

Research Article

Evaluation of Serum Vitamin D Levels in Patients with Hashimoto's Thyroiditis

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ABSTRACT

Objective: Vitamin D belongs to a group of fat soluble steroids responsible for enhancing intestinal absorption of calcium, phosphate to regulate the serum calcium and phosphate, for the normal mineralization of bone, muscle contraction, nerve conduction and general cellular function. New researches suggest that vitamin D plays an important role in autoimmune diseases. Hashimoto thyroiditis is the most common autoimmune disease of the thyroid gland, which is the main cause of hypothyroidism.

Aim of the study: The purpose of this study was to evaluate serum levels of vitamin D in patients with Hashimoto's thyroiditis and its comparison with serum vitamin D levels in healthy control group.

Methods: This was a Case-control study on 45 healthy subjects and 51 patients with Hashimoto's thyroiditis. All subjects were matched for age, sex, BMI. TSH, FT4, Anti TPO-Ab and 25 (OH) D levels were measured in blood samples. Hashimoto thyroiditis was diagnosed by measuring Anti-TPO-Ab titers.

Results: In this study Serum vitamin D levels were measured in 96 people and 77(79.4%) had vitamin D deficiency, 9 (9.3%) had insufficient serum levels of vitamin D and 10(10.3%) did not have any abnormalities in their serum vitamin D levels. Deficient and insufficient vitamin D levels were diagnosed in 45 patients with Hashimoto's thyroiditis and 41 of control group.

Conclusion: There was no relationship between serum vitamin D levels and Hashimoto's thyroiditis in this study and also because of conflicting data's of other studies, and the role of vitamin D in autoimmune disease and autoimmune nature of Hashimoto's thyroiditis, for evaluation of likelihood of serum vitamin D level in relation with Hashimoto's thyroiditis more studies at vast societies are needed.

Keywords: 25-Hydroxyvitamin D, Hashimoto's thyroiditis, Hypothyroidism, Anti thyroid peroxidase Antibody.

INTRUDUCTION

Vitamin D belongs to a group of fat soluble steroids responsible for enhancing intestinal

absorption of calcium, phosphate to regulate the serum calcium and phosphate, for the normal

mineralization of bone, muscle contraction, nerve conduction and general cellular function. Vitamin D First is metabolized to 25 OH D, then to the hormonal form 1,25 dihydroxyvitamin D (1,25(OH)₂D). 1,25(OH)₂D is the ligand for Vitamin D receptor (VDR) a transcription factor, binding to sites in the DNA called Vitamin D response elements (VDREs). With the finding of the Vitamin D receptor VDR in most tissues and the more recent discovery of thousands of VDR binding sites throughout the genome, controlling hundreds of genes, enhances Vitamin D impact on multiple biologic processes. So apart from its traditional actions related to calcium and Vitamin D, it has been recognized for its Anti-proliferative and Pro-differentiation and Immune modulatory effects.(1) Vitamin D deficiency has been identified as a risk factor in many autoimmune diseases such as type 1 diabetes, Multiple sclerosis, Crohn's disease, rheumatoid arthritis, asthma and cardiovascular disease.(2)

Hashimoto's thyroiditis is the most common autoimmune disease of the thyroid gland, and is the main cause of hypothyroidism, is characterized by thyroid cell apoptosis leading to destruction of thyroid follicles. Hashimoto's thyroiditis antibody in the immune response to the antigen-specific activation of thyroid begins to Thelper. Thelper induces production of activated B-cell antibodies against the thyroid. The mechanism of damage to the thyroid gland is done by both humoral and cellular immune system.(3)

1,25 Dihydroxy vitamin D₃ is a modulator of both the innate and adaptive immune system. Immune system cells such as monocytes macrophages, dendritic cells and T cell and B cells are target of activated form of Vitamin D. But it is not exactly known which Vitamin D levels are sufficient for improving the immune regulatory function and to make its response more effective. It should be mentioned that 25OH Vitamin D levels less than 20 ng/ml is defined as Vitamin D deficiency and serum Vitamin D levels <30ng/ml is defined as Vitamin D insufficiency.

In this study we aimed to assess Vitamin D levels in Hashimoto's thyroiditis patients to recognize whether Vitamin D deficiency is related to autoimmune thyroid disease or not. Because Hashimoto's thyroiditis (Known as chronic lymphocytic thyroiditis), the most common form of thyroiditis and the most common cause of hypothyroidism has an autoimmune basis.

MATERIALS AND METHODS:

This Case-control study was designed on 45 healthy subjects and 51 patients with Hashimoto's thyroiditis disease. The target populations were patients with hypothyroidism referred to Imam Reza Hospital University of Medical Sciences of Tabriz. Patients and control subjects were matched in age, sex, and BMI.

Patients with a history of liver disease, kidney disease, diabetes, metabolic bone diseases, hypertension, history of epilepsy or antiepileptic drugs use, glucocorticoids and anti-TB drugs and Calcium-D supplementation which may change the level of 25 (OH) D or 1,25 (OH) D were excluded.(3)

The aim of the study was explained to the patient before entering the study and informed consent was signed by the patients. After screening, 96 patients were eligible for the study and signed a consent form. To document the association of serum vitamin D levels with Hashimoto's Thyroiditis TSH, FT₄, TPO-Ab and 25 (OH) D levels was measured in serum samples. Hashimoto's thyroiditis was diagnosed by measuring Anti-TPO-Ab titers.(3-14)

25-Hydroxyvitamin D level was determined by CLIA (Chemiluminescent immunoassay technology) and Lias on chemiluminescence Auto-analyzer with a Special Diasorin factory Kit. Serum TSH was measured by sandwich chemiluminescence immunoassay. Serum FT₄ was measured by solid phase antigen linked technique and for this purpose liaison kits of Diasorin factory were used.

In this study the Relationship of serum vitamin D levels with autoimmune thyroid disease

biomarkers was performed by statistical analysis of the data using SPSS software version 22, Tables of results were summarized as mean ± SD. For comparison, data were analyzed by Chi-square test between-group comparison of test data on patients and controls. Paired T-test or Wilcoxon signed rank test was used. It was also used to compare quantitative variables between the two groups and the group of patients with Hashimoto's Thyroiditis. T-test or independent Mann-Whitney U TEST was used. To check the data, distribution whether was normal or not, Kolmogorov-Smirnov test was used. For normally distributed data, parametric test and for data with not-normal distribution non-parametric tests were used. The Spearman and Pearson correlation coefficient was used to assess the Correlation. In all analyzes P-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1. blood levels of vitamin D, according to sex

Vit D \ Sex	Control Group		HASHIMOTO'S THYROIDITIS patients	
	female	male	female	male
• 10	22(62.9%)	5(50%)	29(64.4%)	4(66.7%)
10-30	10(28.6%)	4(40%)	10(23.5%)	2(33.33%)
30-100	3(8.6%)	1(10%)	6(11.8%)	0(0%)
• 100	0(0%)	0(0%)	0(0%)	0(0%)
total	35	10	45	6

In Table 2, the mean parameters associated with Hashimoto's Thyroiditis parameters in the two groups of people in the study population are shown as mean ± SD Hashimoto's thyroiditis group and gender breakdown is given.

Table 2- Parameter mean population studied

Group	Gender	N	age	25(OH)D	Anti-TPO-Ab	FT4	TSH
Hashimoto's thyroiditis patients	Male	6	38.3(±17.65)	9.95(±7.95)	595.72(±620.95)	1.22(±0.26)	2.19(±1.08)
	Female	45	37.6(±12.36)	13.16(±12.57)	560.28(±714.67)	1.16(±0.21)	2.12(±1.29)
Control	Male	10	35.51(±15.94)	13.34(±12.71)	2.04 (±2.01)	1.15(±0.19)	2.14(±0.90)
	Female	35	34.00(±12.11)	11.90(±10.66)	4.14(±4.10)	1.11(±0.17)	2.26(±1.22)

DISCUSSION

In this study, serum vitamin D levels in patients with Hashimoto's Thyroiditis and control groups

In this study, with 6 months of duration 96 patients met inclusion criteria, out of 96 people, 51 subjects (54.8%) were Anti-TPO positive and had Hashimoto's thyroiditis. Out of 51 patients with Hashimoto's thyroiditis, 45 were women and 6 were men and out of 45 healthy subjects, 35 were females and 10 were males. Age range was between 4 to 66 years. In control group with Anti TPO negative, 35 were women and 10 were men. According to Tables 1 and 2, 46 people (88.24%) of Hashimoto's thyroiditis patients had some degree of vitamin D deficiency and insufficiency and 39 women and 6 men had Vit D deficiency.

Also subjects (91.12%) in the control group, had vitamin D deficiency which included 32 women and 9 men, respectively. Therefore, vitamin D deficiency was found both in patients and controls group. In none of the two groups, poisonous quantities of vitamin D level were reported

were measured and compared. Vit D deficiency was defined as 25 OH vit D levels <10ng/ml and vitamin D insufficiency was defined as 25 OH vit

D levels 10-30 ng/ml and normal 25 Oh vit D levels was 30-100 ng / ml. 62.5% of men and 65% of women had vit D deficiency and 31.25% of men and 75.23% of women had vit D insufficiency. 75.88% of women and 75.93% of men had inadequate serum levels of vit D, which may be related to factors such as sun exposure and dressing situation or differences of vit D production in both sexes. The results of this study showed that 91.12% of Hashimoto's Thyroiditis patients and 88.24% of healthy control group had some degree of vitamin D deficiency.

Of 51 patients with Hashimoto's Thyroiditis 29 females and 4 males (33 cases), had vitamin D deficiency and 10 females and 2 males (12 cases), only six women had sufficient serum levels of vit D.

In control group, 22 females and 5 males (total n = 27), had vitamin D deficiency and 10 women and 4 men (total 14) had insufficient level of vitamin D and 3 females and 1 male (total 4) had normal levels of 25 OH Vit D.

The study showed that in the prevalence of vitamin D deficiency in patients with Hashimoto's thyroiditis and control group there was not significant association between serum 25-hydroxyvitamin D and positive Anti-TPO- AB titers in individuals with Hashimoto's Thyroiditis. Based on the Pearson coefficient analysis there was no significant difference in serum Vit D levels between Hashimoto's thyroiditis patients and healthy controls. (12.79 ng/ml at equivalent 12.22 ng/ml).

Tamer et al. in a Case-Control study on the 161 patients with Hashimoto's Thyroiditis and 162 healthy control subjects concluded that 92% of people with Hashimoto's thyroiditis had insufficient levels of vitamin D which was more obvious than healthy people. (2)

Dr. Effraimidis et al. in a similar Case-Control study on serum vitamin D levels and its relationship with early stages of Hashimoto's Thyroiditis on 78 women aged 18-65 years 5 years Follow Up concluded that the serum level of 25-

hydroxy vitamin D was not associated with auto-immunity in Hashimoto's Thyroiditis. (3)

Dr. Gowsamiet al. study in India in 5 months, on 642 patients (16-60 Y) concluded that there was an inverse relationship between serum levels of 25-hydroxyvitamin D and Anti-TPO Ab titers in Hashimoto's thyroiditis patients. (14)

Dr. Mnsournia et al. studied the relationship of serum levels of 25 (OH) D in 41 Hashimoto's thyroiditis patients and compared it with 45 subjects in control group, which concluded that there was reverse relationship between serum 25 (OH) Vit D and Hashimoto's thyroiditis. They suggested that high values of serum 25(OH) Vit D is associated with reduced risk of. For every 5 ng/ml increase in the level of serum 25 (OH) D, there was 19% reduced risk for Hashimoto's thyroiditis. (15)

Doctor Buzkurt and colleagues study in Turkey in 2013 to recognize the relationship of vitamin D deficiency and Hashimoto's Thyroiditis on 180 patients with Hashimoto's thyroiditis treated with levothyroxine, 180 patients with Hashimoto's thyroiditis newly diagnosed and 180 healthy controls concluded that 25 (OH) D serum levels in Hashimoto's thyroiditis in patients was significantly lower than control group and the lower values of 25 (OH) Vit D was associated with disease duration and thyroid autoantibodies levels. (16)

In our study according to the vitamin D deficiency in Hashimoto's thyroiditis patients and control group, there is no correlation of Vit D deficiency in occurrence of Hashimoto's thyroiditis. Vitamin D deficiency has variable prevalence in different countries which there is not a clear strategy for Vit D deficiency prevention. (16)

CONCLUSION

According to the results of our study and low serum levels of vitamin D in Hashimoto's thyroiditis patients and control group, we cannot exactly accept or refuse the correlation of Vit D deficiency and occurrence of Hashimoto's thyroiditis. In Iranian population and although

according to other studies, there is a controversy in correlation of Vit D serum level and risk of Hashimoto's thyroiditis. But because of regulatory function of vit D in autoimmune processes and autoimmune nature of Hashimoto's thyroiditis, there is a need for larger studies. So we suggest first, long and seasonal sampling of Vit D serum levels to determine accurate Vit D status in different Populations, then confirm or refuse its correlation with autoimmune disease. Second, it needs a cohort study involving, larger population.

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