

# Study of Thyroid Function Indices (T3, T4, a-Tpo, Tg, a-Tg) During Hepatitis B in Khoy City, Iran, Before Alpha-Interferon Therapy

## Alpha-İnterferon Tedavisinden Önce İran, Khoy Şehrindeki Hepatit B Sırasında Tiroid Fonksiyon Endekslerinin (T3, T4, a-Tpo, Tg, a-Tg) İncelenmesi

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### ABSTRACT

**Objective:** The purpose of this study was to evaluate whether hepatitis B impresses on thyroid function indices (T3, T4, a-Tpo, Tg, a-Tg) levels. Hepatitis B is known as one of the most dangerous and important viral diseases which causes various side-effects on liver and other organs.

**Methods:** In this study, thirty hepatitis B patients which had been diagnosed based on routine test with ELISA technique and ten healthy cases (clinically and para-clinically) were selected (in different age and sex). After blood sampling, all parameters in two groups were detected by electrochemiluminescence technique.

**Results:** The results suggested that significant elevation ( $p<0.01$ ) of a-Tpo, Tg, a-Tg and significant decrease ( $p<0.01$ ) of T3 and T4 in patient group compared with healthy ones.

**Conclusion:** Hepatitis B patients of Khoy city involve with thyroid dysfunction and seems that results may help in the much better management of hepatitis B.

**Keywords:** Thyroid function indices, hepatitis B, Khoy city, Iran

### ÖZ

**Amaç:** Bu araştırmanın amacı Hepatit B'nin tiroid çalışması göstergelerine (T3, T4 , a-Tpo, a-Tg , Tg) etkili olup olmadığını görmektir. Hepatit B en tehlikeli ve en önemli viral hastalıklardan biri olarak tanınır ki vücutta karaciğer ve diğer organlarda önemli arızalara yol açmaktadır.

**Gereç ve Yöntemler:** Bu çalışmada ELISA deney yöntemiyle tespit edilmiş 30 hepatit B hastası ve 10 sağlam kişi ele alınmıştır (değişik yaş ve cinsiyette). Devamında kan örnekleri alındıktan sonra, tüm değerler elektrokemilüminesans teknik ve yöntemiyle ölçüldü.

**Bulgular:** Sonuçlar hasta grupta sağlam olanlara göre, a-Tpo , Tg ve a-Tg değerlerinde anlamlı artış ( $p\leq 0,01$ ) ve T3 ve T4 değerlerinde anlamlı azalma göstermiştir.

**Sonuç:** Khoy ilçesindeki hepatit B hastalarında, tiroid bezi çalışmasında bozulma gözlenmiştir ve görünüşe göre elde olunan sonuçlar hepatit B hastalığının yönetiminde yardımcı olabilir.

**Anahtar Kelimeler:** Tiroid fonksiyon indeksleri, hepatit B, Khoy şehri, İran

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## INTRODUCTION

The liver possesses essential role in metabolism of the thyroid hormones, as synthesizes the major transport protein of thyroid hormones which is known thyroxin binding globulin (TBG), which links 75% of the circulating hormone (1). In addition, deiodination of T4 to T3 carried out mainly in the liver (2). This process thus initiates both action and catabolism of the hormones. Conjugation, deamination and decarboxylation of side chains of T3 and T4 also occur in the liver (3). In Iran, one of the most common viral disease is known to be hepatitis. The hepatitis B virus (HBV) prevalence is approximately 2-3% (4). Thyroid gland dysfunction prevalence has been demonstrated to be high before interferon-alpha (IFN- $\alpha$ ) therapy and after treatment with it in patients with hepatitis C virus (HCV) and some literatures also confirm during autoimmune thyroiditis disease, the prevalence of anti HCV antibody increase in those patients (5), but anti HBV prevalence has been reported to be very low during infection with HBV (6). Different studies not only reported the thyroid dysfunction prevalence but also determined production of anti-thyroid antibodies production in hepatitis C patients. They reported the enhancement of thyroid peroxidase antibody (a-Tpo) and thyroglobulin antibody (a-Tg) levels in patients during IFN- $\alpha$  therapy in comparison with the normal value (6-8). However, there appear no research in respect of anti-thyroid antibodies (ATAs, a-Tpo and a-Tg) during hepatitis B infection before IFN therapy.

In recent years, more attention has been paid on identification of various aspects of hepatitis and no research has been conducted to determine possible thyroid dysfunction in hepatitis B in the West Azerbaijan, Iran. Hence, to our knowledge, evaluation of thyroid function indices during hepatitis B before IFN- $\alpha$  therapy in Khoy city can be useful in hepatitis B management in Iran.

## MATERIALS AND METHODS

This study was carried out in West Azerbaijan Province, Khoy city, (Madani and Gamar Banihashem Hospitals), Iran during 2013. Diagnostic tests of anti-HBV (based on ELISA technique) were performed in the patients' sera: hepatitis B surface antigen, hepatitis B e antigen, hepatitis B surface antibody, hepatitis B e antibody and hepatitis B core antibody. Informed consent of information was confirmed by all patients. After diagnosis of hepatitis B, blood sampling was performed and 10 milliliter of blood

were taken from 30 chronic hepatitis B patients (28-55 age) and 10 samples from clinically and para-clinically healthy cases (28-55 age) and transferred into plain tubes for serum preparation and after 20 minutes standing of blood tubes, these ones were centrifuged in 6000 rpm and then sera removed from samples.

Thyroid function parameters such as, T3, T4, a-Tpo, a-Tg and Tg levels were determined through electrochemiluminescence technique (Elecsys, Roche, 2010) with DIASORIAN kit.

## Statistical Analysis

Statistical analysis was accomplished in all analyses. After normality analysis, mean  $\pm$  standard error of the mean and the determination of variation between the data results were carried out with Student's t-test through SAS v9.1 (SAS Institute Inc., Cary, NC, USA). The significance level was specified at ( $p < 0.01$ ).

## RESULTS

The results denote significant alterations ( $p < 0.01$ ) in those parameters. Increase in the a-Tpo, Tg, a-Tg and decrease of T3 and T4 in patients group in comparison with healthy ones (Table 1).

## DISCUSSION

In present study, elevation of a-Tpo, a-Tg and Tg levels and decrease of T3 and T4 levels were determined in the hepatitis B patients. Ziaee et al. in 2009 reported alterations in the thyroid function parameters in the hepatitis C and B patients during IFN- $\alpha$  therapy (9). As thyroid dysfunction was not observed in the hepatitis B group in the Ziaee et al. in 2009 and Lisker-Melman et al. study in 1997 which is not in accordance in present study (9,10). Ziaee

**Table 1:** Alterations of thyroid function indices in patient and healthy group

Parameters/groups	Healthy group	Patient group	p
T3, ng/dL	13.56 $\pm$ 0.9	4.85 $\pm$ 0.16	0.003
T4, $\mu$ g/dL	10.95 $\pm$ 1.02	3.89 $\pm$ 0.56	0.001
Tg, ng/mL	0.069 $\pm$ 0.01	0.31 $\pm$ 0.5	0.004
a-Tg, IU/mL	3.75 $\pm$ 0.51	9.49 $\pm$ 0.10	0.005
a-Tpo, IU/mL	0.03 $\pm$ 0.019	0.15 $\pm$ 0.006	0.001

Data are expressed as mean  $\pm$  standard error of mean. P value was set as ( $p < 0.01$ ).

a-Tg: Thyroglobulin antibody, a-Tpo: Thyroid peroxidase antibody

et al. concluded that hepatitis C patients more prone to dysfunction of thyroid gland during IFN- $\alpha$  therapy in comparison of patients with hepatitis B ones (9). Also, Ziaee et al. attributed cause of thyroid dysfunction to IFN- $\alpha$  therapy (9). In previous reports, the prevalence of thyroid dysfunction differed remarkably from 3.4% to 31.4% (7,8). Several agents can develop on thyroid dysfunction, for example, genetic diversity, geographical distribution and environmental factors such as viral infection and iodine intake (11). We did not consider age and sex role in this study, but others reported significant differences based on age and sex. Ziaee et al. in 2009 demonstrated the relationship of hepatitis B prevalence with age of patients which may be attributed to the vertical transmission route in Iran (9). Also, Koh et al. in 1997 determined that female sex was found to be susceptible for developing thyroid dysfunction in HCV patients (12).

Zafar et al. in 2015 and Gardner et al. in 1985 reported high level of T3 and T4 during acute hepatitis B virus infection which are not in accordance with present study (13,14). However, Yamanska et al. in 1980 clarified occurrence of low levels of T3 during decompensated liver cirrhosis that agrees with present study (15). Zafar et al. expressed that the elevation of T3 and T4 firstly can be proportional attributed to hepatocyte necrosis (due to icterus and high activity of transaminases and ALP) and secondly cause of T4 elevation can be due to decreased conversion of T4 to T3, because this conversion is performed in the liver (13). This might be a correct description in the severe hepatitis and not in mild to moderate ones.

Kano et al. in 1987 reported high levels of T4 and FT4 along with reference value of FT4 in patients with acute hepatitis of mild or moderate severity and contributed it to elevated TBG, which is synthesized as an acute-phase reactant in the liver (16). The same study revealed low levels of total T4 in impending liver failure and may reflect decreased hepatocellular synthesis of TBG. Furthermore, Kano et al. in 1987 presented prognostic value of free T3:T4 ratio in the liver disease and showed negative correlation of T3:T4 ratio with liver disease (16).

Anti-thyroid antibodies (ATAs) (a-Tg and a-Tpo) are known to play as markers of auto-immune thyroid disease and thyroid dysfunction resulting in different degrees of hypothyroidism from subclinical to overt are attributed to ATAs (17). There appears to be few studies on the levels of these indices to compare with the present findings in the

hepatitis B patients before IFN- $\alpha$  therapy. Some studies have exhibited ATAs in different disorders such as, positive a-Tg in patients with premature menopause and the relation of autoimmune thyroiditis and minor hypothyroidism with systemic lupus erythematosus (18). Ziaee et al. reported that from 58 hepatitis C patients, four cases (6.9%) and in the hepatitis B group only one patient (5.5%) possess high levels of a-Tpo before IFN- $\alpha$  therapy and a-Tpo levels increased after administration of IFN- $\alpha$  therapy (9). Fernandez-Soto et al. in 1998 determined positive levels of anti-thyroperoxidase (a-Tpo) and anti-thyroglobulin (a-Tg) in 5% and 3% of HBV patients respectively (6). In the study of Deutsch et al. in 1997, 7 patients (4%) of the 170 HBV patients showed dysfunction of thyroid gland (19). Preziati et al. in 1995 studied on 51 HBV patients who treated with IFN- $\alpha$  therapy, primarily reported positive concentrations of anti-thyroperoxidase (a-Tpo) and anti-thyroglobulin (a-Tg) in zero and 5 (9.8%) patients, respectively (7).

The possible mechanism of IFN- $\alpha$  therapy effect on thyroid dysfunction has been almost curtailed in the hepatitis C disease. There are interestingly some suggestions that a portion of the HCV genome could share partial sequence homology with thyroid tissue antigens (20). Thus, patients with chronic hepatitis C infection might be more prone to autoimmune thyroid diseases. It is possible that the same mechanism and/or a bit similar mechanism occurred during hepatitis B infection in this study.

## CONCLUSION

In conclusion, since, we were faced with alterations of Tg, a-tg, a-Tpo and T3, T4 in the hepatitis B, therefore, it is possible that we can utilize these results for understanding of hepatitis B associated complications and how to deal with them for reduction of possible implications of hepatitis B. In addition, thyroid gland dysfunction and elevation of thyroid antibodies may aggravate hepatitis B conditions along with treatment protocol and seems to be aware of these changes involves a significant impact on the management of hepatitis B therapy.

**Ethics Committee Approval:** All procedures carried out in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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