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Evaluation of Serum Trace Elements and Vitamin Levels in Hashimoto's Thyroiditis: Single Centre Experience from Turkey

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ABSTRACT

Aim: To determine levels of serum trace elements and vitamins, and to find out possible correlations between these elements and vitamins with thyroid function tests and thyroid autoantibody levels in patients having Hashimoto's thyroiditis (HT). **Methods:** The study included 51 premenauposal women with untreated HT, aged 18 to 56 years without any known chronic diseases or chronic medicine usage, and 27 healthy premenauposal women aged 19 to 42 years old. Trace elements (selenium, zinc, copper, iron levels) and vitamins [A, E, B12, 25-OH-D, $1,25(OH)_2D$ and folic acid levels] were evaluated in patient and control groups. **Results:** Consequently, serum trace elements and vitamin B12 levels did not significantly differ in patients with HT and control group. Thyroid functioning tests and autoantibody levels did not show any correlation with the levels of trace elements, vitamin A, vitamin E and 25-OH vitamin D. A correlation was detected between vitamin B12 and Anti thyroid peroxidase levels. **Conclusion:** The negative correlation between vitamin B12 and Anti thyroid peroxidase levels may demonstrate the necessity to screen the patients with HT for atrophic gastritis. We believe that more comprehensive studies with larger sample sizes are needed in which patients are randomized according to their nutritional status.

Keywords: Hashimoto's Thyroiditis; Trace Element; Vitamin, Vitamin B12, Atrophic Gastritis; Anti Thyroid Peroxidase Antibody

1. Introduction

Hashimoto's thyroiditis (HT) is an autoimmune disease caused by the destruction of thyroid gland in various degrees via numerous immune mechanisms. HT is diagnosed with the elevated thyroid antibodies in serum. Autoantibodies, genetic tendency, intracellular oxidative mechanisms and cytokines lead to cellular apoptosis and thus result in follicular destruction. Hypothyroidism may develop due to the destruction of thyroid gland in HT.

Trace elements are necessary for development, growth and physiology of the organism. They take part in various mechanisms in the body, but cannot be synthesized in the organism. These elements are iron, zinc, copper, selenium, chloride, florid, iodine, chrome, manganese, bore, cobalt, molybdenum, vanadium, spelter and silisium. They take part in functions like immune regulation, nerve conduction, regulation of membrane potential and maintenance of mithocondrial activity.

Zinc is an essential element for thyroid hormone functions [1]. Copper is the vital component of numerous oxidative enzymes. [2]. Free copper takes role on cellular membranes as a pro-oxidant agent. Selenium is essential for deiodinase activities and thyroid hormone synthesis and metabolism. Selenium acts as a co-factor in the structure of glutation peroxidase which has anti-oxidant features. Glutation peroxidase takes role in degradation of hydrogen peroxide to water. After interacting with vitamin E, selenium protects the cellular membrane against oxidative damages caused by lipid metabolism [3]. Iron takes place in structures of many enzymes in the body.

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Vitamins are the essential elements which are necessary for occurrence of metabolic events and maintenance of health status, while they cannot be synthesized in the body or synthesized inadequately, and need to be intaken.

Non-enzymatic anti-oxidants, like vitamin E and A, contribute to decrease the oxidative damage caused by oxygen radicals by taking their high-energy electrons [4]. Another function of vitamin E is to increase the absorption of vitamin A from the intestines and its level in the tissues. Concomitance of hypothyroidism and pernicious anemia is very frequent, and vitamin B12 deficiency is observed in pernicious anemia. Due to its antiinflammatory and immunomodulatory features and potential effects on cytokine levels, decreased levels of vitamin D is associated with the increased risks of many disorders, particularly autoimmune diseases [5,6]. Folic acid, which is actually a pro-vitamin, is changed to dihydrofolat by dehydrofolat reductase enzyme after being absorbed, and then it is converted to tetrahydrofolate. Using single carbon units, the nascent tetrahydrofolate transfers single carbon to some endogenous substances via various oxidating mechanisms.

In this study, we aimed to determine the levels of serum trace elements like selenium, zinc, copper and iron, and vitamins like A, E, B12, 25-OH-D, 1,25$(OH)_2$D, folic acid in patients with HT and evaluate the association between thyroid antibodies and these elements and vitamins.

2. Material and Methods

This prospective study included 51 premenopausal women aged between 18 to 56 years and 27 healthy premenopausal women aged between 19 to 42 years, who had applied to our clinic. Only female participants are involved in order to create a homogeneous group. Patients were newly diagnosed and untreated with L-thyroxine. Patients with any known diseases (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, chronic liver or kidney diseases, gastrointestinal absorption problems, collagen tissue disease, bone metabolism disease, thyroid disease or malignancy) or chronic medicine users were excluded. Demographic characteristics, information on current smoking and alcohol consumption and personal and familial histories were recorded, and detailed physical examinations were performed. Informed consent forms were obtained from all patients. Approval of Local Ethics Committee was taken. The study was performed in accordance with Helsinki Declaration and Good Clinical Practice.

HT was diagnosed by elevated anti thyroid peroxidase (anti-TPO), anti thyroglobulin (anti-TG) levels and thyroid ultrasonography evaluation which revealed heterogeneity and fibrotic bands in thyroid glands [7]. Subjects with normal thyroid antibodies were considered to be healthy.

Weight, waist circumference, hip circumference and height were measured in fasting status and with daily clothes by the same person. The waist circumference was accepted as the narrowest diameter between the arcus costarum and spina iliaca anterior superior, and the hip circumference was considered as the largest diameter over the gluteus maximus posteriorly and symphysis pubis anteriorly. Body mass index (BMI) was the ratio of the weight to the square of height (weight/heigh^2- kg/m^2).

Blood samples were collected following 12 hours of fasting. In order to study selenium levels (N: 46 - 143 µg/L), the collected blood samples were centrifuged at 5000 rpm/min after coagulation and stored at −80˚C until testing. The test was performed manually by AAS Hydro System Management. Blood samples were collected from antecubital veins to evaluate iron, copper, zinc, albumin, thyroid stimulating hormone (TSH), Anti-TG, Anti-TPO, TSH receptor antibody (TRAB), vitamin A, vitamin E, vitamin B12, 25-OH vitamin D, 1.25-$(OH)_2$ vitamin D and folic acid. Iron (N: 70 - 180 µg/dL), copper (N: 12.6 - 24 µmol/L) and zinc (N: 10.4 - 22.9 µmol/L) were detected by Olympus AU 2700 equipment using the original kits. 25-OH vitamin D (N: 10 - 80 ng/mL), 1.25-$(OH)_2$ vitamin D (N: 10 - 60 pg/mL) and TRAB (N: 0 - 14 U/L) levels were detected by radioimmunaassay (RIA) method using Dia Source kit. fT3 (N: 2.3 - 4.2 pg/mL), sT4 (N: 0.7 - 1.76 ng/dL), TSH (N: µIU/mL), anti-TPO (N: 0 - 60 U/mL), anti-TG (N: 0 - 60 U/mL), vitamin B12 (N: 190 - 911 pg/mL), folic acid (N: 5.38 - 20 ng/mL) levels were detected using Advia Centaur System (Siemens) and its original kits by chemiluscent method. Vitamin A (N: 1.05 - 2.8 µmol/L) and vitamin E (N: 11.6 - 46.4 µmol/L) were tested by HPLC method using Agilent 1200 equipment and Chromosystems kits.

Statistical analyzes were performed by SPSS 16 program. The values were presented as mean ± standard deviation. Mann Whitney U test was used to compare the means between the two groups. $P < 0.05$ was accepted to be significant.

3. Results

Features of Hashimoto and control groups are presented on **Table 1**.

While there was a significant difference between Hashimoto and control groups regarding TSH, fT4, Anti-TPO, Anti-TG and TRAB, there was no significant difference in terms of FT3 (**Table 2**).

The levels of serum selenium, zinc, copper, iron, vitamin E, vitamin A, vitamin B12, folic acid, 25-OH vitamin D and 1.25-$(OH)_2$ vitamin D did not differ between Hashimoto and the control groups (**Table 3**).

A correlation was detected between vitamin B12 and Anti-TPO levels ($r = -0.226$, $p = 0.04$, **Figure 1**).

Table 1. Features of patient and control group.

	Control	Patient	p
Age (year)	33.14 ± 6.87	35.37 ± 8.00	0.2
BMI (kg/m²)	26.76 ± 7.08	27.48 ± 5.17	0.64
Waist circumference (cm)	87.08 ± 14.14	87.14 ± 11.68	0.98
Hip circumference (cm)	105.57 ± 12.23	106.89 ± 9.49	0.63

Table 2. Thyroid function tests and thyroid autoantibody levels of patient and control group.

	Control	Patient	p
TSH (µIU/mL)	1.99 ± 1.22	5.64 ± 6,32	**0.0001**
fT3 (pg/mL)	3.37 ± 0.33	3.26 ± 0.27	0.132
fT4 (ng/dL)	1.04 ± 0.15	0.91 ± 0.16	**0.002**
Anti-TPO (U/mL)	41.56 ± 13.72	236.74 ± 266.95	**0.0001**
Anti-TG (U/mL)	31.53 ± 12.48	145.03 ± 118.98	**0.0001**
TRAB (U/L)	7.4 ± 4.16	4.92 ± 3.32	**0.019**

Normal ranges: TSH: µIU/Ml, fT3: 2.3 - 4.2 pg/mL, fT4: 0.7 - 1.76 ng/dL, anti-TPO: 0 - 60 U/mL, anti-TG: 0 - 60 U/mL, TRAB: 0 - 14 U/L.

Table 3. Trace elements and vitamin levels of patient and control group.

	Control	Patient	p
Selenium (µg/L)	70.03 ± 11.43	67.32 ± 10.29	0.34
Zinc (µmol/L)	13.26 ± 1.77	12.85 ± 2.58	0.42
Copper (µmol/L)	15.75 ± 3.19	16.57 ± 3.57	0.31
Iron (µg/dL)	69.51 ± 40.23	68.68 ± 36.94	0.92
Vitamin E (µmol/L)	27.64 ± 6.99	29.20 ± 7.22	0.36
Vitamin A (µmol/L)	1.50 ± 0.35	1.61 ± 0.49	0.25
Vitamin B12 (pg/mL)	298.33 ± 88.17	279.09 ± 98.16	0.38
Folic acid (ng/mL)	9.64 ± 3.13	9.76 ± 4.37	0.86
25-OH vitamin D (ng/mL)	17.3 ± 8.0	21.8 ± 15.2	0.18
1.25-$(OH)_2$ vitamin D(pg/mL)	23.76 ± 16.75	17.18 ± 11.64	0.09

Normal ranges: selenium: 46 - 143 µg/L, zinc: 10.4 - 22.9 µmol/L, iron: 70 - 180 µg/dL, copper: 12.6 - 24 µmol/L, vitamin E: 11.6 - 46.4 µmol/L, vitamin A: 1.05 - 2.8 µmol/L, vitamin B12: 190 - 911 pg/mL, folic acid: 5.38 - 20 ng/mL, 25-OH vitamin D: 10 - 80 ng/mL, 1.25-$(OH)_2$ vitamin D: 10 - 60 pg/mL.

4. Discussion

Levels of serum trace elements and vitamins did not differ between HT and control groups in our study. We also did not determine a correlation between the levels of trace elements and thyroid antibodies. We determined a negative correlation only between vitamin B12 and Anti-TPO levels.

In the recent studies, oxidative mechanisms are considered to play a role in thyroid autoimmunity. In this case, thyroid autoantibodies could be expected to be associated with selenium, vitamin E and vitamin A, which are called antioxidants, as well as zinc and copper, which are called antioxidant enzyme co-factors. However, we could not detect such an association in our study. There was also no association between vitamin D, folic acid and iron with thyroid autoantibodies. We did not find any reports demonstrating correlations between thyroid autoantibodies and vitamin E, vitamin A, vitamin, D folic acid, copper and zinc. While some reports showed an association between the levels of selenium [8] and autoantibodies, some did not [9-11]. Different outcomes in these studies might be due to nutrition alterations among the individuals, genetic tendency, different stages of thyroid diseases, differences in numbers of patients and their distributions and/or alterations in laboratory techniques.

There are a few reports regarding the association between thyroid and vitamin B12. It is known that HT may accompany other autoimmune diseases. Pernicious anemia is one of them. Of the patients with hypothyroidism, 7% to 12% have evident pernicious anemia and 10% have latent pernicious anemia [12]. Vitamin B12 deficiency is observed in pernicious anemia [13]. Ness-Abramof *et al.* suggested that patients with autoimmune diseases should be screened for pernicious anemia by screening vitamin B12 levels in every 3 or 5 years [14]. We did not determine any vitamin B12 deficiency among patients in our study, but detected a correlation between vitamin B12 and Anti-TPO levels ($r = -0.226$). This relationship might be indicative of an underlying similar autoimmune pathology. By these results, necessities appear for the investigation of the level of gastric parietal cell antibody and for the determination of the co-morbidity of atrophic gastritis, which also an autoimmune disease, in patients with high levels of Anti-TPO.

Our study had some limitations. Selenoprotein levels for selenium status, seruloplasmin for copper status, and zinc levels in urine, erythrocyte for zinc status and parietal cell antibody could not be detected. Dietary habits of patients were not asked.

Consequently, serum trace elements and vitamin levels did not significantly differ in patients with HT and the control group. Thyroid function tests (TSH, fT3, fT4) did not show any correlation between the levels of trace ele-

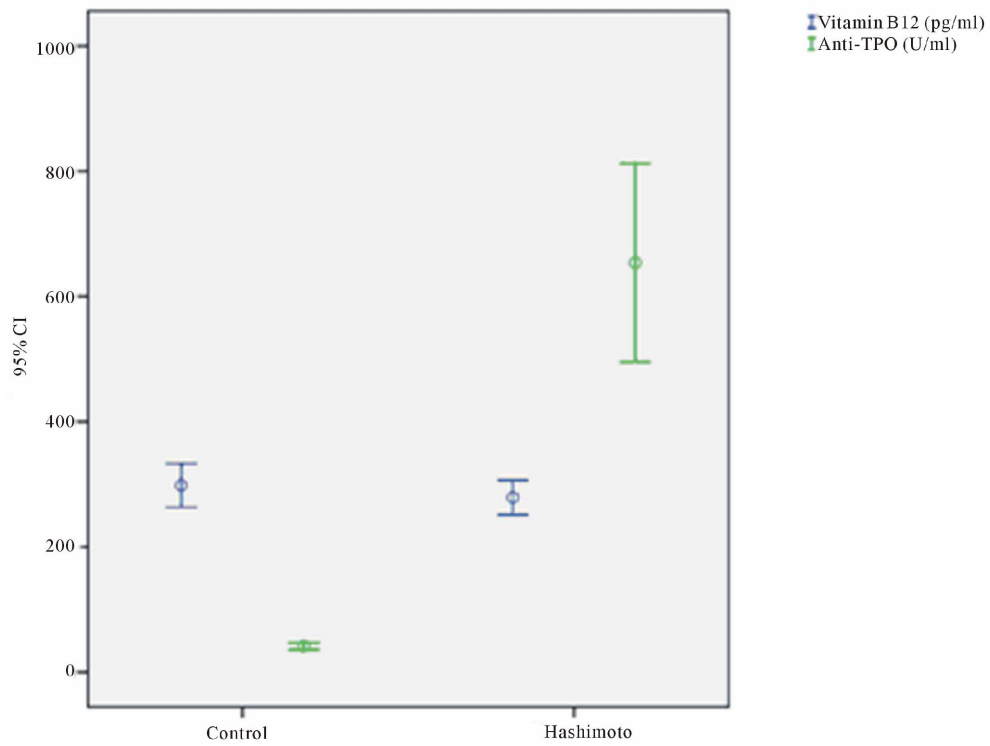

Figure 1. Vitamin B12 and Anti-tpo levels in patient and control groups.

ments and vitamins. Thyroid autoantibody levels did not show any correlation between the levels of trace elements and vitamin A, vitamin E and 25-OH vitamin D. A correlation was detected between vitamin B12 and Anti-TPO levels. This result may show that patients with HT should be screened for atrophic gastritis. We believe that more comprehensive studies with larger sample sizes are needed.

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Abbreviations

Anti-TG: Anti thyroglobulin;
Anti-TPO: Anti thyroid peroxidase;
BMI: Body mass index;
HT: Hashimoto's thyroiditis;
TSH: Thyroid stimulating hormone;
TRAB: Thyroid stimulating hormone receptor antibody.

