Incidence of Autoimmune Thyroid Disorders Following Treatment with Pegylated Interferon Therapy for HCV Infection among Egyptian Patients

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Background: Thyroid autoimmunity is a common side effect of interferon treatment for chronic hepatitis C (HCV). There are currently no reliable parameters to predict the occurrence of thyroid dysfunctions in patients undergoing IFN therapy. The risk might be closely correlated with mixed HCV genotype infection and lower HCV RNA levels, female gender, pre-treatment positivity for thyroid antibodies (particularly TPO Ab) and a hypoechoic pattern of the thyroid gland at ultrasound, none of the above features has enough specificity and sensitivity to reliably predict the occurrence of thyroid dysfunction. CXC chemokine ligand 10 (CXCL10) is a chemokine known to play a role in both thyroid autoimmune disease and hepatitis C virus (HCV) hepatitis. Possible relation between serum chemokines and treatment outcome in patients with HCV-hepatitis has been suggested.

Aim of the Work: to assess the incidence of autoimmune thyroid disorder following treatment of chronic HCV infection with Pegylated Interferon among Egyptian cases, and to investigate the role of CXCL10 in predicting a favourable response to the treatment with IFN.

Patients and Methods: Forty (40) patients were participated in the study twenty two (22) males and eighteen (18) females. All patients were diagnosed as chronic viral C hepatitis. These patients received IFN therapy (Pegasys) 180 microgram per week plus Ribavirin 1200 mg daily for 6 months. History evaluation and full clinical examination with stress on symptoms and signs of thyroid dysfunction were done before and after six months of treatment. All patients had complete blood picture, ALT, AST, serum albumin, serum creatinine.HCV antibody detection using ELISA, HCV-RNA.FT3, FT4, TSH, Thyroid ultrasound, anti-thyroid peroxidase (ATPO) antibodies, antithyroglobulin antibodies (ATA) and CXCL10 before treatment and after 6 months of treatment.

Exclusion criteria: Pretreatment history of any thyroid disease, history of autoimmune disorders as SLE, rheumatoid arthritis and malignancy.

Results:

At the end of the study (after 6 months of IFN therapy), participants were divided into 3 groups according to their response to IFN therapy and developing of thyroid dysfunction. **Group A:** Twenty four (24) patients 60% (14 male and 10 females) responded to Interferon treatment and their AST, ALT and PCR turned to normal values without developing thyroid dysfunction. **Group B:** Ten (10) patients (25%) (6 males and 4 females) didn't respond to IFN treatment with AST, ALT and PCR still elevated, without developing thyroid dysfunction. **Group C:** Six (6) patients 15% (2 males and 4 females) responded to Interferon treatment and became PCR negative but had elevated Anti TPO and Anti TG and they developed echogenic changes in neck ultrasound of the thyroid gland (Fig 2).

Fig. (1): Patients groups

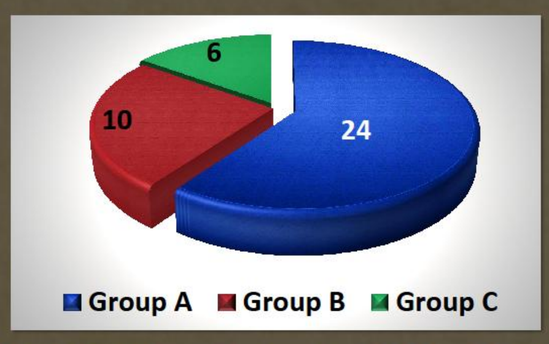
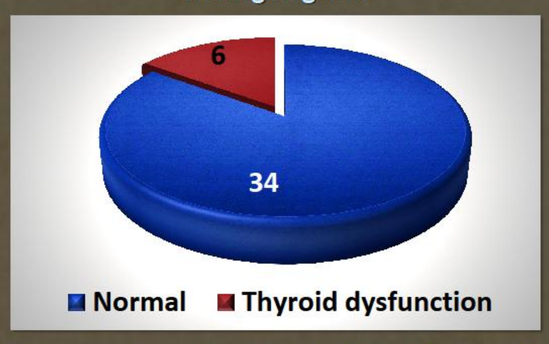


Fig. (2): Incidence of thyroid dysfunction in patients undergoing IFN.



At the beginning of the study: Group C had the highest level of Anti TPO and Anti TG in comparison with group A and B (Fig. 3, 4). The lowest level of PCR in comparison with group A and B, while group B had the highest level of PCR in comparison with group A and group C. Group C had the lowest level of CXCL10 in comparison with group A and B (Fig. 6), while group B had the highest level of CXCL10 pg/dl in comparison with group A and C (Tables 1).

After 6 months of therapy: Group A and group C respond to IFN therapy and became PCR negative and the liver enzymes became normal, while group B remained having elevated PCR, AST and ALT level. Group A and group C show marked decrease in CXCL10 level in comparison with group B(Fig 6).Group C showed marked elevation of Anti TG and Anti TPO level in comparison with group A and B (Fig 3, 4) (Table 2).

The correlation between CXCL10 and AST, ALT and PCR was significantly positive direct correlation at the beginning of the study and after 6 months of therapy, but insignificant with thyroid profile and antibodies.

Table (1): Comparison between Groups A, B and C at the beginning of the study as regard clinical data, liver profile and thyroid profile using ANOVA test.

	Group A (n=24)	Group B (n=10)	Group C (n=6)	F	P	Sig.
General						
Age (years)	30.5±6.3	32.3±6.3	30.3± 1.5	0.49	0.61	NS
BMI	27.2±2.5	28.4± 4.2	28.3 ± 1.5	0.59	0.56	NS
Liver profile						
AST (u/l)	81.2±15.4	91.3 ± 20.4	68.3 ± 13.05	1.478	0.244	NS
ALT (u/l)	82.8±21.2	94.4 ± 29.3	71 ± 13.2	2.069	0.144	NS
PCR x10^6	1.4±0.9	5.57 ± 0.67	0.63 ± 0.31	82.82	<0.01	HS
Thyroid profile						
TSH (u/ml)	3±1.1	2.7 ± 1.1	2.8 ± 1.3	0.291	0.749	NS
FT3 (pg/dl)	3.1±0.4	3.04 ± 0.6	2.93 ± 0.05	0.233	0.793	NS
FT4 (ng/dl)	1.3±0.4	1.2 ± 0.4	1.13 ± 0.25	0.190	0.828	NS
Anti TPO (IU/ml)	22.04±10.1	20.75 ± 6.2	33.47 ± 4.72	2.97	0.067	NS
Anti TG (IU/ml)	36.1±10.5	41.4 ± 13.7	52.67 ± 21	2.56	0.094	NS
CXCL10 (pg/ml)	308.2 ± 83.7	395.9 ± 24.2	250.3 ± 12.5	7.28	<0.01	HS

Table (2): Comparison between Groups A, B Group C as regard clinical data, liver and thyroid profile after 6 months of IFN therapy using ANOVA test.

	Group A (n=24)	Group B (n=10)	Group C (n=6)	F	P	Sig.
General						
Age	30.5 ± 6.3	32.3±6.3	30.3± 1.5	0.49	0.61	NS
BMI	27.4 ± 3.2	27.7 ± 3.3	29.1±2.5	0.57	0.56	NS
Liver profile						
AST (u/l)	23.5 ± 4.7	82.4 ± 11.3	25.3 ± 6.65	47.43	<0.01	HS
ALT (u/l)	26.9 ± 5.3	85.8 ± 16.4	22 ± 1.73	87.67	<0.01	HS
PCR x10^6	0	5.39 ± 2.2	0		<0.01	HS
Thyroid profile						
TSH (u/ml)	3.4 ± 0.6	3.1 ± 0.5	9.5 ± 4.19	13.52	<0.01	HS
FT3 (pg/dl)	3.06 ± 0.36	3.06 ± 0.5	2.4 ± 0.43	1.62	0.21	NS
FT4 (ng/dl)	1.3 ± 0.2	1.1 ± 0.3	0.9 ± 0.37	2.09	0.14	NS
Anti TPO (IU/ml)	30 ± 5.8	22.78 ± 4.7	80 ± 11.53	75.91	<0.01	HS
Anti TG (IU/ml)	45 ± 9.1	46.5 ± 7.3	210 ± 68.2	117.56	<0.01	HS
CXCL10 (pg/ml)	165.47 ± 36.6	372 ± 48	185.3 ± 10.4	48.84	<0.01	HS

Fig 3: Comparison between group A, B and C as regard Anti TPO at the beginning of study and after 6 months of therapy.

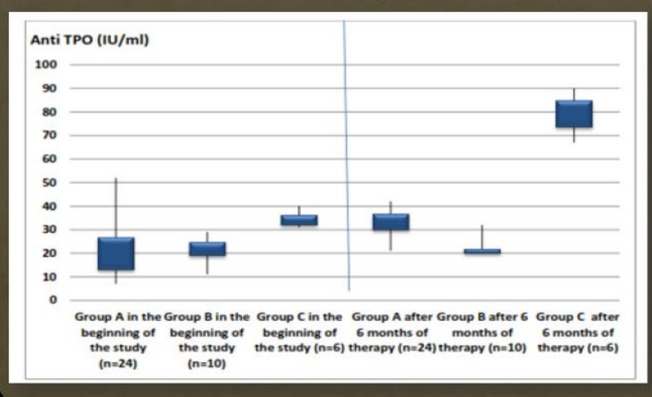


Fig (4): Comparison between group A, B and C as regard Anti TG level at the beginning of study and after 6 months of therapy.

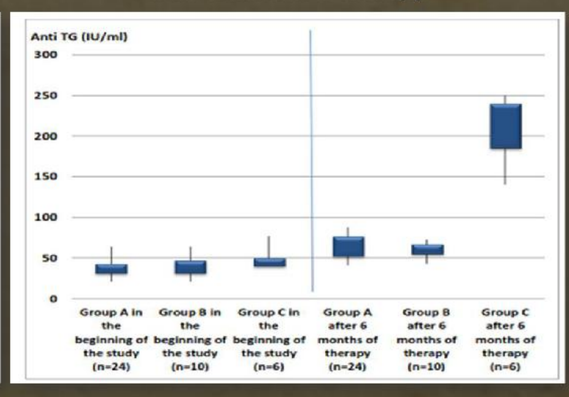


Fig (5): Comparison between group A, B and C as regard TSH at the beginning of study and after 6 months of therapy.

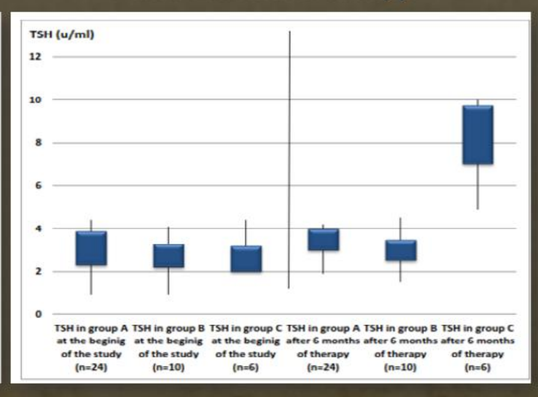
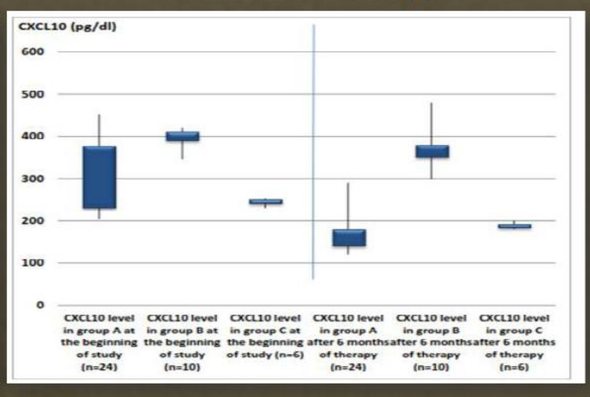


Fig (6) : Comparison between group A, B and C as regard CXCL10 level at the beginning of study and after 6 months of therapy.



Conclusion:

- Incidence of thyroid dysfunction in patients received IFN therapy with Ribavirin for treatment of HCV infection for 6 months is not uncommon 15%.
- Pretreatment thyroid antibodies and female gender seems to be a risk factor in predicting the occurrence of thyroid dysfunction during IFN therapy.
- CXCL10 is expected to be decreased after IFN therapy, and lower pre-treatment level of CXCL10 level indicates better response to IFN therapy and is less likely to be related to thyroid dysfunction.

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Thyroid non-cancer

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