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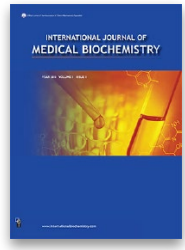

Research Article

Evaluation of vitamin D status and the relationship with thyroid disease

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Abstract

Objectives: Vitamin D is known to be an essential element for calcium metabolism and bone health. Recent studies have also identified vitamin D deficiency as a risk factor for cancers, autoimmune diseases, and cardiovascular disorders. The aim of this study was to investigate the relationship between vitamin D status and thyroid disease.

Methods: A total of 1197 adults aged 18-45 years were enrolled in this retrospective study. Data of serum levels of vitamin D, free triiodothyronine, free thyroxine, and thyroid-stimulating hormone were retrieved and analyzed. The individuals were divided into 3 groups: euthyroid state (n=940), hypothyroidism (n=206), and hyperthyroidism (n=51). The vitamin D status of the groups was compared.

Results: The study population had a mean serum vitamin D concentration of 18.33±14.53 ng/mL. The mean vitamin D level was 16.01±14.37 ng/mL in females (n=921) and 26.04±12.26 ng/mL in males (n=276) ($p<0.001$). The mean vitamin D level in the euthyroid, hypothyroidism, and hyperthyroidism groups was 8.79±15.04 ng/mL, 15.72±11.71 ng/mL, and 20.4±14.23 ng/mL, respectively. There was a statistically significant difference in the vitamin D level between the hyperthyroidism and hypothyroidism groups ($p<0.05$).

Conclusion: Vitamin D deficiency/insufficiency is an important public health problem in Turkey, especially in females. The hypothyroid patients had significantly lower vitamin D levels compared with the other groups. Vitamin D supplementation may be considered in the treatment of thyroid disease; however, additional prospective studies with a larger number of subjects are needed.

Keywords: Hyperthyroidism, hypothyroidism, thyroid disease, vitamin D, vitamin D deficiency

Vitamin D is recognized as an important, fat-soluble vitamin for calcium metabolism and bone health [1]. However, in recent years it has also been shown to have a variety of effects on extraskeletal health, including an influence on cell growth and cellular differentiation, maturation, proliferation, apoptosis, angiogenesis, etc. [2, 3]. Vitamin D deficiency is defined as a level of <20 ng/mL, and it is a global health problem [4]. Deficiency can cause bone diseases, including rickets in children and osteomalacia in adults, and it has also been associated with cancers, autoimmune diseases, cardiovascular disorders, respiratory illnesses, and infectious diseases [5, 6]. The vitamin D receptor (VDR) plays a significant role in modulation of the immune system, enhancing the innate immune response while exerting an inhibitory action on the adaptive immune system [7]. Several studies have demonstrated that there is a significant relationship between vitamin D and autoimmune diseases, such as insulin-dependent diabetes mellitus, rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, and inflammatory bowel disease [8]. Low vitamin D levels have been associated with autoimmune thyroid diseases (AITD), and an impaired vitamin D signal has been reported to promote the formation of thyroid cancers [9]. Vitamin D supplementation has been shown to decrease the prevalence of autoimmune diseases and provide benefi-

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cial effects against autoimmune diseases [10, 11]. The present study is an examination of the vitamin D level in young and middle-aged individuals and an analysis of the relationship between vitamin D status and thyroid hormone levels.

Materials and Methods

A total of 1197 adults, aged 18-45 years and who presented at Ahi Evran University Training and Research Hospital were enrolled in this retrospective study. Serum measurements of free triiodothyronine (FT3), free thyroxine (FT4), thyroid-stimulating hormone (TSH), 25-hydroxyvitamin D3 were assessed using an enzyme chemiluminescence immunoassay method with a commercially available kit (F. Hoffmann-La Roche Ltd., Basel, Switzerland) and an immunoassay autoanalyzer. The normal range of the tests were TSH: 0.27-4.2 mIU/mL; FT4: 0.93-1.7 ng/dL; FT3: 2.6-4.4 ng/L; and vitamin D >30 ng/mL. Laboratory test results were collected retrospectively from the hospital electronic information system.

The individuals were divided into 3 classic groups of euthyroid state, hypothyroidism, and hyperthyroidism. Hypothyroidism was defined as normal or decreased free hormone levels and a TSH value of >4.20 µIU/mL. Hyperthyroidism was defined as elevated or normal levels of FT4 and FT3, and a TSH level of <0.27 µIU/mL. Euthyroidism was defined as the absence of hypothyroidism or hyperthyroidism and within the normal range of thyroid hormones levels. The vitamin D status in the groups was compared. The vitamin D level in the overall study group was also evaluated. The study was performed in accordance with the Declaration of Helsinki Good Clinical Practice guidelines and was approved by the Ahi Evran University Ethical Committee (2017-10/92).

Statistical analysis

Continuous and categorical data were reported as mean±SD and percentages, respectively. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess normality. Kruskal-Wallis analysis of variance and the Mann-Whitney U test were used for independent group comparisons. For categorical variables, a chi-square test was used. Relationships between continuous variables were assessed using Spearman's rank correlation coefficient. All of the statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA) and a p value of <0.05 was considered statistically significant.

Table 1. Descriptive and laboratory characteristics of the study group

	Female (n=921)	Male (n=276)	Total (n=1197)	p
Age (years)	33.3±7.8	34.1±7.2	33.5±7.8	0.264
FT3 (ng/L)	3.2±1.02	3.39±0.48	3.25±0.9	<0.001
FT4 (ng/dL)	1.26±0.37	1.27±0.18	1.26±0.3	<0.001
TSH (mIU/L)	3.24±6.41	2.85±6.3	3.15±6.4	0.186
Vitamin D (ng/mL)	16.01±14.37	26.04±12.7	18.3±14.5	<0.001

p<0.05: Statistically significant. FT3: Free triiodothyronine; FT4: Free thyroxine; TSH: Thyroid-stimulating hormone.

Results

A total of 1197 subjects (77% female, 23% male) were enrolled in this study. The mean age was 33.5±7.8 years, and was similar in the female and male patients (Table 1). The study population had a mean serum vitamin D concentration of 18.33±14.53 ng/mL. The mean vitamin D level was 16.01±14.37 ng/mL in females (n=921) and 26.04±12.26 ng/mL in males (n=276) (p<0.001). The mean TSH, FT3, and FT4 levels of the study group were 3.15 (±6.4) mIU/mL, 3.25 (±0.9) ng/L, and 1.26 (±0.3) ng/dL, respectively. The FT3 and FT4 levels in the female patients were significantly lower than those of the males (p<0.001) (Table 1).

In all, 78.5% were classified as in the euthyroid group (n=940), 17.2% in the hypothyroidism group (n=206), and 4.3% in the hyperthyroidism group (n=51). The mean vitamin D level in the euthyroid, hypothyroidism, and hyperthyroidism groups was 18.79±15.04 ng/mL, 15.72±11.71 ng/mL, and 20.4±14.23 ng/mL, respectively (Fig. 1). There was a statistically significant difference between the hyperthyroidism and hypothyroidism groups (p=0.037) (Table 2).

The correlation analysis between vitamin D levels and serum thyroid hormone levels is shown in detail in Table 3. In the euthyroid group, there was a significant positive correlation with FT3 and FT4 and a negative correlation with TSH (Table 3) (p<0.05).

Table 2. Comparison of group characteristics according to thyroid hormone level

	Euthyroid (n=940; 78.5%)	Hypothyroidism (n=206; 17.2%)	Hyperthyroidism (n=51; 4.3%)	p
Female	711	164	46	0.034
Male	229	42	5	
Age (years)	33.5±7.8	33.3±7.8	33.9±7.5	0.843
Vitamin D (ng/mL)	18.7±15.0	15.7±11.7*	20.4±14.2*	0.037

p<0.05: Statistically significant. *Difference between hypothyroidism and hyperthyroidism: p<0.05.

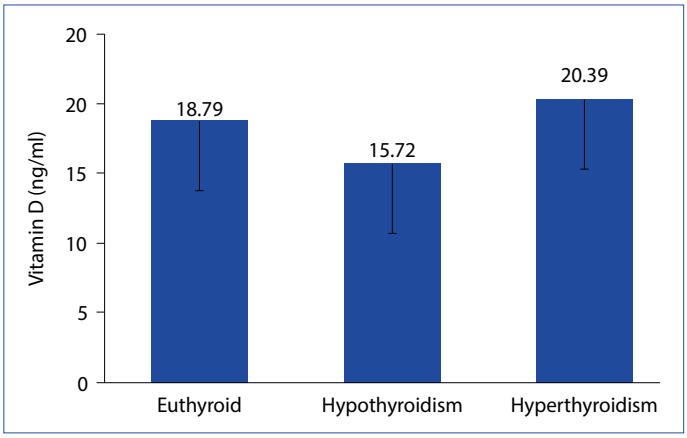

Figure 1. The mean vitamin D level by group.

Discussion

In the present study, we aimed to investigate the relationship between vitamin D status and thyroid hormones levels in a young and middle-aged Turkish population categorized as euthyroid, hypothyroidism, and hyperthyroidism. Our results demonstrated that 57.8% of the study population had vitamin D deficiency and 23.3% had insufficiency. An adequate vitamin D level is defined as >30 ng/mL, deficiency is defined as <20 ng/mL, and insufficiency is a value 21-29 ng/mL [12].

Vitamin D deficiency/insufficiency is an important health issue in our country. Hekimsoy et al. [13] reported that among adults in the Aegean region of Turkey, the mean serum vitamin D concentration was 16.9±13.09 ng/mL and 74.9% of the subjects had vitamin D deficiency. In another study performed by Solak et al. [14] in Konya, which is located in the Central Anatolia region of Turkey, the mean serum vitamin D level of all of the individuals included in the study was 15.2±8.8 ng/mL and 76.25% had vitamin D deficiency. In an another study performed by Erkan et al., [15] which included Turkish residents of Turkey and Turkish immigrants living in Germany, females had a higher prevalence of vitamin D deficiency than males. In this study, sex, limited exposure to sunlight, living at a higher latitude, and clothing style were found to be the most significant determinants for deficiency.

Consistent with other studies in the literature, a gender comparison in our study indicated that the female subjects mean vitamin D was significantly lower than that of the male subjects. Arasil et al. [16] demonstrated that the prevalence of vitamin D deficiency was approximately 80% in reproductive-age women and elderly women in Ankara, Turkey. Similarly, several other studies of the Turkish population have reported that vitamin D deficiency is more prevalent among females [14, 17, 18]. Personal factors, such as a clothing style that limits exposure to sunlight, more time spent indoors, and a greater body surface area in men may be sources of the difference.

Vitamin D deficiency has been associated with several autoimmune diseases, including AITD [19]. Gene polymorphism of the vitamin D receptor, vitamin D-binding protein, and 1α-hydroxylase may also predispose to the development of autoimmune thyroiditis [20, 21].

Bozkurt et al. [22] evaluated 25-hydroxyvitamin D status in subjects with Hashimoto's thyroiditis (HT) and healthy controls. They reported that the HT patients had significantly lower vitamin D values than the healthy controls and that low vitamin D levels were correlated with disease duration, thyroid volume, and antibody levels. In an another study performed by Yasuda et al. [23], vitamin D levels in female patients with newly onset Graves' disease (GD) were low and significantly associated with thyroid gland volume. Vitamin D mediates its effect on immune system cells, including monocytes, dendritic cells, and T and B lymphocytes, through binding to the VDR and regulating the proliferation and differentiation of immune cells [21]. Vitamin D deficiency is prevalent in AITD patients, but the association between vitamin D level and thyroid disease is still not clear. Due to the influence on the immune system it is possible that vitamin D deficiency may be a cause or a consequence of thyroid disease [24, 25].

In our study groups, the vitamin D levels were lower in the hypothyroid patients than in the other 2 groups, and significantly lower compared with the hyperthyroid patients. Similarly, Mackawy et al. [26] compared the vitamin D level of hypothyroid patients and healthy controls and found that the vitamin D levels were significantly lower in hypothyroid patients compared with the controls (14.79±2.11 ng/mL and 44.53±14.91 ng/mL, respectively). The study also reported that the deficiency of vitamin D in hypothyroid patients was significantly associated with the degree and severity of thyroid disease. Ke et al. [27] evaluated the serum vitamin D levels in AITD patients with overt hyperthyroidism GD, HT with normal thyroid function, and control subjects. The findings indicated that the HT patients had significantly lower vitamin D levels

Table 3. Correlation of serum vitamin D and thyroid hormone level by group

	Vitamin D (Euthyroid)		Vitamin D (Hypothyroidism)		Vitamin D (Hyperthyroidism)	
	r	P	r	P	r	P
FT3 (ng/L)	0.100	0.002	0.074	0.292	0.131	0.361
FT4 (ng/dL)	0.104	0.001	0.118	0.090	0.089	0.537
TSH (mIU/L)	-0.066	0.042	-0.012	0.869	-0.016	0.911

P<0.05: Statistically significant. FT3: Free triiodothyronine; FT4: Free thyroxine; TSH: Thyroid-stimulating hormone.

compared with the GD patients and control subjects. The presence of vitamin D deficiency was significantly different (>55%; p<0.001) in HT patients compared with the controls (24.1%) and GD patients (22.9%). The authors concluded that thyroid hormone levels may indirectly affect vitamin D status in AITD.

In our study, vitamin D had a significant negative correlation with serum TSH and a significant positive correlation with FT3 and FT4 in the euthyroid group (p<0.05), but there was no correlation in the other groups. Zhang et al. [28] reported that TSH levels were inversely correlated with vitamin D levels independent of thyroid hormone levels in a study of a population-based health survey of middle-aged and elderly individuals. Mackawy et al. [26] and Sinha et al. [29] reported that there was a significant positive correlation between the serum level of vitamin D and thyroid hormones and a significant negative correlation with TSH levels in hypothyroid patients. They concluded that there may be a significant association between vitamin D deficiency and hypothyroidism. However, the findings of other research did not indicate any correlation between vitamin D level and thyroid function [22, 28].

Several studies recommend vitamin D supplementation for AITD patients, but it is still a controversial issue. Talaei et al. [11] demonstrated that vitamin D supplementation in hypothyroid patients for 12 weeks improved serum TSH levels and calcium concentrations compared with a placebo. In another study by Simsek et al. [30] reported a significant reduction in antibody titers in GD and HT patients after vitamin D replacement. Vitamin D is an inexpensive compound that is easy to intake, and administration may improve AITD symptoms and progression; however, there are few clinical studies on vitamin D supplementation in AITD patients and supplementation may lead to hypercalcemia [24,31]. Consequently, further research is needed to confirm the role of vitamin D in AITD pathogenesis before beginning vitamin D supplementation.

Limitations

A retrospective design and limited recorded information are the primary limitations of this study. In addition, TSH receptor-stimulating antibodies, thyroid peroxidase antibodies, and thyroglobulin antibodies were not measured. We also couldn't assess other factors that may affect the 25-hydroxyvitamin D level, such as seasonal change, lack of sun exposure, malnutrition, skin color, sunscreen use, covered clothing, obesity, dietary habits, and vitamin D supplementation history.

Conclusion

In conclusion, vitamin D deficiency is an important public health problem. The vitamin D levels in patients with hypothyroidism were lower than those of the other groups. There may also be a relationship between vitamin D deficiency and the progression of hypothyroidism. Vitamin D supplementation may be considered in treatment of thyroid disease, but additional prospective studies with a larger number of subjects are needed.

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Conflict of interest: There is no conflict of interest between the authors.

Ethics Committee Approval: Ahi Evran University Ethical Committee (2017-10/92).

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Authorship contributions: Concept – R.N., E.A.; Design – R.N., E.A.; Supervision – R.N.; Data collection &/or processing – R.N.; Analysis and/or interpretation – R.N., E.A.; Literature search – R.N.; Writing – R.N.; Critical review – R.N., E.A.

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