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Research Article

Vitamin D Levels and Inflammatory Markers in Patients with Active Graves Disease and a Possible Role of Vitamin D for Ophtalmopathy

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Abstract

Objectives: This study investigated the role of vitamin D in Graves' disease and autoimmune thyroid disease and examined the relationship between vitamin D levels and thyroid ophthalmopathy, inflammation, body mass, and thyroid autoantibodies.

Methods: The study included 80 participants: 40 active Graves' disease patients before treatment, 20 patients with euthyroid autoimmune thyroid disease, and 20 healthy individuals. All Graves' disease patients were evaluated for ophthalmopathy. Measurements included 25(OH)D, high-sensitivity CRP, erythrocyte sedimentation rate, fibrinogen, and anthropometric assessments. Thyroid function tests and autoantibodies were evaluated in the autoimmune thyroid disease group.

Results: Vitamin D levels were significantly lower in Graves' disease and autoimmune thyroid disorder patients compared to healthy controls. Lower vitamin D correlated with higher thyroid receptor and anti-thyroid peroxidase antibodies. Patients with thyroid ophthalmopathy had even lower vitamin D levels. Vitamin D deficiency was associated with inflammation and higher body mass index.

Conclusion: Lower vitamin D levels were linked to Graves' disease, autoimmune thyroid disorders, and thyroid ophthalmopathy. Vitamin D deficiency was also associated with increased inflammation in these conditions, suggesting a potential role for vitamin D in the pathogenesis of autoimmune thyroid disorders, particularly thyroid ophthalmopathy.

Keywords: Autoimmune thyroid disease, Graves disease, inflammation, ophthalmopathy, vitamin D

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Autoimmune thyroid disorders include Graves disease (GD), Hashimoto thyroiditis, and postpartum thyroiditis. The major pathogenesis in Graves disease is TSH receptor antibodies (TRAb) acting against the TSH receptor (TSHR), similar to TSH.[1–3] Diffuse goiter and thyrotoxicosis occur due to autoimmune stimulation of the thyroid gland. Besides, retroorbital and dermal infiltrations lead to other characteristics of the disease, which are ophthalmopathy and dermatopathy.[4,5]

Graves disease is the most common cause of hyperthyroidism.[6] Graves ophthalmopathy is also observed in almost half of the patients.[7] Preferred treatment alternatives for Graves disease are antithyroid treatment, radioactive io-

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dine (RAI), and/or surgery. However, these treatments do not target the pathogenesis but only provide symptomatic cure. Mostly, permanent remission is not achieved after long-term therapies.[8]

The main function of vitamin D is the absorption of calcium and phosphate and maintenance of body calcium/phosphate balance along with PTH. It is well proven that, besides calcium and phosphate metabolism, vitamin D has many effects on growth and development, such as cell differentiation, brain development, and the immune system. Vitamin D deficiency is implicated in rickets and osteomalacia, as well as multiple sclerosis, type 1 diabetes, several cancers, immune system disorders, and a tendency toward infectious diseases.[9] The discovery of vitamin D receptors (VDR) in many tissues led to additional studies beyond calcium and phosphate metabolism. Identification of VDRs on almost all immune system cells, mainly on active T and B lymphocytes and antigen-presenting cells such as activated macrophages and dendritic cells, suggested its role in immune regulation.[10]

After the discovery of the relationship between vitamin D, immune function, and autoimmune disorders, its association with autoimmune thyroid disorders has also been taken into consideration.[11] In animal models, if cyclosporin was given with vitamin D supplements for the treatment of autoimmune thyroid disorder, disease remission was accelerated. Also, in a study on mice, subjects with vitamin D deficiency had a tendency toward thyrotoxicosis.[12] In studies on humans, vitamin D levels in Graves patients were significantly lower than in control groups.[13] In various studies, vitamin D levels have been found to be associated with obesity, inflammation, and thyroid function tests.[13]

In this study, we aimed to evaluate the role of vitamin D in the activation of Graves disease and the pathogenesis of autoimmune thyroid disorders. Besides, we planned to investigate whether a significant alteration existed in inflammatory markers with Graves disease activation or autoimmune thyroid disorder and also the possible relation of inflammatory markers and thyroid ophthalmopathy with vitamin D.

Methods

Study Design and Participants

The study consisted of three groups, the first of which included 40 active Graves patients; the second, 20 euthyroid patients with autoimmune thyroid disease (ATD); and the third, 20 healthy controls. In all groups, patients had similar age and gender characteristics. In the Graves group, newly diagnosed Graves patients who had thyrotoxicosis and TRAb positivity or remitted Graves patients who were reactivated and had thyrotoxicosis were included before starting antithyroid treatment. The autoimmune thyroid disease group included patients who were under follow-up and euthyroid while using L-thyroxin treatment. The control group consisted of healthy volunteers who did not have a goiter on physical examination and were euthyroid.

Clinical Assessments

Body weight, height, and waist measurements were taken, and body mass index (BMI) was calculated according to the body weight (kg)/height (m^2) formula for all patients. All patients admitted with active Graves disease were evaluated for ophthalmopathy by ophthalmological examination and orbital MRI if required. According to the findings, patients with Graves disease were classified as with and without ophthalmopathy. None of the euthyroid patients with autoimmune thyroid disease or the control group had ophthalmopathy.

Laboratory Measurements

Blood tests were performed after at least 8 hours of fasting. In all patients, 25(OH)D, serum calcium, phosphate, total alkaline phosphatase (ALP), parathormone, albumin, as well as inflammatory markers, including high-sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), and fibrinogen levels, were measured. Serum calcium, phosphorus, albumin, and parathormone (PTH) levels were also studied since the levels might be affected by vitamin D. Serum calcium levels were corrected according to serum albumin levels.

In the active Graves group, TSH receptor antibody (TRAb), anti-thyroid peroxidase antibody (anti-TPO), anti-thyroglobulin antibody (anti-Tg), free T3 (FT3), free T4 (FT4), and TSH levels were recorded. In the autoimmune thyroid disease group and the control group, anti-TPO, anti-Tg, FT3, FT4, and TSH levels were also measured. In all patients, 24-hour urine was collected, and urinary calcium excretion was calculated.

Patients were included in the study during fall and winter in order to exclude seasonal effects on vitamin D measurements. Patients using drugs that may affect vitamin D levels, those who have diseases related to calcium, phosphate, or bone metabolism, renal or hepatic failure, or chronic inflammatory conditions were not included in the study.

To measure 25(OH)D levels, blood was centrifuged for 10 minutes at 3000 rpm, and sera were separated, stored, and frozen at -20°C until analysis. 25(OH)D was measured by the ELISA method using immunodiagnostic kits with a Biotech Microplate (Biotech ELx 800, USA) analyzer.

Ethical Approval

This study was undertaken at Eskisehir Osmangazi University Medical Faculty, Department of Endocrinology and Metabolism, and the study was evaluated and approved by the Eskisehir Osmangazi University Medical Faculty Ethical Committee (29.06.2015, No: 80558721/207). Written informed consent was obtained from each participant.

Statistical Analysis

Statistical analysis of the variables was performed using SPSS 21.0. Categorical measures were presented as numbers and percentages; numerical outcomes as mean and standard deviation. The chi-square test was used for comparison of categorical variables between groups. Distribution of numerical variables was evaluated with the Kolmogorov–Smirnov test.

If assumptions were met, independent t-tests were used for between-group comparisons of numerical values (patient–control, vitamin D deficiency +/–, etc.); otherwise, the Mann–Whitney U test was used. For comparisons of numerical values between more than two groups, one-way analysis of variance was used if assumptions were met; otherwise, the Kruskal–Wallis test was applied.

For significant cases, dual subgroup comparisons were performed using relevant post hoc tests (Scheffé, Bonferroni, Tamhane, etc.) or Bonferroni-corrected Mann–Whitney U tests. Correlations between numerical variables were assessed using Spearman correlation coefficients. In all tests, statistical significance was accepted as $p<0.05$, $p<0.01$, or $p<0.001$.

Results

Biochemical and Anthropometric Parameters

Serum phosphate levels of the patients with active Graves disease were significantly lower than those of healthy subjects ($p=0.026$). Serum corrected calcium, total alkaline phosphatase, parathormone, 24-hour urinary calcium excretion level, and inflammatory parameters, including ESR, hsCRP, and fibrinogen levels, did not differ significantly between the groups. BMI and waist circumference of the patients with active Graves disease were significantly lower than those of patients with autoimmune thyroid disease and the healthy group ($p=0.024$, $p<0.001$, respectively) (Table 1).

Serum 25(OH)D Levels in Study Groups

The mean 25(OH)D levels were found to be 13.56 ng/ml in patients with active Graves disease, 13.26 ng/ml in patients with autoimmune thyroid disease, and 22.09 ng/ml in the healthy control group. Serum 25(OH)D levels of the patients with active Graves disease and those with autoimmune thyroid disorders were significantly lower than those of the healthy group ($p=0.03$) (Table 1–3, Fig. 1).

In our study, 30 of 40 active Graves disease patients (75%), 17 of 20 autoimmune thyroid disease patients (85%), and 10 of 20 individuals in the healthy control group (50%) had 25(OH)D levels below 20 ng/ml and had severe vitamin D deficiency. Moreover, when 30 ng/ml was selected as the lower limit for 25(OH)D level, 39 of 40 active Graves disease patients (97.5%), 19 of 20 autoimmune thyroid disease patients (75%), and 5 of 20 individuals in the healthy group

Table 1. Anthropometric measurements and biochemical parameters of the study groups

Parameter	Active graves (n=40)	ATD (n=20)	Healthy control (n=20)	p	Significant comparisons
25(OH)D (ng/mL)	13.50±7.77	13.26±7.98	22.09±16.54	0.030*	1 vs. 3, 2 vs. 3
Calcium (mg/dL)	9.35±0.43	9.49±0.43	9.43 ± 0.35	0.263	–
Phosphorus (mg/dL)	3.13±0.69	3.43±0.60	3.59±0.55	0.026*	1 vs. 3
ALP (U/L)	74.45±34.26	72.70±31.40	64.65±27.27	0.399	–
PTH (pg/mL)	49.42±17.85	51.85±17.50	49.40±14.62	0.635	–
ESR (mm/h)	6.75±3.84	4.80±4.34	7.55±6.30	0.135	–
hsCRP (mg/dL)	3.19±2.65	2.45±1.98	3.60±2.23	0.232	–
Fibrinogen (mg/dL)	301.70±33.58	286.75±43.10	294.25±36.02	0.414	–
Urinary Calcium (mg/day)	110.32±63.70	107.50±48.90	132.80±78.02	0.720	–
BMI (kg/m^2)	25.67±4.05	28.45±3.48	27.70±4.05	0.024*	1 vs. 2, 1 vs. 3
Waist Circumference (cm)	92.15±13.32	103.75±11.80	105.20±8.09	0.001***	1 vs. 2, 1 vs. 3

Data are presented as mean ± standard deviation. ATD: Autoimmune thyroid disease; ALP: Alkaline phosphatase; PTH: Parathormone; ESR: Erythrocyte sedimentation rate; hsCRP: High-sensitivity C-reactive protein; BMI: Body mass index. *p<0.05, **p<0.01, ***p<0.001 indicate statistical significance. Group comparisons: 1 = Active graves, 2 = ATD, 3 = Healthy control.

Table 2. Comparison of parameters between graves patients with 25(OH)D Levels ≤ 20 ng/mL and > 20 ng/mL

Parameter	25(OH)D ≤ 20 ng/mL	25(OH)D > 20 ng/mL	p
Phosphorus (mg/dL)	3.14±0.61	3.77±0.54	<0.001***
ALP (U/L)	79.82±32.87	51.08±16.38	<0.001***
PTH (pg/mL)	53.17±17.40	42.21±12.55	0.008**
ESR (mm/h)	6.59±4.66	6.13±4.99	0.693
hsCRP (mg/dL)	3.20±2.61	2.86±1.81	0.574
Fibrinogen (mg/dL)	294.35±37.66	300.43±35.09	0.507
Urinary Calcium (mg/day)	92.35±44.27	171.95±72.02	<0.001***
TRAb (U/L)	11.92±12.30	2.94±1.21	0.028**

Data are presented as mean ± standard deviation. ALP: Alkaline phosphatase; PTH: Parathormone; ESR: Erythrocyte sedimentation rate; U Calcium: Urinary calcium; TRAb: Thyroid-stimulating hormone receptor antibody; Phos: Serum phosphorus. *p<0.05, **p<0.01, ***p<0.001 indicate statistical significance.

Table 3. Correlations between 25(OH)D levels and biochemical parameters in active graves patients

Parameter	r	p
Calcium (mg/dL)	0.565	<0.001***
Phosphorus (mg/dL)	0.551	<0.001***
ALP (U/L)	–0.669	<0.001***
PTH (pg/mL)	–0.648	<0.001***
ESR (mm/h)	–0.402	0.010*
hsCRP (mg/dL)	–0.502	<0.001***
Urinary Calcium (mg/day)	0.658	<0.001***
TRAb (U/L)	–0.363	0.021*

r: Pearson correlation coefficient. ALP: Alkaline phosphatase; PTH: Parathormone; ESR: Erythrocyte sedimentation rate; U Calcium: Urinary calcium; TRAb: Thyroid-stimulating hormone receptor antibody. *p<0.05, **p<0.01, ***p<0.001 indicate statistical significance.

(25%) had 25(OH)D levels below 30 ng/ml and had insufficient vitamin D levels. The ratio of the patients with vitamin D levels below 20 ng/ml and 30 ng/ml to the total number of patients in the groups is shown in Figure 2.

Vitamin D Levels and Thyroid Ophthalmopathy

Among Graves disease patients, 21 patients had thyroid ophthalmopathy, and 19 did not have thyroid ophthalmopathy. The mean 25(OH)D level was 10.66 ng/ml in patients with thyroid ophthalmopathy and 16.64 ng/ml in patients without thyroid ophthalmopathy. 25(OH)D levels of the Graves disease patients with ophthalmopathy were significantly lower than those of the Graves disease patients without ophthalmopathy (p=0.016) (Fig. 3). Serum TRAb levels were also significantly higher in patients with

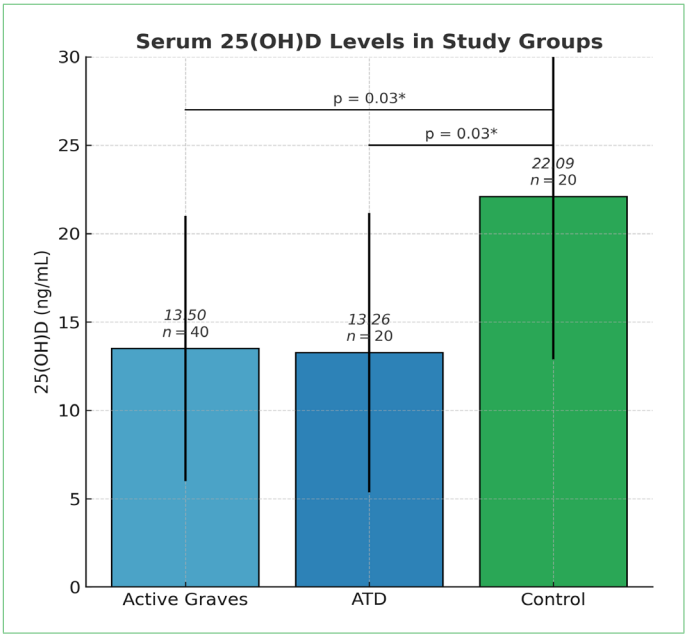

Figure 1. 25(OH)D levels in active Graves disease (n=40, 13.50±7.7 ng/ml), autoimmune thyroid disease (n=20, 13.26±7.9 ng/ml), and the control group (n=20, 22.09±16.5 ng/ml, p=0.03).

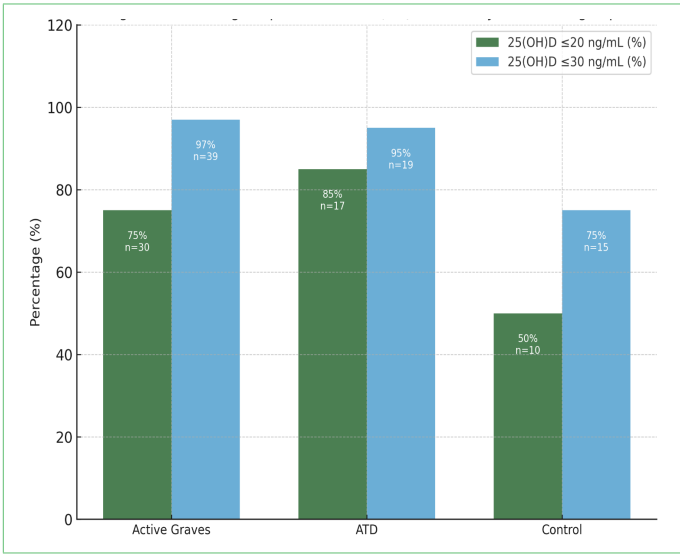

Figure 2. Percentage of 25(OH)D level less than or equal to 20 ng/ml and 30 mg/dl in active Graves disease [(n=40, n=30(≤20 ng/ml), n=39 (≤30 ng/ml)], autoimmune thyroid disease (ATD) [(n=20, n=17(≤20 ng/ml), n=19 (≤30 ng/ml)] and the control group [(n =20, n=10(≤20 ng/ml), n=15(≤30 ng/ml), p<0.05].

Graves disease who had 25(OH)D levels ≤20 ng/ml compared to Graves patients with 25(OH)D levels >20 ng/ml (11.92±12.30 vs. 2.94±1.21, p=0.028).

Correlation Analyses in Graves' Disease

In patients with Graves disease, 25(OH)D levels correlated positively with serum calcium (r=0.565, p<0.001), uri-

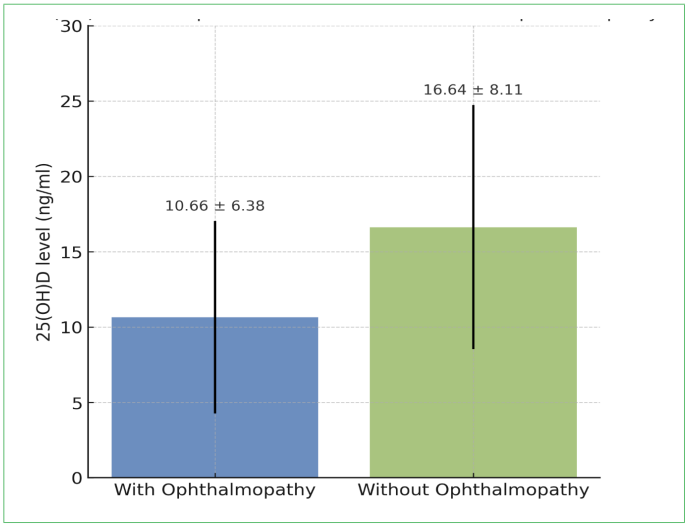

Figure 3. 25(OH)D levels in patients with Graves ophtalmopathy (n=21, 10.66±6.38 ng/ml), and without ophthalmopathy (n=19, 16.64±8.11 ng/ml, p=0.016).

nary calcium (r=0.363, p=0.021), and serum phosphorus (r=0.551, p<0.001) levels. There was also a significant negative correlation between 25(OH)D levels and serum total ALP (r=-0.669, p<0.001), PTH (r=-0.648, p<0.001), ESR (r=-0.402, p=0.01), hsCRP (r=-0.502, p<0.001), and TRAb (r=-0.363, p=0.021) levels. In all patients, including those with autoimmune thyroid disease and Graves disease, 25(OH)D levels also correlated negatively with anti-TPO levels (r=-0.310, p=0.016).

Discussion

The prevalence of vitamin D deficiency is globally rising, and it is becoming an important health problem. Many ecological factors, such as seasonal change, local climate, characteristics of the atmosphere and altitude, and lifestyle features including clothing, diet, and exposure to sunlight, all affect plasma vitamin D levels.[14,15]

In recent years, it has been shown that vitamin D has not only effects on calcium, bone, and mineral metabolism but also on many other organ systems. Vitamin D has been implicated in cardiovascular function and blood pressure, innate and adaptive immunity, insulin secretion, occurrence of metabolic syndrome and diabetes, muscle function and strength, production of cancer cells, and counteraction of infectious diseases. Vitamin D deficiency has been associated with many diseases that have an autoimmune pathogenesis.[16] This relationship between autoimmune disorders and vitamin D deficiency has led to studies in autoimmune thyroid disorders, and many researchers have found associations that might be valuable in shedding light on the pathogenesis.[17–21]

In our study, we found that vitamin D levels of patients with active Graves disease and those with autoimmune thyroid disease were lower than those of healthy controls. Also, more patients with Graves disease and autoimmune thyroid disorders had vitamin D levels below 20 ng/ml and below 30 ng/ml compared to the healthy group. However, there was no significant difference between active Graves disease patients and autoimmune thyroid disease patients regarding vitamin D levels. This shows that vitamin D may play a role in the emergence of thyroid autoimmunity.

However, low levels of vitamin D do not seem to be as operative in the activation of Graves disease, since the achievement of the euthyroid state does not alter its serum levels. Besides, it may be the consequence of not testing and replacing vitamin D after the onset of autoimmune thyroid disease as a routine practice. We, like previous studies, found that vitamin D deficiency might be a risk factor for autoimmune thyroid disorders. Meanwhile, since no difference was found between vitamin D levels of the active Graves group and the autoimmune thyroid group, it may suggest that vitamin D deficiency generally leads to autoimmune pathologies and that its unique role in Graves pathogenesis is less apparent.

Supporting the role of vitamin D deficiency in the development of autoimmune thyroid disease, the induction of experimental thyroiditis was shown to be prevented by the administration of active vitamin D.[1] In another study conducted on animals, vitamin D-deficient mice were found to be more susceptible to resistant hyperthyroidism after induction with TSH receptor antibody compared to mice replaced with adequate vitamin D.[2] In human studies, abnormal thyroid function tests and thyroid antibody titers were found to be more prevalent in patients with deficient vitamin D levels.[3] There are data showing polymorphism in the VDR gene to play a role in Graves pathogenesis.[18]

In a study, vitamin D levels of newly diagnosed Graves disease patients and patients with Hashimoto thyroiditis and postpartum thyroiditis, all of which are considered autoimmune thyroid disorders, were found to be lower than those of the control group.[19] There are also studies showing no difference in 25(OH)D levels between anti-TPO antibody-positive and negative subjects.[4] However, overall data about thyroid autoimmunity and vitamin D suggest a link between the two, and our findings support this evidence.

In our study, waist circumference and BMI were lower in patients with active Graves disease. These findings may be related to the weight loss experienced by Graves disease patients during the activation phase of the disease. Also, serum phosphorus levels were significantly lower in pa-

tients with Graves disease compared to both the autoimmune thyroid disease group and the healthy control group. Although the reason for this finding is not apparently clear, it may be related to the phosphaturic effect of PTH increase secondary to low vitamin D levels or the high rates of bone turnover seen in hyperthyroid patients.

When patients with vitamin D deficiency (25(OH)D <20 ng/ml) were compared to patients with 25(OH)D levels >20 ng/ml, serum phosphorus level and urinary calcium excretion rates were significantly lower, and total alkaline phosphatase and PTH levels were significantly higher in patients with deficient vitamin D levels. There was also a positive correlation between 25(OH)D levels and serum calcium, phosphate, and urinary calcium excretion, and a negative correlation between 25(OH)D levels and total alkaline phosphatase and PTH levels. These findings reflect the secondary effects of vitamin D deficiency.

Another important result obtained from this study was that the TRAb levels of patients with Graves disease and vitamin D deficiency were significantly higher compared to those of Graves disease patients with relatively higher vitamin D levels. In accordance with these findings, 25(OH)D levels correlated negatively with TRAb levels and also with inflammatory markers hsCRP and ESR. Also, anti-TPO levels correlated with 25(OH)D levels in all patients with autoimmune thyroid disease. This is an important finding that suggests a role of vitamin D in the emergence of thyroid antibodies. These findings also indicate that low vitamin D levels may induce low-grade inflammation seen in autoimmune thyroid disorders.

In a study, the adaptive immune response developed by dendritic cells stimulated by endogenous antigens such as TSH receptor peptide was shown to have a preventive role in the pathogenesis of Graves disease.[22,23] IL-4 rise due to an increase in T helper 2 activity is a mechanism effective in the pathogenesis of Graves disease. However, in Hashimoto thyroiditis, IFN-γ rise due to T helper 1 activity is observed. Moreover, T helper 17 and IL-17 were shown to have a role in autoimmune thyroid disorder development. Vitamin D is closely related to T helper 1, T helper 2, and T helper 17 levels and IL-4, IFN-γ, and IL-17 levels. Therefore, it is possible that vitamin D deficiency might have a role in the pathogenesis of autoimmune thyroid disorders, including Graves disease.[24]

In a previous study, it was shown that vitamin D levels of TRAb-positive Graves patients were significantly lower than those of TRAb-negative patients. In that study, no significant relation was found between vitamin D levels and thyroid antibodies anti-TPO and anti-thyroglobulin levels.[25] Ünal et al.[26] showed a negative correlation between vitamin D levels and anti-TPO and anti-thyroglobulin levels in a study conducted on newly diagnosed autoimmune thyroid disease patients, including newly diagnosed Graves disease patients.

In our study, in patients with Graves disease activation, a significant negative correlation was found between vitamin D and TRAb levels. Identification of a negative correlation between vitamin D and TRAb levels may indicate that vitamin D deficiency has a role in immune activation.

Another interesting finding of our study was that 25(OH) D levels of Graves disease patients with ophthalmopathy were significantly lower compared to those without ophthalmopathy. To the best of our knowledge, this is the first study to show the relationship between Graves ophthalmopathy, TSH receptor antibodies, and vitamin D deficiency. Main risk factors for ophthalmopathy are suggested to be smoking, male gender, and exposure to radioiodine in Graves disease patients. TSH receptor antibody levels are also valuable in predicting the course of the disease. Our findings suggest that vitamin D deficiency might be listed among the risk factors for ophthalmopathy. Since our study includes a small number of Graves disease patients with ophthalmopathy, larger studies are required to test our hypothesis.

In a study, Mellenthin et al.[27] observed a relationship between vitamin D levels and inflammatory parameters. Correlation was investigated between vitamin D, hsCRP, fibrinogen, and total leukocyte count. A negative correlation was observed between vitamin D and hsCRP and fibrinogen. In our study, ESR and hsCRP levels were higher in patients with vitamin D levels ≤20 ng/ml than in patients with vitamin D levels >20 ng/ml. Moreover, in the active Graves disease group, there was a negative correlation between vitamin D and ESR and hsCRP. Also, in our study, patients with vitamin D deficiency can be considered to have a tendency toward inflammation. However, there were additional factors that might have a relationship with inflammatory markers, such as Graves disease activation and thyroid ophthalmopathy. For more reliable results, advanced studies are required that specifically target the relationship between vitamin D and inflammation.

There are some limitations to our study that should be acknowledged. First, the relatively small number of patients may limit the generalizability of our findings, and the results should therefore be interpreted with caution. Nevertheless, the study carries clinical value, as it specifically included patients with Graves' disease during the activation period and prior to the initiation of any antithyroid medication, thereby minimizing the potential confounding effects of treatment on vitamin D status and inflammatory mark-

ers. In addition, the cross-sectional design of the study precludes causal inferences; longitudinal studies would be required to establish a definitive relationship between vitamin D deficiency and the pathogenesis of Graves' disease or ophthalmopathy. Despite these limitations, the results provide important preliminary insights and may serve as a basis for future larger-scale, prospective studies.

Conclusion

In conclusion, our study suggests that vitamin D deficiency is associated with an increased tendency toward systemic inflammation and may play an important role in the pathogenesis of Graves' disease and other autoimmune thyroid disorders. Furthermore, vitamin D deficiency might also contribute to the development and severity of Graves' ophthalmopathy, as indicated by its correlation with both inflammatory markers and higher TRAb levels in affected patients. These findings highlight the possibility that vitamin D status could be an important, yet often overlooked, factor influencing both disease activity and clinical outcomes in patients with autoimmune thyroid disorders. From a clinical perspective, assessment and correction of vitamin D deficiency may represent a simple and cost-effective strategy that could potentially improve disease management and reduce the risk of ophthalmopathy progression. Future research should further clarify the mechanistic role of vitamin D in thyroid autoimmunity and investigate whether vitamin D supplementation, either alone or in combination with standard antithyroid therapy, can provide therapeutic benefits. Longitudinal and interventional studies are warranted to determine whether maintaining adequate vitamin D levels could help prevent disease recurrence, modulate inflammatory activity, and improve quality of life in patients with Graves' disease.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethical Committee of Eskisehir Osmangazi University with an approval date and number of (29.06.2015, No:80558721/207).

Informed Consent: Written consent was obtained from all participants.

Conflict of Interest: The authors have no conflicts of interest to declare.

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