Prevalence of thyroid dysfunction in Egyptian chronic hepatitis C patients treated with Pegylated interferon and Ribavirin

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Abstract

Background: Hepatitis C is a major cause of liver-related morbidity and mortality and represents a major public health problem in Egypt and worldwide. INF therapy is the most popular treatment for HCV. INF has many side effects most of them still under study. The development of thyroid dysfunction during IFN and Ribavirin combination therapy has been reported.

Aim: The aim of this study is to assess the Prevalence of thyroid dysfunction in Egyptian chronic hepatitis C patient treated with pegylated interferon and Ribavirin

Materials & Methods: The study was conducted in cooperation between Internal Medicine Department, Faculty of Medicine, Cairo University and Internal Medicine Department, out patients' clinic of National Hepatology and Tropical Medicine Research Institute (NHTMRI) in the period from January 2009 to June 2010. The current study included 200 patients who fulfilled the predesigned inclusion criteria. TSH was done pre treatment, every 3 months during treatment and 3 months following termination of treatment also were done for all cases. Also, FT3 and FT4 were done if there is abnormal TSH.

Results: The prevalence of thyroid dysfunction in chronic hepatitis C patients treated with pegylated INF and Ribavirin reaching 19% in this study.

Key words: HCV- pegylated interferon-thyroid dysfunction.

Introduction:

Hepatitis C is a major cause of liver-related morbidity and mortality and represents a major public health problem in Egypt and worldwide ***(Alberti and Benvegnu, 2003)*** and there is a large underlying reservoir of HCV-caused liver disease ***(Strickland et al., 2002).*** The main goal of treatment is permanent eradication of the virus, secondary goal is histological improvement of liver inflammation and fibrosis to delay cirrhosis and prevent decompansation and HCC ***(Strader et al.,2004).*** The current standard of care for the treatment of patients with chronic hepatitis C is combination pegylated interferon (PEG-IFN) alfa by subcutaneous injection once a week and oral ribavirin daily for patients with contraindications to ribavirin ***(Rebetol, 2004).*** Two PEG-IFN alfa preparations are available ***(McHutchinson et al., 2006 & Manns, 2001)***

PEG-IFN alfa-2b, administered at a weight-based. 1.5µg/kg dose.

PEG IFN alfa-2a, administered at a fixed 180-µg dose.

Randomized controlled trials (RCTs) have shown that combination PEG-IFN alfa and ribavirin therapy can achieve a sustained virologic response (SVR) in 54%-56% of patients for genotype 1 and 4 and (76%-84%)

of those with genotypes 2 and 3 ***(Ward et al., 2004)*.**

The hypothyroidism and thyroid autoimmunity were significantly more common in patients with hepatitis C compared to controls ***(Antonelli A et al., 2004)***.Further evidence for this association came from a recent study that found that the prevalence of non-autoimmune hypothyroidism, as well as the presence of Tg-Ab, was higher in untreated children with HCV compared to healthy non-HCV infected controls. This increased prevalence was not associated with other parameters (family history of autoimmune diseases, duration of HCV infection, viral genotype, viral load or liver function) except active HCV infection ***(Inolfi et al., 2008)*.**

Thyroid dysfunction is reportly an uncommon side effect of interferon alpha (IFN-α) treatment of chronic hepatitis C but the prevalence, natural history and cause of dysfunction is unclear ***(Roberts et al., 1996***). More commonly observed is the development of biochemical and on occasion clinical thyroid dysfunction while patients are being treated for chronic HCV infection with interferon α ***(Baudin et al., 1993.,Watanabe et al., 1994.,Marcellin et al., 1995).*** IFN therapy induced antithyroid auto-antibodies and thyroid dysfunction *de-novo* in patients with chronic hepatitis without pre-existing thyroid abnormalities as there is no significant association was found between chronic hepatitis C and the presence of thyroid auto-immunity in female patients.

Thyroid dysfunction secondary to IFN was reversible after discontinuation of therapy ***(Marazurla et al., 1996).*** Thyroid dysfunction typically manifesting as hypothyroidism occurs *de- novo* in 8% of chronic hepatitis C patient under IFN therapy. It is usually reversible and does not necessarily specific treatment or cessation of interferon. TSH receptor antibodies, either blocking or stimulating, do not appear to play a pathogenic role in interferon induced thyroid dysfunction ***(Roberts et al., 1996)*** **.** IFN-α therapy in chronic viral hepatitis, particularly hepatitis C accentuates and makes clinically manifest preexisting auto-immune thyroid abnormalitits ***(Marcellin et al., 1992., Kodayama et al., 1994 .,Watanabe et al., 1994).***

Patients and methods:

It is a prospective cross-sectional study conducted on 200chronic hepatitis C patients treated with pegylated interferon and ribavirin. between (January 2009 and May 2010) in chronic HCV treatment centre (National Hepatology & and Tropical Medicine Research Institute,Cairo ,Egypt).

Inclusion criteria including -Adult patients >18 years old,positive serology for HCV and HCV viremia,compensated liver disease, ,euthyroid by TSH.

Exclusion criteria including -Adult patients >60 years old,decompensated liver disease,autoimmune disease by ANA,patients discovered to have TSH abnormalities during treatment (tested at 12, 24, 36 and 48 weeks of treatment) will be subjected to freeT3 and free T4 then sub classified into 4 groups:

1-clinical hypothyroidism (elevated TSH with decreased levels of FT3orFT4)

2-subclinical hypothyroidism (elevated TSH with normal FT3, FT4)

3- Clinical hyperthyroidism (decreased TSH with elevated levels of FT3orFT4)

4- Subclinical hyperthyroidism(decreased TSH with normal levels of FT3,FT4).

All participating subjects, after a written consent, were subjected to Careful history taking, Thorough clinical examination, laboratory assays which including:

a) AST,ALT,Bilirubin,Albumin,ALP,Creatinin,FBS,CBC and INR.

b) Viral markers: HBs Ag and HCV Ab.

c)) ANA, AFP.

d)) Quantitative HCV RNA by PCR.

e) Histopathological examination of liver biopsy.

ff)) TSH

g)) FT3, FT4 for patients showed thyroid abnormalities.

TSH:

SAMPLE COLLECTION AND STORAGE-TECHNIQUE:

Five ml of venous blood were withdrawn from patients; allow blood samples to clot for 30 min before centrifugation for 15 min. Aliquoted serum into 1 aliquot and store samples at -80°C.The test done using (ACCU-Bind kit-Lake Forest,USA). The assay was run fully automated in the Commander Parallel Processing Center (Abbott) machine. Normal

level= (0.3-5.0 uIU/ml) ***(Hopton &Harrap,1986)***

FT3:

SAMPLE COLLECTION AND STORAGE-TECHNIQUE:

The test done using (ACCU-Bind kit-Lake Forest,USA). The assay was run fully automated in the Commander Parallel Processing Center (Abbott) machine. Normal level= (2.0-4.7 pg/ml) ***(Pederson, 1974).***

FT4:

SAMPLE COLLECTION AND STORAGE-TECHNIQUE:

The test done using (ACCU-Bind kit-Lake Forest,USA). The assay was run fully automated in the Commander Parallel Processing Center (Abbott) machine. Normal level= (0.8-1.8 pg/ml) ***(Barker, 1948).***

Statistical Analysis:

Analysis of data was performed using SPSS 17 (Statistical Package for Scientific Studies) for Windows.

Description of variables was presented as follows:

- Description of quantitative variables was in the form of mean, standard deviation (SD), minimum and maximum.
- Description of qualitative variables was in the form of numbers (No.) and percents (%).

Data were explored for normality using Kolmogorov-Smirnov test of normality. The results of Kolmogorov-Smirnov test indicated that most of data were normally distributed (parametric data) so parametric tests were used for the comparisons.

- Comparison between quantitative variables was carried out by student T-test of two independent samples. Repeated measures Analysis of Variance (ANOVA) test was used instead of T-test when comparing between 4 groups of independent variables. Results were expressed in the form P-values.
- Comparison between qualitative variables was carried out by Chi-Square test (X2). Fisher exact test was used instead of Chi-square test when one expected cell or more were ≤5.

The significance of the results was assessed in the form of P value

that was differentiated into:

- Non-significant when P-value > 0.05
- Significant when P-value ≤0.05
- Highly significant when P-value ≤ 0.01

Results

Age distribution of the studied patients was ranged between 20 and 59 years (mean 43 ± 9.9 years).there was male predominance being there is male predominance being77.5% versus 22.5% for females. The mean BMI was (28.78±4.78).29 % of the studied patients were chronic cigarette smokers.105 patient treated with INF alpha 2a (52.5%) and 95 patients treated with INF alpha 2b (47.5). The studied groups showed a mean ALT of (70.95±54.89), a mean AST of (58.01±36.96), a mean ALKPh of (96.51±46.55), a mean T.Bil of (0.81±0.27) and a mean Alb of (4.16±0.38). 95% of the studied patients have no family history of thyroid abnormalities and only 5 % do have.

	Frequency	Percent
F0	6	3.0
F1	93	46.5
F2	57	28.5
F3	26	13.0
F4	18	9.0
Total	200	100.0

Table (1) showed the fibrosis grading by Metavir score for histopathological examination of the studied patients.

The sub clinical hypothyroidism occurred to 25 patients (12.5%) and the clinical hypothyroidism occurred to 3 patients (1.5%) and the sub clinical hyperthyroidism occurred to 5 patients (2.5%) and the clinical hyperthyroidism occurred to 5 patients (2.5%).

	Frequency	Percent
No dysfunction	162	81.0
Dysfunction	38	19.0
Total	200	100.0

Table (2) showed the overall thyroid dysfunction for the studied patients during treatment.

Type of IFN	Dysfunction		No dysfunction		Total		P value
	N.	%	N.	%	N.	%	
IFN Alpha 2 a	18	17.1%	87	82.9%	105	100%	**0.48**
IFN Alpha 2 b	20	21.1%	75	78.9%	95	100%	
Total	38	19%	162	81%	200	100%	

Table (3) showed the relation between thyroid dysfunction and type of INF received among the studied patients.

Table (3) shows that there is no significant relation between type of INF and thyroid dysfunction with p=0.482.

Gender	Dysfunction		No dysfunction		Total		P value
	N.	%	N.	%	N.	%	
Male	29	18.7%	126	81.3%	155	100%	0.846
Female	9	20%	36	80%	45	100%	
Total	38	19%	162	81%	200	100%	

Table (4) showed the relation thyroid dysfunction and the gender for the studied patients

Table (4) shows that there is no significant relation between the gender and thyroid dysfunction with p=0.846

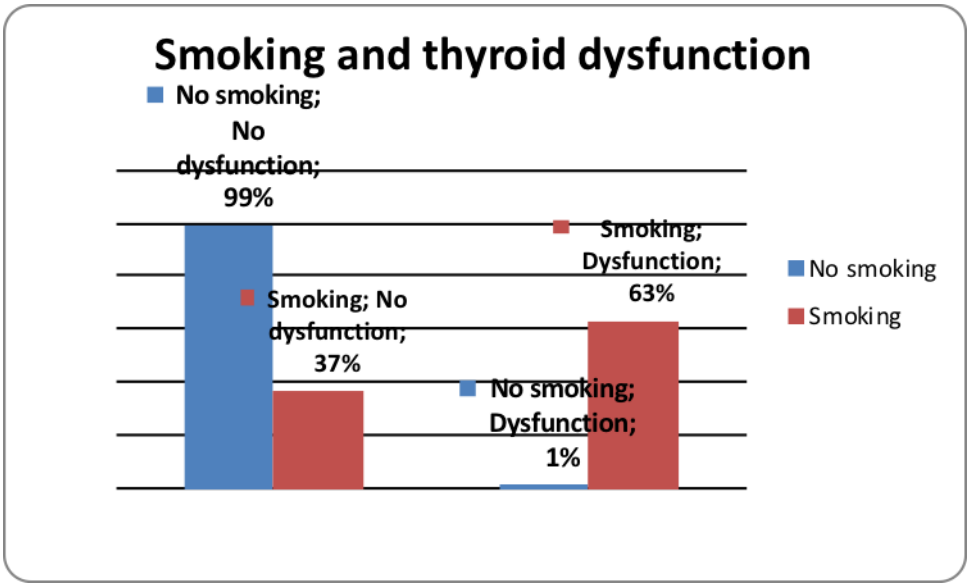

***Fig (1)* showed the relation between thyroid dysfunction and smoking among the studied patients**

There is significant relation between smoking and thyroid dysfunction with p<0.001.
There is significant relation between body mass index and thyroid dysfunction with p=0.004.
Also there is significant relation between biopsy grading from F0 and F4 and thyroid dysfunction with p=0.009 for relation between grade 0 and 4, it is highly significant p. P<0.001.**Fig (2)**
No significant relation between family history of thyroid abnormalities and thyroid dysfunction with p=0.023.

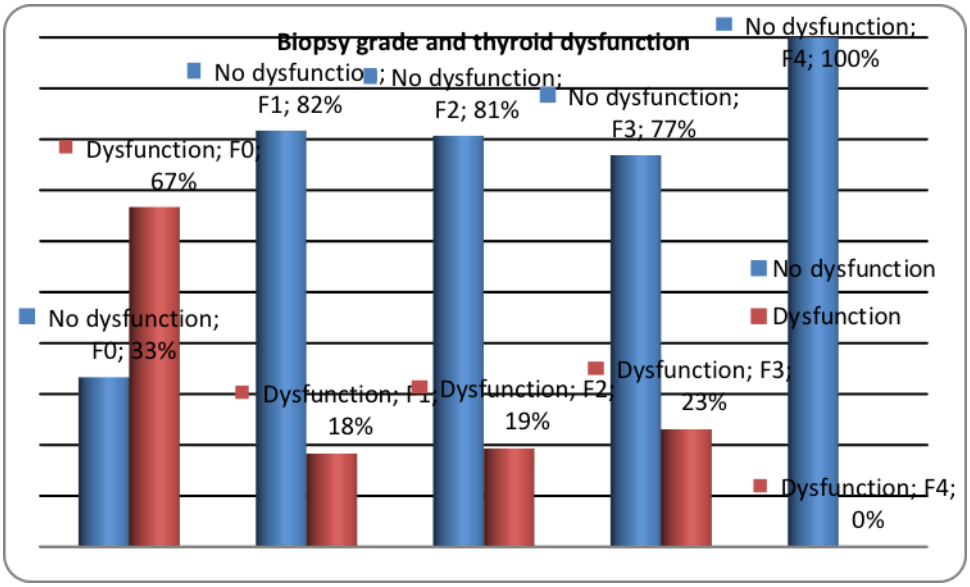

***Fig (2)* showed the relation between thyroid dysfunction and biopsy staging among the studied patients.**

			Sub clinical Hypothyroidism	Clinical Hypothyroidism	Sub clinical Hyperthyroidism	Clinical Hyperthyroidism	Total
Family History	Negative	N.	25	0	4	4	33
		%	75.8%	.0%	12.1%	12.1%	100.0%
	Positive	N.	0	3	1	1	5
		%	.0%	60.0%	20.0%	20.0%	100.0%
Total		N.	25	3	5	5	38
		%	65.8%	7.9%	13.2%	13.2%	100.0%
P value				**< 0.001**			

***Table (5)* showed the relation between the family history and different groups of thyroid dysfunction for the studied patients.**

Table (5) shows that there is high significant relation between the family history and different groups of thyroid dysfunction with p<0.001.

	Frequency	Percent
Normalized	29	76.3%
Not Normalized	9	23.7%
Total	38	100.0

***Table (6)* Present the normalization of thyroid function at 3 months follow up after termination of treatment**

Table (6) shows that there is predominance of normalization 76.3% versus 23.7%.

			Sub clinical Hypothyroidism	Clinical Hypothyroidism	Sub clinical Hyperthyroidism	Clinical Hyperthyroidism	Total
Follow up	Not normalized	N.	25	0	4	0	29
		%	86.2%	.0%	13.8%	.0%	100.0%
	normalized	N.	0	3	1	5	9
		%	.0%	33.3%	11.1%	55.6%	100.0%
Total		N.	25	3	5	5	38
		%	65.8%	7.9%	13.2%	13.2%	100.0%
P value				**< 0.001**			

Table (7) **Present the relation between the normalization of thyroid function at follow up and different groups of thyroid dysfunction for the studied patients**

Table (7) shows that there is significant relation between the normalization of thyroid function and different groups of thyroid dysfunction with p<0.001.

			Time of dysfunction				Total
			12	24	36	48	
Follow up	Not normalized	N.	2	8	2	17	29
		%	6.9%	27.6%	6.9%	58.6%	100.0 %
	normalized	N.	0	4	1	4	9
		%	.0%	44.4%	11.1%	44.4%	100.0 %
Total		N.	2	12	3	21	38
		%	5.3%	31.6%	7.9%	55.3%	100.0 %
P value			**0.650**				

Table (8) **presents the relation between the normalization of thyroid function and time of occurrence of thyroid dysfunction for the studied patients**

Table (8) shows that there is no significant relation between the normalization of thyroid function and time of occurrence of thyroid dysfunction with p=0.650.

			Sub clinical	clinical	Total
Follow up	Normalized	N.	29	0	29
		%	100.0%	.0%	100.0%
	Not Normalized	N.	1	8	9
		%	11.1%	88.9%	100.0%
Total		N.	30	8	38
		%	78.9%	21.1%	100.0%
P value			**< 0.001**		

***Table (9)* present the relation between the normalization of thyroid function and sub clinical versus clinical of thyroid dysfunction for the studied patients**

Table (9) shows that there is highly significant relation between the normalization of thyroid function and sub clinical versus clinical of thyroid dysfunction p<0.001.

	Time of occurrence of dysfunction	Sub clinical hypothyroidism	Clinical hypothyroidism	Sub clinical hyperthyroidism	Clinical Hyperthyroidism	Total	P value
12w	N.	1	0	1	0	2	
	%	50.0%	.0%	50.0%	.0%	100.0%	
24w	N.	6	1	2	3	12	
	%	50.0%	8.3%	16.7%	25.0%	100.0%	0.670
36w	N.	2	1	0	0	3	
	%	66.7%	33.3%	.0%	.0%	100.0%	0.475
48w	N.	16	1	2	2	21	
	%	76.2%	4.8%	9.5%	9.5%	100.0%	0.365
Total	N.	25	3	5	5	38	
	%	65.8%	7.9%	13.2%	13.2%	100.0%	0.467

***Table (10)* presents the relation between the time of occurrence of thyroid dysfunction and different 4 groups of thyroid dysfunction for the studied patients**

Even there is no significant relation between the clinical outcomes of 12th and 48th weeks P= 0.432, This table shows that there is no significant relation between the

time of occurrence of thyroid dysfunction and different 4 groups of thyroid dysfunction p=0.432.

Discussion

Hepatitis C virus (HCV) has been estimated by the World Health Organization (WHO) to infect 170 million patients worldwide, with the highest prevalence rate among Egyptians (14% - 18 %) approximately 10 folds greater than in the United States and Europe) ***(Mohamed, 2004).*** Because of the very high prevalence rate of HCV in the general Egyptian population, it accounts for most chronic liver disease and HCC cases in Egypt ***(Strickland et al., 2002).***

The aim of the current study is to assess the Prevalence of thyroid dysfunction in Egyptian chronic hepatitis C patient treated with pegylated interferon and Ribavirin.For better assessment, this study was designed to be cross sectional study in order to rule out any possible factors that may interrupt, strengthen or weaken the laboratory and or pathological judgment. The current study included 200 patients; there were male predominance being 155 male patients (77.5%) and 45 female patients (22.5%). Their age ranged between 20 and 59 years (mean 43 ±9.9 years). This agrees to ***Clark et al.. (2006)*** study which was conducted on ninety patients included (55 men and 35 women) with a mean age of (45±13 years). In the present study, there were 24 diabetic patients (12%) and 186 non diabetic patients (93%), this is relatively agrees with ***Bahtiyar.,et al 2004*** which mentioned that about one third of patients with chronic hepatitis C virus (HCV) develop type 2 diabetes mellitus (DM) ,this relatively small percentage may be attributed to the small sample size , young aged studied patients and compensated liver functions (policy of NHTMRI in treatment of chronic hepatitis C with INF). In the present study, the thyroid dysfunction occurred in 38 patients (19%) and not occurred in 162 patients (81%). This is relatively agrees with ***Edmund. et al. (2004)*** which mentioned that among the 225 male patients, thyroid disease developed in 10.7% with HCV infection treated with interferon and Ribavirin this relatively small percentage may

be attributed to the gender in Edmund J study where all studied subjects were males and used one type of interferon, Interferon Alfa-2b. Also, relatively agrees with ***Jamil et al,(2009)*** which mentioned that treatment of chronic hepatitis C with interferon is known to be associated with thyroid dysfunction (TD) in 8.8% of patients (45 patients out of 511 patients), this
relatively small percentage difference may be attributed to the larger number of cases and contains patient treated by un-pegylated INF and Pegylated INF.
Also, relatively agrees with ***Deutch et al.(2003)*** which mentioned that IFN-a treatment significantly increased the prevalence of thyroid dysfunction up to 9.7%,), this relatively percentage difference may be attributed to the patient
of this study was chronic hepatitis not only due to viral hepatitis C but also due to viral hepatitis B and D. Also, relatively agrees with ***Hsieh et al.(2000)*** which mentioned that the virologic features of HCV may be associated with thyroid dysfunction in chronic hepatitis C patients treated with IFN-alpha. In this study 28 patients out of 150 patients (18.7%) have thyroid dysfunction during INF alpha treatment. Also, relatively agrees with ***Carella et al.(2004)*** which mentioned that the prevalence of thyroid disease during IFN treatment is extremely variable, ranging between 1 and 35%. This is relatively disagrees with ***Tran et al.(2006)*** which concluded that the pegylated IFN, in combination with Ribavirin, did not aggravate thyroid diseases in the hepatitis C
population. This disagreement may be due to his very small sample group and the previous treatment of his group by un-pegylated INF. In the present study, there was no significant relation between treatment response and thyroid dysfunction. This is relatively agrees with ***Ming-Chia Hsieh et al.(2000)*** which concluded that thyroid dysfunction was not associated with the response of chronic hepatitis C to IFN-a therapy. This is relatively disagrees with ***Nadeem A et al.(2010)*** which concluded that the development of hypothyroidism in patients who undergo treatment with IFN-alpha plus Ribavirin is significantly associated with better treatment response in CHC patients. This difference may be attributed to focusing only on hypothyroidism. In the present study, the type of pegylated INF weather INF alpha 2 a or INF alpha 2 b did not affect the incidence of thyroid dysfunction occurrence; no significant relation with p=
0.482. 18 patients (17.1%) from total 105 patients treated with INF alpha 2a had thyroid dysfunction versus 20 patients (21.1%) from total 95 patients treated with INF alpha 2b had thyroid dysfunction. In the present study, there was no significant relation between gender and prevalence of thyroid dysfunction. This is in difference with ***Ming-Chia Hsieh et al.(2000)*** and ***Maribel Rodríguez-Torres et al.(2008).*** The first reported that the prevalence of thyroid abnormalities was 12.8% (males 5.8%, females 19.8%) ,so Gender (female) is a strong risk factor for thyroid dysfunction induced by IFN-alpha. The second reported that it has been reported to be more frequent in females, and to be mostly hypothyroidism (both clinical and biochemical). The difference with the second study may be attributed to single type of INF and the concentration on hypothyroidism.
In the present study, diabetes mellitus is not a risk factor for thyroid dysfunction in the studied group, where 36 patients (94.7%) who have thyroid dysfunction have no DM versus 2 patients (5.3%) who have thyroid dysfunction & DM.
In the present study, there is highly significant relation between smoking and thyroid dysfunction 36 patients (94.7%) of cases developed thyroid dysfunction were smoker versus 2 patients (5.3%) were non smoker (P< 0.001). In the present study, there is no significant relation between family history of thyroid disease and thyroid dysfunction 5 patients (13.2%) of cases have family history of thyroid disease versus 33 patients (86.8%) were not having family history of thyroid disease (P: 0.010). In the present study, chi-square test was done between different fibrosis stages and thyroid dysfunction occurrence with no significant relation, But there is highly significant relation between F0 and F4 staging with thyroid dysfunction occurrence with P<0.001. This is relatively agrees with ***Maribel Rodríguez-Torres et al.(2008)*** who concluded that Patients with severe fibrosis have more thyroid dysfunction events at baseline and during treatment with Peg IFN alfa-2a.In the present study, there is significant

relation between body mass index and thyroid dysfunction .In the present study, the hypothyroidism occurred to 28 patients (14%) and hyperthyroidism occurred to 10 patients (5%) which mean occurrence of hypothyroidism 73.7% versus occurrence of hyperthyroidism 26.3% between all cases of thyroid dysfunction. This is relatively agrees with ***Astushi Inoue et al.(2005)*** who concluded that hypothyroidism (62%) seems to be the more frequent than hyperthyroidism (28%). In the present study, the sub clinical hypothyroidism occurred to 25 patients (12.5%) and the clinical hypothyroidism occurred to 3 patients (1.5%) and the sub clinical hyperthyroidism occurred to 5 patients (2.5%) and the clinical hyperthyroidism occurred to 3 patients (2.5%). That means 65.7% of thyroid dysfunction was sub clinical hypothyroidism, 7.8% of thyroid dysfunction was clinical hypothyroidism, 13.2% of thyroid dysfunction was sub clinical hyperthyroidism and 13.2% of thyroid dysfunction was sub clinical hypothyroidism. In the present study, there is no significant relation between type of INF and different types of thyroid dysfunction.

In sub clinical hypothyroidism group there is 15 cases (60%) treated with INF alpha 2b and 10 cases (40%) with INF alpha 2a.

In clinical hypothyroidism group ,there is 1 cases (33.6%) treated with INF alpha 2b and 2 cases (66.7%) with INF alpha 2a. In subclinical hyperthyroidism group there is 2 cases (40%) treated with INF alpha 2b and 3 cases (60%) with INF alpha 2a.In clinical hypothyroidism group there is 2 cases (40%) treated with INF alpha 2b and 3 cases (60%) with INF alpha 2a.In the present study, there is male predominance in different groups of thyroid dysfunction with no significant relation between gender and different types of thyroid dysfunction. In sub clinical hypothyroidism group there is 18 male (72%) versus 7 female (28%). In clinical hypothyroidism group there is 3 male (100%) versus 0 female. In subclinical hyperthyroidism group there is 4 male (80%) versus 1 female (20%). In clinical hyperthyroidism group there is 4 male (80%) versus 1 female (20%).

In the present study, there is highly significant relation between family history of thyroid abnormalities and different groups of thyroid dysfunction with P<0.001. In the present study, there is no significant relation between occurrence of different types of thyroid dysfunction and the duration of treatment. In subclinical hypothyroidism group there is 1 case (4%) discovered in week12, 6 cases (24%) discovered in week24, 2 cases (8%) discovered in week36 and 16 cases (64%) discovered in week48. In clinical hypothyroidism group there is no case discovered in week12, 1 case (33.3%) discovered in week24, 1 case (33.3%) discovered in week36 and 1 case (33.3%) discovered in week48. In subclinical hyperthyroidism group there is 1 case (20%) discovered in week12, 2 cases (40%) discovered in week24, no case discovered in week36 and 2 cases (40%) discovered in week48. The only group in opposite direction is the clinical hyperthyroidism group where there is no case discovered in week12, 3cases (60%) discovered in week24, no case discovered in week36 and 2 cases (40%) discovered in week48. In the present study, in most of cases thyroid function normalized after 3 months of treatment stoppage. 29 cases (76.3%) normalized versus 9 cases (23.7%) continue with thyroid dysfunction.

In the present study, there is highly significant relation between thyroid function normalized after 3 months of treatment stoppage and type of dysfunction whether clinical or sub clinical with P<0.001. All 29 patients (100%) who normalized at follow up was subclinical thyroid dysfunction.

Summary

The prevalence of thyroid dysfunction in chronic hepatitis C patients treated with pegylated INF and Ribavirin reaching 19% in this study.

Conclusion

The prevalence of thyroid dysfunction in chronic hepatitis C patients treated with pegylated INF and Ribavirin is 19%. Smoking and high body mass index are risk factors for thyroid dysfunction in chronic hepatitis C patients treated with pegylated INF and Ribavirin. Patients with more hepatic fibrosis require careful attention to diagnose and manage thyroid dysfunction. Almost all cases of subclinical thyroid dysfunction normalized within 3 months of stoppage of INF.

Recommendations

Patients received pegylated INF and Ribavirin should done regular TSH analysis every 3 months at least. Patients with more hepatic fibrosis require careful attention to diagnose and manage thyroid dysfunction. More research in the immune mechanisms of hepatic fibrosis progression and autoimmune complications is needed. Further researches with a larger group numbers and
longer period of follow up after termination of pegylated INF and Ribavirin must be done.

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إنتشار إختلال الغدة الدرقيةفى مرضى الإلتهاب الكبدي الفيروسي(سي)الذين يتم علاجهم بالأنترفيرون طويل المفعول والريبافيرين

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الالتهاب الكبدى الناتج من الاصابه بفيروس سى من اكثر الامراض المنتشرة فى العالم و تعد مصر من اعلى الدول فى معدلات الاصابة كما ان العلاج بالانترفيرون طويل المدى و الريبافيرين هو الاكثر شيوعا الان و ما زال الكثير من اثاره الجانبيه ما زالت تحت الدراسة حتى الان و منها تاثيره على الغدة الدرقيه .
هذه الدراسة تم تصميمها لتحديد انتشار اختلال الغدة الدرقية في مرضى الألتهاب الكبدى الفيروسى (سى) اللذين يتم علاجهم بواسطة الأنترفيرون طويل المدى و الريبافيرين و ذلك بالتعاون ما بين قسم الباطنة بكلية الطب جامعة القاهرة و قسم الباطنة بالمعهد القومى للامراض المتوطنة و الكبد فى الفترة بين بناير2009 و حتى يونيو 2010.

أجريت هذه الدراسة علي ٢00 مريضا تتراوح اعمارهم من 18 الى 60 عام و وظائف الكبد متكافئة و الغدة الدرقية طبيعية .

و لقد اوضحت الدراسة وجود اختلال فى وظائف الغدة الدرقية في 38 مريض اي بنسبة19% .
كما أوضحت الدراسة ايضا ان هناك علاقة قوية بين درجة التليف المتقدمة و التدخين من ناحية و حدوث اختلال فى وظائف الغدة الدرقية من الناحية الاخرى.

وكذلك اوضحت الدراسة ايضا ان هناك علاقة بين معدل كتلة الجسم و حدوث اختلال فى وظائف الغدة الدرقية.
كما أن انخفاض افرازات الغدة الدرقية حدث ل 28 مريض اى بنسبة 14% و زيادة افرازات الغدة الدرقية حدث ل 10 مريض اى بنسبة 5% .

كما اوضحت الدراسة بانه لا يوجد علاقه بين مدة العلاج بالانترفيرون و حدوث الخلل فى وظائف الغدة الدرقية .

و لقد اوضحت الدراسة ايضا ان اغلب الحالات تعود فيها وظائف الغدة الدرقية الى طبيعتها فى خلال ثلاث اشهر من انتهاء العلاج بالانترفيرون و الريبافيرين.

هذه الدراسة توصى بضرورة التأكد بخلو المريض من اى اختلال فى وظائف الغدة الدرقية قبل بدأ العلاج بالانترفيرون طويل المدى و الريبافيرين و كذلك عمل متابعة دوريه طول فترة العلاج على الاقل كل ثلاث شهور للتأكد من سلامة الغدة الدرقيه.