The role of vitamin D3 deficiency in the etiopathogenesis of autoimmune thyroid diseases.

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Abstract

Vitamin D is now recognized not only for promoting bone health in children and adults, but also for other health benefits, including reducing the risk of chronic diseases such as autoimmune diseases, malignancies, and cardiovascular disease.

The aim of our study is to investigate whether there is a correlation between autoimmune thyroid disease and vitamin D 3 deficiency in the population of Georgia.

The study cohort included a total of 306 patients aged 18–65 years (mean age 37.6 ± 11.3 years) referred to the National Institute of Endocrinology from 2018 to 2019The cohort included 87 men (total 28.4%) and 219 women (total 71.6%). A retrospective selection of the study population was made based on patient history. The study protocol was approved by the Medical Ethics Committee of our institute (Protocol N 448) and informed consent was signed by all patients.

Results: Compared to controls the study droup were characterized by significantly higher frequencies of following factors: hair loss, brittle nails, dizziness, general weakness, mood swings.

Compared to controls the study group were characterized by significantly higher frequencies of Anti-TPO (236.44+44 vs 0.409.65$\pm$84.22, $p<0.0001$). The mean value of vitamin D and TSh are unsatisfactory higher in the study group(6.1+8.64 vs 5.6+9.20, $p=0.5161$).

Conclusion:

- The role of vitamin D deficiency in thyroid autoimmune diseases was not confirmed in the population of Georgia.
- Since no reliable difference in vitamin D 3 deficiency was detected in both groups, larger-scale studies are needed to study vitamin D references in the Georgian population.
- Keywords: D vitamin, Autoimmune Thyroiditis, Immune system

ვიტამინი D3-ის დეფიციტის როლი ფარისებრი ჯირკვლის აუტოიმუნური დაავადებების ეტიოპათოგენეზში.

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ივ. ჯავახიშვილის სახელობის თბილისის სახელმწიფო უნივერსიტეტის ენდოკრინოლოგიის დეპარტამენტი, ენდოკრინოლოგიის ეროვნული ინსტიტუტი.

დღეისათვის აღიარებულია D ვიტამინის მნიშვნელოვანი როლი ქრონიკული დაავადებების რისკის შემცირებაში, როგორიცაა აუტოიმუნური დაავადებები, ავთვისებიანი სიმსივნეები და გულ-სისხლძარღვთა დაავადებები.

ჩვენი კვლევის მიზანია გამოვიკვლიოთ არის თუ არა კორელაცია ფარისებრი ჯირკვლის აუტოიმუნურ დაავადებასა და D 3 ვიტამინის დეფიციტს შორის საქართველოს მოსახლეობაში.

საკვლევი კოჰორტა მოიცავდა 18-65 წლის 306 პაციენტს (საშუალო ასაკი 37.6 ± 11.3 წელი), რომლებიც მიმართეს ენდოკრინოლოგიის ეროვნულ ინსტიტუტს 2018 წლიდან 2019 წლამდე. კოჰორტა მოიცავდა 87 მამაკაცს (სულ 28.4%) და 219 ქალს (სულ 71.6%). . საკვლევი პოპულაციის რეტროსპექტული შერჩევა მოხდა პაციენტის ისტორიის საფუძველზე. კვლევის ოქმი დამტკიცდა ინსტიტუტის სამედიცინო ეთიკის კომიტეტის მიერ (ოქმი N 448) და ინფორმირებული თანხმობა გაფორმდა ყველა პაციენტთან.

შედეგები: საკონტროლო ჯგუფთან შედარებით, საკვლევ ჯგუფს ახასიათებდა შემდეგი ფაქტორების მნიშვნელოვნად მაღალი სიხშირე: თმის ცვენა, მტვრევადი ფრჩხილები, თავბრუსხვევა, ზოგადი სისუსტე, განწყობის ცვალებადობა.

საკონტროლო ჯგუფთან შედარებით საკვლევ ჯგუფში სარწმუნოდ მაღალი იყო Anti-TPO-ს სიხშირე (236.44+44 vs 0.409.65+84.22, p<0.0001).ხოლო D ვიტამინის მნიშვნელობა არასარწმუნოდ მაღალია საკვლევ ჯგუფში (6.1+8.64 vs 5.6+9.20, p=0.5161).

დასკვნები:

• საქართველოს მოსახლეობაში არ დადასტურებულა D ვიტამინის დეფიციტის როლი ფარისებრი ჯირკვლის აუტოიმუნურ დაავადებებში.

• ვინაიდან D3 ვიტამინის დეფიციტის სარწმუნო განსხვავება ორივე ჯგუფში არ გამოვლენილა, საჭიროა უფრო ფართომასშტაბიანი კვლევები D ვიტამინის როლის შესასწავლად საქართველოს პოპულაციაში.

საკვანძო სიტყვები: D ვიტამინი, აუტოიმუნური თირეოიდიტი, იმუნური სისტემა

Introduction: Over the past decade, and especially in recent years, there has been a dramatic increase in interest in vitamin D in the biomedical world. [1]. Vitamin D is one of the oldest hormones, and most plants and animals that are exposed to sunlight have the ability to produce vitamin D. Vitamin D is critically important for growth and development, as well as maintaining healthy bones from birth to death [2].

The steroid hormone vitamin D is required for normal calcium and phosphorus metabolism and therefore contributes significantly to the health of the musculoskeletal system. According to recent data, low levels of vitamin D are associated with: malignant diseases, cardiovascular diseases, autoimmune diseases and an increase in infections. Adequate levels of vitamin D are maintained through photosynthesis in the skin and through oral intake. According to some estimates, one billion people worldwide are vitamin D deficient or deficient[3]. Vitamin D3 is synthesized in the skin by exposure to ultraviolet light from the sun, or obtained from food, especially oily fish. After hydroxylation in the liver to 25-hydroxyvitamin D (25(OH)D) and in

the kidneys to 1,25-dihydroxyvitamin D (1,25(OH)2D), the active metabolite enters the cell and binds to the vitamin D receptor. [4].

Vitamin D is now recognized not only for promoting bone health in children and adults, but also for other health benefits, including reducing the risk of chronic diseases such as autoimmune diseases, malignancies, and cardiovascular disease. [5].

It has been observed that diseases such as: Autoimmune diseases: including type 1 diabetes, multiple sclerosis and Crohn's disease are common in vitamin D deficient regions. [6]. There are many correlational studies showing that living near the equator reduces the risk of developing various autoimmune diseases. [7].

Autoimmune disease has been on the rise in recent decades [8]. Among the organ-specific autoimmune diseases (ADS), the most widespread is autoimmune thyroid disease (AITD) [9,10] It affects 2-5% of the population, the frequency varies by gender - women 5-15%, and men 1-5%[10].

The etiology of autoimmune thyroid disease is multifactorial and includes genetic and environmental factors [11]. The immune system is an integral part of fundamental physiological processes [12].

It has been established that a complex, integrated immune system requires many specific micronutrients, including vitamins A, D, C, E, B6 and B12, folate, zinc, iron, copper and selenium, which play important, often synergistic roles at all stages of the immune response. [13].

The aim of our study is to investigate whether there is a correlation between autoimmune thyroid disease and vitamin D 3 deficiency in the population of Georgia.

Materials and methods.

The study cohort included a total of 306 patients aged 18–65 years (mean age 37.6 ± 11.3 years) referred to the National Institute of Endocrinology from 2018 to 2019The cohort included 87 men (total 28.4%) and 219 women (total 71.6%). A retrospective selection of the study population was made based on patient history. The study protocol was approved by the Medical Ethics Committee of our institute (Protocol N 448) and informed consent was signed by all patients.

Inclusion Criteria: Patients with Autoimmune Thyroid Diseases

Exclusion Criteria: Iodine deficiency (detected by urine), iron deficiency anemia, vitamin B12 deficiency, diabetes mellitus type 2, diabetes mellitus type 1, pregnancy or breastfeeding, chronic kidney, liver or heart failure, recent vitamin D therapy, immunosuppressive therapy, treatment with metformin or estrogens.

Study variables included: age, sex, social status, body mass index (BMIcm/m2), clinical signs observed included: sweating, dry skin, hair loss, brittle nails, headache, dizziness, fatigue, mood and appetite. Laboratory tests included: vitamin D, TSH, anti-TPO and thyroid ultrasonography.Abbreviations and normal ranges provided by the laboratory for the various tests were: TSH _ thyroid stimulating hormone (0.4-4.2 IU/L), anti-TP0_ antithyroid peroxidase (<3.2 IU/mL), D vit _ vitamin 25(OH).) D (≥30 ng/mL), thyroid volume _ total thyroid volume >18 cm3 in women and >25 cm3 in men indicates thyroid enlargement.Biochemical analyzes were performed using HumaCount 5D analyzer (general blood test), biosystems ALB 80 FLEX and BIO-RAD, human hormone analysis was performed using fluorescence enzyme immunoassay (Tosoh AIA-900) and chemiluminescence immunoassay magiluminescence immunoassay.

Thyroid anatomical dimensions were measured by ultrasonography (GE Philips Affiniti 70G). Patients were divided into groups with AITD (serum anti-TPO>3.2 IU/ml _study group) and patients without AITD (serum anti-TPO<3.2 IU/ml -control group). Quantitative values are presented as the mean ± SD and qualitative values as absolute values and percentages. For qualitative variables the difference between groups was analyzed by Fishers' exact test,while for quantitative variables it was analyzed by the _Student's t-test. Correlations between quantitative factors determined by the Pearson correlation coefficient, and between qualitative factors using – Spearmans' correlation analysis. Sensitivity and specificity was calculated by ROC analysis. The clinical material was calculated using the SPSS 23 package of statistical programs.

Results:

Clinical features in the study(autoimmune thyroid disease) and control groups are shown in Table 1

Table 1. Clinical signs in the study(autoimmune thyroid disease) and control groups

	Control group		Study group		F	p
	n	%	n	%		
Oversweating	45	29.80	45	29.03	0.02	0.8831
Dry skin	66	43.71	65	41.94	0.10	0.7549
Hear loss	46	30.46	65	41.94	4.39	0.0370
Fragility of nails	27	17.88	43	27.74	4.25	0.0402
Headache	58	38.41	70	45.16	1.43	0.2327
Dizziness	37	24.50	68	43.87	13.19	0.0003

Fatigue	65	43.05	104	67.10	18.88	0.0000
Decreased mood	51	33.77	95	61.29	24.95	0.0000
Increased Apepetite	96	63.58	91	58.71	0.76	0.3843

Compared to controls the study droup were characterized by significantly higher frequencies of following factors: hair loss, brittle nails, dizziness, general weakness, mood swings.

Correlation of autoimmune thyroid disease with laboratory parameters given in Table 2.

Table 2. laboratory parameters in the study and Control group

	Control group		**Study group**		t	p
	Mean	SD	Mean	SD		
TSh	3.16	10.42	5.14	8.82	-1.79	0.0744
Anti-TPO	9.65	84.22	236.44	440.40	-6.22	< 0.0001
D vitamin	5.6	9.20	6.1	8.64	2.42	0.5161

Compared to controls the study group were characterized by significantly higher frequencies of Anti-TPO (236.44+44 vs 0.409.65$\pm$84.22, $p<0.0001$).

The mean value of vitamin D and TSh are unsatisfactory higher in the study group(6.1+8.64 vs 5.6+9.20, p=0.5161).

Discussion:Dermopathies, hair loss, onycholysis are common in autoimmune thyroid diseases. [14] Research shows a significant link between thyroid autoimmunity and alopecia [15].

Dizziness is common in thyroid diseases [16]. In our study, the autoimmune thyroid group has significantly more hair loss and brittle nails, dizziness compared to the non-autoimmune group. A significant association between vitamin D deficiency and Hashimoto's thyroiditis has been demonstrated [17]. Vitamin D deficiency shows that vitamin D deficiency is more associated with autoimmunity than with thyroid dysfunction [18]. Our study also revealed vitamin D deficiency in the group with autoimmune thyroid disease. In the USA, autoimmune thyroiditis is one of the leading etiologies of hypothyroidism [19]. In our study, an increase in hypothyroidism is also

found in the group of autoimmune thyroid disease. Vitamin D deficiency is associated with decreased mood in elderly patients [20]. Symptoms and signs associated with hypothyroidism are: weakness, constipation, weight gain, carpal tunnel syndrome, menorrhagia, dysphagia, edema, dry skin [21,22]. Our research shows that diffuse goiter, hypothyroidism, hair loss, brittle nails, headache, dizziness, general weakness, low mood show a reliable positive correlation with anti-TPO (>3.2iu/ml). And with diffuse gout: excessive sweating, low mood, male gender, hypothyroidism. General weakness also correlates with hypothyroidism.

Conclusion:

- The role of vitamin D deficiency in thyroid autoimmune diseases was not confirmed in the population of Georgia.
- Since no reliable difference in vitamin D 3 deficiency was detected in both groups, larger-scale studies are needed to study vitamin D references in the Georgian population.

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