

Evaluation of Triiodothyronine (T3) and Lipid Peroxidation in Hepatitis C Patients Receiving Interferon and Ribavirin

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ABSTRACT

Background: Hepatitis is an inflammatory disorder of the liver and liver is considered as vital organ of the body. Hepatitis C virus affects 3% of the world population in which 170 million people are affected chronically and 3 to 4 million affected per year. Interferon-alpha is a cytokine, which is produced by white blood cells and T lymphocytes. Destructive thyroiditis in patients receiving interferon- α therapy is analyzed based on negative TSH receptor antibodies (TRAbs) and low thyroid radioactive iodine uptake. **Methodology:** Fifty-Five patients of Hepatitis C and Twenty-five age and sex-matched clinically apparently healthy individuals were eligible for inclusion in the study at Jinnah Hospital Lahore. 5.0 ml blood samples were taken and subjected to centrifuge at 3000-4000 rpm for 10-15 minutes for the separation of serum. The estimation of AST, ALT and ALP, FT3, Total Protein (TP), Total bilirubin (TB) and MDA were estimated. **Results:** FT3 level in HCV patients was elevated remarkably (16.63 ± 7.14) as compared to control (4.25 ± 0.72) and statistically significant (p -value < 0.05). MDA level was also increased in HCV patients (8.58 ± 1.19) as compared to healthy persons (1.47 ± 0.54) and statistically significant (p -value < 0.05). The level of total protein (TP) in HCV patients was decreased (4.20 ± 0.61) as compared to healthy individuals (6.23 ± 0.51) and also statistically significant (p -value < 0.05). **Conclusion:** Present study concluded that HCV patients treated with interferon therapy have remarkably elevated lipid peroxidation rate which caused high level of MDA and FT3 level also elevated and play significant role in HCV patients which is causative agent for the progression of the disease.

Keywords: Hepatitis C, Interferon, Ribavirin, Triiodothyronine, Lipid Peroxidation

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INTRODUCTION

Liver is a vital organ of the body. Its main functions include food metabolism, filtration of blood and protection against toxins. Hepatitis is an inflammatory disorder of the liver that is affecting worldwide population. There are five types of hepatitis namely A,B,C,D and E while virus-related hepatitis are A,B and C. Hepatitis A affects 1.4 million people per year all over the world but the actual number is 3-10 times greater.¹ Two billion people are affected by hepatitis B while more than 350 million people are victims of chronic hepatitis B. Hepatitis B and C causes liver fibrosis, cirrhosis and hepatocellular carcinoma. Interferon-alpha belongs to cytokine family which is produced by white blood cells and T-lymphocytes.² Interferon has three types' alpha, beta and gamma. Type 1 interferon comprises both interferon-alpha and beta, which is produced by white blood cells. Interferon gamma which is produced by T cells is known as type 2 interferon.³ Interferon inhibits proliferation of tumor cells, multiplication of virus and changes in host

immune system which plays important role in combating viruses.⁴

Ribavirin is a nucleoside analogue and has greater combating potential against DNA and RNA viruses. It has immunomodulatory effects and stimulates immune system. Thyroid dysfunction is caused by combination of ribavirin with interferon-alpha through an auto-immune mechanism.⁵ Ribavirin is activated by cellular kinases and converts into 5'triphosphate nucleotide which interferes with RNA metabolism related to viral replication. Adenosine kinase phosphorylates intracellular ribavirin into ribavirin mono, di and triphosphate metabolites.⁶

Thyroid gland, a large endocrine gland produces thyroid hormones and are of two types, triiodothyronine (T3) and thyroxin (T4). Affinity of T3 is greater for thyroid hormone receptor than T4. It is thought that T4 is the precursor of T3 and it consists of four iodine atoms while T3 has three atoms. Thyroid glands surrounds 90% iodine and out of this 20-40% is in the thyroid hormone.⁷ Hormones are synthesized in the thyroid follicles which are

cuboidal in shape consisting of a group of epithelial cells that are aligned around the lumen. Most of the thyroid hormone is bound with serum proteins and in inactive form while 0.3% and 0.03% T3 and T4 is present in active form in plasma respectively.

Interferon- α and Ribavirin therapy has many side effects including headache, fever, lassitude, influenza like conditions, neuropsychiatric effects and hematological instabilities.⁸ One of the common side-effects of this therapy is thyroiditis while the relation between interferon- α and thyroid disease was firstly studied more than two eras ago.⁹ Without clinical symptoms, the most common form of thyroid autoimmunity is the presence of thyroid antibodies consisting of thyroid peroxidase antibodies (TPO-Ab) and thyroglobulin antibodies (Tg-Ab). Negative TSH receptor antibodies (TRAb) and low thyroid radioactive iodine uptake was analyzed in destructive thyroiditis patients receiving interferon- α and Ribavirin therapy.¹⁰ If treatment is restarted, thyroid functions should be carefully monitored as patients mostly recover from thyroiditis.¹¹

METHODOLOGY

SOURCE OF DATA

Fifty Five (55) Patients of HCV positive were recruited for this study at Jinnah Hospital Lahore and all experimental work was performed in Biochemistry Department, Minhaj University Lahore. Detailed history with any clinical complications and smokers habits in particular smoking and tobacco chewing were collected from participants of the study, by giving them a questionnaire. Clinical diagnosis of the patient was also taken into consideration.

Twenty Five (25) age and sex-matched clinically apparently healthy individuals were included as controls.

Method of collection of data

Informed consent from subjects was obtained before collection of blood samples. Blood samples were collected with aseptic precaution.

Sample and Sampling Technique

5ml blood sample of the study participants were collected in EDTA-vacutainers and centrifuge at 3000-4000 rpm for 15 minutes to separate of the serum.

Chemicals

All chemical reagents of analytical grades were purchased from Sigma Chemical Co. (St. Louis, Mo, USA).

Following Parameters were Estimated Biochemical Assays for Liver Function Tests

The estimation of AST, ALT and ALP, FT3, total protein (TP) and total Bilirubin (TB) were estimated

by using commercially available Bio Merux and Randox kits.

Estimation of Thiobarbituric Acid Reactive Substances (TBARS)

Lipid peroxidation in liver tissues was estimated calorimetrically by measuring Thiobarbituric acid reactive substances (TBARS) by the method of Ohkawa et al., 1979.¹²

RESULTS

The data presented in Table 1 shows the picture of the different parameters measured in Hepatitis C patients receiving Interferon and Ribavirin. When the age profile was observed, it was noticed that it increased remarkably in the patients (40.94 \pm 11.53) as compared to healthy persons (33.04 \pm 6.63) and also observed that it was statistically significant (p-value <0.002). When the FT3 level was measured it was noticed that FT3 level was elevated remarkably in the HCV patients (16.63 \pm 7.14) as compared to control objects (4.25 \pm 0.72) and statistically significant (p-value <0.000). Similarly MDA level in patients was recorded as (8.58 \pm 1.19) while in healthy individuals (1.47 \pm 0.54).

Table 1: Comparison of different parameters in hepatitis C (HCV) patients receiving interferon and ribavirin

Parameters	Control (n=25)	Patients (n=55)	P-value <0.05
Age	33.04 \pm 6.63	40.94 \pm 11.53	0.002
FT3	4.25 \pm 0.72	16.63 \pm 7.14	0.000
MDA	1.47 \pm 0.54	8.58 \pm 1.19	0.000
ALT	32.78 \pm 20.46	40.51 \pm 41.69	0.413
AST	31.43 \pm 7.31	47.88 \pm 40.49	0.024
ALP	1.84 \pm 71.00	2.02 \pm 76.26	0.375
TP	6.23 \pm 0.51	4.20 \pm 0.61	0.000
TB	0.88 \pm 0.27	0.95 \pm 0.466	0.492

It shows that lipid peroxidation level in patients was elevated than control persons and it was statistically significant (p-value <0.05). Serum ALT level in patients was (40.51 \pm 41.69) while in healthy individuals (32.78 \pm 20.46) and it was statistically non-significant (p-value >0.413). When serum AST level was measured, it was observed that AST level was increased remarkably in patients (47.88 \pm 40.49) as compared to control objects (31.43 \pm 7.31) and it was statistically significant (p-value <0.02). Serum ALP level in HCV patients was recorded as (2.02 \pm 76.26) while in healthy persons it was (1.84 \pm 71.00) and statistically non-significant (p-value >0.375). Total Protein (TP) level was

decreased in HCV patients (4.20±0.61) as compared to Control persons (6.23±0.51) and also noticed that it was statistically significant (p-value <0.05). The values of total Bilirubin (TB) in patients was (0.95±0.46) while in healthy individuals (0.88±0.27) and statistically non-significant (p-value >0.492).

The data presented in Table 2 is the comparison of different parameters in HCV patients according to gender. When the Age profile was observed in male patients it was (35.71±10.36) and in female patients it was (39.76±10.53). FT3 level in males was (9.72±6.79) and in females (13.58±9.11). MDA level in male HCV patients was (5.05±3.86) while in females it was (6.43±3.36). When ALT level was observed in males, it was recorded as (38.75±40.25) and in females (36.23±29.54). AST level in males was (40.82±30.14) while in females (41.86±35.50). Serum ALP level in HCV infected males was (1.92±71.16) while in females (1.98±77.85). Total Protein (TP) level in male patients was (5.26±1.17) and in female patients (4.78±1.09). When total Bilirubin (TB) level was measured in Male patients it was recorded as (0.94±0.32) while in case of females it was recorded as (0.91±0.46). It was also observed that all the parameters were statistically non-significant (P-value >0.05) which showed that in the progression of the Hepatitis C (HCV), gender does not matter. It can be infected both either males or females.

Table 2: Comparison of different parameters in hepatitis C (HCV) patients receiving interferon and ribavirin according to gender

Parameters	Females (n= 30)	Males (n= 25)	P-value < 0.05
AGE	39.76±10.53	35.71±10.36	0.146
FT3	13.58±9.11	9.72±6.79	0.075
MDA	6.43±3.36	5.05±3.86	0.154
ALT	36.23±29.54	38.75±40.25	0.786
AST	41.86±35.50	40.82±30.14	0.904
ALP	1.98±77.85	1.92±71.16	0.756
TP	4.78±1.09	5.26±1.17	0.114
TB	0.91±0.46	0.94±0.32	0.782

DISCUSSION

HCV was treated with interferon-alpha and Ribavirin therapy. This therapy induced thyroid dysfunction in HCV patients. In the previous studies, it is clear that thyroid dysfunction occurred in females mostly when compared with male.¹³ Thyroiditis is of two types: Autoimmune interferon induced thyroiditis (IIT) and non-autoimmune interferon induced thyroiditis.¹⁴

Autoimmune IIT can appear as Graves' disease (GD) and Hashimoto's thyroiditis (HT) while non-autoimmune IIT can be presented as destructive thyroiditis or non-autoimmune hypothyroidism. Hypothyroiditis occurred commonly.¹⁵

It was clear that T3 is inversely proportional to the severity of disease. If levels of T3 are low it means disease is severe. If levels of T3 are increased it means disease less severe. Present study shows that FT3 levels increased in HCV patients. Malondialdehyde is the end-product of lipid peroxidation and produce by degradation of the polyunsaturated lipids by Reactive Oxygen Species (ROS). The previous studies described that MDA level in chronic hepatitis C patients increased in serum and in liver tissues. Present study has shown that the MDA level in chronic hepatitis C patients was statistically significantly higher when compared to the healthy control group. This finding is compatible with previous reports.

Present study showed that there was no more difference in the levels of ALP in HCV patients. It was noticed that there was no variation in the level of ALP in patients (2.02 ± 76.26) when compared with controls (1.84 ± 71.00). It was observed that ALP levels were statistically non-significant in HCV patients (P=0.375>0.05). The levels of ALP observed in 55 subjects. 30 were female and 25 were male. There was no variation in the level ALP in female (1.98 ± 77.85) when compared with male (1.92 ± 71.16). So level of ALP shows that it is statistically non-significant (P=0.756>0.05).

CONCLUSION

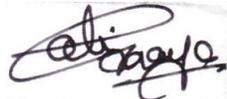
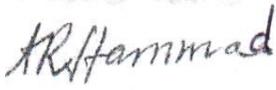
Thyroid dysfunction occurred in chronic hepatitis C patients when treated with interferon-alpha and Ribavirin therapy. In a multivariate analysis, it was confirmed that thyroid dysfunction occurs mostly in females as compared to males. Female gender is an independent predictor of the development of biochemical thyroid dysfunction during interferon-alpha and Ribavirin treatment. In present study, Age, MDA, FT3, ALT, AST, ALP, TP and TB parameters were studied. Biochemical studies express that oxidative stress play a key role in the development of disease. It is concluded that HCV patients have remarkably increased lipid peroxidation due to which MDA is increases. Age is significant and FT3 levels also increased. AST and TP are significant. TB and ALP values are highly non-significant.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

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