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KLİNİK ARAŞTIRMA

Evaluation of the frequency of vitamin D deficiency and its relationship with disease involvement in patients with systemic sclerosis

Sklerodermalı hastalarda D vitamini eksikliğinin sıklığı ve hastalık tutulumları ile ilişkisinin değerlendirilmesi

Kezban Armagan Alpturker[1], Ozgul Soysal Gunduz[2]
[1]Mengucek Gazi Training and Research Hospital, Departments Of Rheumatology, Erzincan, Turkey
[2]Celal Bayar University Hospital, Department of Internal Medicine, Division of Rheumatology, Manisa, Turkey

Correspondence: Kezban Armagan Alpturker
Mengucek Gazi Training and Research Hospital, Departments Of Rheumatology, Erzincan, Turkey
e-mail: kezban887@gmail.com

ORCID ID:
KAA 0000-0001-7380-6097
OSG 0000-0002-8149-9311

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SUMMARY

Aim: Systemic sclerosis is a chronic autoimmune disease characterized by vasculopathy, visceral and cutaneous fibrosis. Vitamin D has various functions in the immunological system and different studies have shown a potential role in triggering autoimmune diseases. Patients with systemic sclerosis may present with low serum vitamin D levels, but the relationship between low vitamin D levels and disease and clinical manifestations is still unclear. Our aim is to determine the frequency of vitamin D deficiency in patients with scleroderma and to analyze the relationship between vitamin D concentration and organ involvement in systemic sclerosis.

Material and Methods: This study retrospectively scanned the files of 54 patients with systemic sclerosis and compared them with the control group. Serum levels of 25-hydroxyvitamin D were measured and the two groups and systemic sclerosis subgroups were compared. Systemic sclerosis subgroups were also analyzed for organ involvement.

Results: Fifty-four systemic sclerosis patients (49 females, mean age 53.25±10.77 years, and the median disease duration 8 (1-25) years) and 50 controls (45 females, mean age 51.02±9.14 years) were included. In the systemic sclerosis group, seven patients (12.9%) had severe vitamin D deficiency (<5 ng/ml) and 46 patients (85.1%) had vitamin D deficiency (20-5 ng/ml), while optimal vitamin D level was not found. There was a significant decrease in vitamin D in the patient group compared to the healthy control (p=0.001). There was no significant difference in the analysis of systemic sclerosis subgroups except for pulmonary involvement (p=0.019) and DLCO (p=0.023). The correlation between 25-hydroxyvitamin D concentration and age, acute phase reactants, autoantibody profile, degree of skin involvement, disease activity and respiratory tests, and vitamin D was not found.

Conclusion: Serum vitamin D concentrations of patients with systemic sclerosis were significantly lower than healthy controls. There was no significant correlation between skin involvement, disease activity, and 25-hydroxyvitamin D level.

Keywords: 25-hydroxyvitamin D, pulmonary involvement, skin involvement, systemic sclerosis

ÖZET

Amaç: Sistemik skleroz, vaskülopati, visseral ve kutanöz fibrozis ile karakterize kronik otoimmün bir hastalıktır. D vitamininin immünolojik sistemde çeşitli işlevleri vardır ve farklı çalışmalar otoimmün hastalıkları tetiklemede potansiyel bir rolü olduğunu göstermiştir. Sistemik sklerozlu hastalar düşük serum D vitamini seviyeleri ile başvurabilirler, ancak vitamin D düşüklüğü ile hastalık ve klinik belirti arasındaki ilişki hala belirsizdir. Amacımız, sklerodermalı hastalarda D vitamini eksikliğinin sıklığını belirlemek ve D vitamini konsantrasyonu ile sistemik sklerozun organ tutulumu ile arasındaki ilişkileri analiz etmektir.

Materyal ve Metotlar: Bu çalışmada retrospektif olarak 54 Sistemik skleroz tanılı hastanın dosyası tarandı. Kontrol grubu olarak da metabolik kemik hastalığı ve romatolojik öyküsü bulunmayan 50 sağlıklı gönüllü alındı. D vitamini durumu, 25-hidroksivitamin D serum seviyeleri ölçülerek değerlendirildi. Skleroderma hastaları alt grupları ve organ tutulumu açısından veriler analiz edildi.

Bulgular: Elli dört sistemik skleroz hastası (49 kadın, ortalama yaş 53,25±10,77 yıl ve hastalık süresi 8 (1-25) yıl) ve 50 kontrol (45 kadın, ortalama yaş 51,02±9,14 yıl) dahil edildi. Sistemik skleroz grubunda ortalama D vitamini düzeyi 11,35±4,09 ng/dL idi. Yedi hastada (%12,9) ağır D vitamini eksikliği (<5 ng/ml) ve 46 hastada (%85,1) D vitamini eksikliği (20-5 ng/ml) varken optimal yeterli D vitamini düzeyi saptanmadı. Sağlıklı kontrolle kıyasla hasta grubunda anlamlı olarak D vitamini düşüklüğü saptandı (p=0,001). Sistemik skleroz alt gruplarındaki analizde pulmoner tutulum (p=0,019) ve DLCO (p=0,023) dışında anlamlı fark yoktu. 25-hidroksivitamin D konsantrasyonu ile yaş, akut faz reaktanları, otoantikor profili, cilt tutulumunun derecesi, hastalık aktivitesi ve solunum testleri ile D vitamini arasındaki korelasyon bakıldı, anlamlı korelasyon saptanmadı.

Sonuç: Sistemik skleroz hastalarının serum D vitamini konsantrasyonları sağlıklı kontrollere göre anlamlı derecede daha düşüktü. Cilt tutulumu, hastalık aktivitesi ile 25-hidroksivitamin D düzeyi arasında ise anlamlı bir korelasyon saptanmadı.

Anahtar kelimeler: 25-hidroksivitamin D, cilt tutulumu, pulmoner tutulum, sistemik skleroz

INTRODUCTION

Although the etiology of Systemic Sclerosis (SSc) is not known exactly, it progresses with multi-organ involvement; it is a chronic disease characterized by vasculopathy, fibrosis and autoimmunity affecting the connective tissue (1).

It is manifested by clinical findings that occur with connective tissue accumulation and skin thickening (scleroderma) due to fibrosis, involvement of organs such as lung, gastrointestinal system (GIS), kidney and heart. Although the most common clinical finding is skin involvement, it can lead to serious loss of function due to the involvement of the internal organs (2,3).

Vitamin D is a vitamin that increases intestinal calcium absorption and has effects on bone storage and bone resorption (4). In recent years, a role of vitamin D as a regulator of the immune system has been proposed and its deficiency has been observed in many autoimmune diseases, including type 1 diabetes mellitus, multiple sclerosis, inflammatory bowel disease, and systemic rheumatic disorders such as rheumatoid arthritis, SLE, and SSc (5). In some studies, the immunosuppressive effects of vitamin D are mainly by inhibiting T helper-1 (Th1) lymphocytes and proinflammatory cytokines such as Interleukin (IL)-6 and IL-17 and stimulating the production of anti-inflammatory cytokines (IL-4 and IL-10). indicated is indicated. Therefore, vitamin D seems to play a protective role in the development of autoimmunity due to its immunomodulatory effects. In addition, vitamin D has antifibrotic properties. Transforming Growth Factor-β (TGF-β) is thought to have this property by inhibiting profibrotic skin and lung fibroblasts (6,7).

Many factors have been reported that may affect the onset and disease process of SSc, which has an autoimmune character; In recent studies, one of these factors is seen as low serum vitamin D level (8). Due to the immunomodulatory and antifibrotic effects of vitamin D, it is thought to be related to pathophysiological mechanisms such as active autoimmunity, peripheral vasculopathy and fibrosis that cause SSc (9). Vitamin D malabsorption can also lead to low 25 (OH) vitamin D levels. Therefore vitamin D levels are very common in SSc and inversely proportional to disease activity, and it is also reported to have a modulating feature on the disease (8,10).

Because of the very different clinical manifestations of the disease, low vitamin D levels in SSc may be associated with different systemic manifestations of the disease, SSc activity and severity, or disease subtype. For this purpose, we wanted to compare the difference in vitamin levels with the control group and also to evaluate a possible relationship between different clinical features in subtypes and organ involvement.

MATERIAL AND METHODS

Patient and Control Group

In this retrospective, cross-sectional study, 54 patients (49 female, 5 male) SSc patients who applied to our rheumatology outpatient clinics between May 2020 and May 2022 and 50 (45 females, 5 males) healthy control with similar demographic characteristics as the patient group was included. According to the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) 2013 criteria, the patients with a score of 9 and above were classified as SSc (11). Fifty healthy volunteers (45 females, 5 males) over 18 years of age, who had not had any systemic additional disease and had not received vitamin D replacement in the last 3 months, and who had a serum vitamin D test, who came to the Physical Medicine and Rehabilitation Algology outpatient clinic for any reason, were included. Patients who had a history of taking vitamin D supplements in the last 3 months and who had kidney failure, liver disease, or endocrinological disease that would affect vitamin D metabolism were excluded from the study. Two groups homogeneous in terms of age and gender were formed.

This study was carried out with the permission of Manisa Celal Bayar University Medical Faculty Clinical Researches Ethics Committee (Date: 30.05.2022, Decision No. E-85252386-050.04.04-313927). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Necessary information about the scales to be applied, physical examination, blood sample was given to all patients, and a written consent form was obtained.

Patient files were reviewed retrospectively. Demographic information of the patients, other comorbidities, treatments they are receiving, physical examination findings between the specified dates, laboratory features such as complete blood count, parathormone (PTH), calcium, phosphorus, creatinine 25 (OH) vitamin D levels can be accessed via the computer system and taken from the records in the polyclinic file. Patients whose file information could not be accessed from the hospital registry system were excluded from the study.

Measurement of serum 25 (OH) vitamin D levels

In the biochemistry laboratory of our hospital, 25 (OH) vitamin D levels in serum were measured with enzyme-linked immunosorbent assay (ELISA) kit (25- Hydroxyvitamin D total ELISA test; ADVIA Centaur XP Immunoassay System, Siemens, Germany. 25 (OH) vitamin D level between 21 and 29 ng/ml “Vitamin D deficiency”, between 5-20 ng/ml “Vitamin D deficiency”, between <5 ng/ml “severe vitamin D deficiency”, ≥30 ng/ml was defined as “adequate vitamin D level” (11).

Anti-nuclear antibodies (ANA) of the patients were examined by indirect fluorescent antibody (IFA) (hep-

2 cells) and other antibodies including anti-centromere antibodies, Anti-Scl 70 (Topoisomerase 1), Anti-centromere antibody (ACA), SSA/ Ro, SSB/La, anti-Sm-RNP were measured by ELISA (enzyme-liked immunosorbent assay) (ELISA method. ANA titer above 1/160 was considered significant.

Pulmonary involvement findings (ground glass, honeycomb image) were evaluated with high-resolution thin-section chest tomography (HRCT), and forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) were evaluated in pulmonary function test.

Skin thickness was assessed using the Modified Rodnan Skin Score (mRSS). In mRSS measurement, the whole skin area is divided into 17 different regions (fingers, hands, forearms, upper arms, face, chest, abdomen, upper legs, lower legs and feet) and the score of each area is calculated by manual palpation. Skin index finger on palpation gently squeezed or rolled between thumb and thumb. Scoring is done by giving a score between 0 and 3. The skin is scored as 0=Normal, 1=Mild thickening, 2=Moderate thickening and 3=Severe thickening according to the degree of thickness, and the maximum score is 51. The total skin score is obtained by summing the skin score of each region (12).

Disease activity was developed by the European Scleroderma Study Group (EScSG), in order to distinguish between active and inactive disease, a scoring system consisting of ten criteria and evaluated over 10 points, which is the total activity index, was determined. As determined initially, this weighted 10-point activity index records activity in individual organs or systems. In this study, activity scoring and EScSG were calculated by the activity measurement method. The patients with cut-off point ≥2.5 were accepted to have the active disease (13).

Statistics

Statistical analysis was performed using SPSS 22.0 package program Continuous variables were expressed as mean±sd and categorical variables as percentages Normal distribution of continuous variables was tested with the Kolmogorov-Smirnov test Independent samples t-test or Mann Whitney test for continuous variables U-test was used appropriately Correlation between data was analyzed by Spearman and Pearson correlation analysis (r-value). Categorical variables of patients and healthy volunteers were chi-square (x2) test. The significance threshold was set at 0.05. Two-sided p-values are presented throughout.

RESULTS

Fifty-four patients meeting ACR-EULAR 2013 classification criteria were included in the SSc group and 49 (88.9%) were female. The female gender was dominant in both groups. The mean age was 53.25±10.77 (18-70) years in the SSc group and the median diagnosis duration of the patients was calculated as 8 (1-25) years. The demographic findings of the patients, other comorbid chronic diseases, and other treatments they are receiving are presented in Table 1.

There was a significant difference between the groups in smoking status (p=0.001), PTH level 84.48±17.49 pg/mL (p=0.001), CRP (p=0.010), and ESH (p=0.009) values (Table 1).

The 25 (OH) vitamin D levels in the group diagnosed with systemic scleroderma was 11.35±4.09 ng/ml (2.5 71.90) and was significantly lower than the control group (p=0.001).

In the scleroderma group, 7 patients (12.9%) had severe vitamin D deficiency (<5 ng/ml), 46 patients (85.1%) had vitamin D deficiency (20-5 ng/ml), 1 patient (1.8%) had vitamin D deficiency (29-21 ng/ml) was detected. A comparison with the control group is given in Table 2.

Demographic and laboratory data of systemic sclerosis subgroups (limited and diffuse) are given in Table 3. There was a significant difference between the groups with regard to pulmonary involvement (ground glass changes) (p=0.019).

When the antinuclear antibody staining pattern was examined, granular staining was observed more frequently in 21 patients (70%) in the dSSc group and in 17 patients (70.8%) in the lSSc group. The number of patients with positive anti-centromere antibodies was 20 (37.0%). Anti-Scl 70 antibody was positive in 24 (44.4%) patients. Considering the frequency of digital ulcers, it was found in 5 (16.6%) patients in the dSSc group. In the dSSc group, 16 (53.3%) patients had sclerodactyly, and 23 (76.6 %) patients in this group had ground glass changes on HRCT, and 7 (23.3%) patients had honeycombing.

Considering other accompanying systemic diseases and clinical conditions, 16 (29.6%) of the patients had hypertension, 14 (25.9%) had cardiovascular disease, 6 (11.1%) had hyperlipidemia and 8 (14.8%) had asthma.

Considering the treatments, calcium channel blocker in 40 patients (74%), bosentan in 4 patients (7.4%), sildenafil in 2 patients (3.7%), steroid in 20 patients (37%), immunosuppressive drug (azathioprine, mycophenolate mofetil, rituximab, and cyclophosphamide) in 27 patients (50%), were used.

When the laboratory data in the Systemic sclerosis group were analyzed in terms of the correlation between organ involvement and activities, no significant correlation was found (p>0.05, Table 4). Only, 25 (OH) vitamin D levels are inversely correlated with PTH (p=0.001, Table 4).

Table 1. Demographic and clinical data of Systemic sclerosis and control patients

Parameters	Control (n:50)	Scleroderma (n:54)	p
Age (years, Mean±SD)	51.02 ± 9.14	53.25 ± 10.77	0.259
Gender (F) (n, %)	45 (90%)	49 (91%)	0.898
Smoking (n, %)			
Current smoker	13 (26%)	6 (11.1%)	
Former smoker	20 (40%)	17 (31.4%)	0.001
Never smoked	17 (34%)	39 (72.2%)	
BMI (kg/m2)	26.19 ±1.89	25.89 ± 4.84	0.649
Hgb (g/dL)	12.84 ± 0.99	12.54 ± 1.54	0.256
Albumin (g/dL)	4.24 ± 0.47	4.34 ± 0.45	0.934
CRP (mg/dL)	0.39 ± 0.27	1.24 ± 2.27	0.010
ESR (mm/h)	22.04 ± 18.75	33.38 ± 24.3	0.009
Ca (mg/dl)	9.34 ± 1.26	8.89 ± 0.53	0.024
P (mg/dl)	3.62 ± 0.58	3.65 ± 0.53	0.803
PTH (pg/ml)	67.14 ± 14.79	84.48 ±17.49	0.001
ALP (u/lt)	59.85±33.46	64.21 ± 22.83	0.102
25 (OH) vitamin D (ng/ml)	22.36 ± 4.50	11.35 ± 4.09	0.001

**BMI: Body Mass Index, Hbg: Hemoglobin, ESH: erythrocyte sedimentation rate, CRP : C-reactive protein Ca: calcium; P: phosphorus;*
ALP: alkaline phosphatase, PTH: parathormone, 25 (OH) vitamin D :25-hydroxyvitamin D, (Mean±SD: Mean ± standard deviation was considered significant at p<0.05)

Table 2. 25-hydroxyvitamin D levels of Systemic sclerosis and control patients

25-hydroxyvitamin D levels	Systemic sclerosis (n:54)	Control (n:50)	p
Sufficient level of Vitamin D (>30 ng/ml)	0	2	0.001
Vitamin D insufficiency (29 – 21 ng/ml)	1	31	
Vitamin D deficiency (20 – 5 ng/ml)	46	17	
Severe Vitamin D deficiency (<5 ng/ml)	7	0	

**Mean±SD: Mean ± standard deviation was considered significant at p<0.05*

Table 3. Laboratory data of Scleroderma patients

Parameters	Localized Scleroderma (lSSc) n:24	Diffuse scleroderma (dSSc) n:30	p
Age (years, Mean±SD)	53.16 ± 8.54	53.33 ± 12.42	0.956
Gender (F) (n, %)	22 (91.6%)	27 (90%)	0.838
Disease duration(years)	8.0 (1-20)	8.0 (3-25)	0.976
BMI (kg/m2)	26.39 ± 4.68	25.44 ± 4.90	0.476
Smoking (n, %)			
Current smoker	3 (12.5%)	3(10%)	
Former smoker	10(41.7%)	7(23.3%)	0.355
Never smoked	11(45.8%)	25(66.7%)	
ESR (mm/hr)	39.2 ±26.54	28.80 ± 2.15	0.118
CRP (mg/dL)	1.47 ± 2.97	1.05 ±1.54	0.506
25 (OH) vitamin D (ng/ml)	11.79 ± 4.43	11.00 ± 3.84	0.485
FVC (%)	94.86 ± 43.14	81.40 ± 9.84	0.103
DLCO (%)	72.8 ± 4.80	68.6± 5.40	0.023
Pulmonary involvement (ground glass changes) n (%)	6 (25%)	17 (56.6%)	0.019
mRSS	22.50 ±12.68	20.90 ± 13.05	0.652
EScSG activity index	3.12 ± 2.09	3.53 ± 2.23	0.638

**ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, 25 (OH) vitamin D: 25-Hydroxyvitamin D, FVC: Forced Vital Capacity,*
DLCO: Diffusing capacity of the lungs for carbon monoxide mRSS: Modified Rodnan Skin Score, EScSG: European Scleroderma Study Group

Table 4. Correlation of vitamin D with demographic and clinical disease variables in patients with scleroderma

Variables	r	p
Age (years)	-0.046	0.108
ESR (mm/hour)	-0.040	0.742
CRP (mg/dL)	0.105	0.439
Smoking	0.124	0.374
PTH level	-0.483	0.001
ANA positivity	-0.114	0.412
Anti-SCL70 antibody	-0.127	0.510
mRSS	-0.086	0.534
FVC (%)	-0.113	0.418
DLCO (%)	-0.289	0.326
EScSG activity index	-0.108	0.089

**ESR: erythrocyte sedimentation rate, CRP: C-reactive protein PTH: parathyroid hormone ANA: Antinuclear Antibody, FVC: Forced Vital Capacity, mRSS: Modified Rodnan Skin Score, DLCO: Diffusing capacity of the lungs for carbon monoxid, EScSG : European Scleroderma Study Group*

DISCUSSION

In this study, we evaluated the frequency of low 25 (OH) vitamin D levels in SSc patients, the difference between vitamin levels in disease subgroups, and possible relationships with clinical features of the disease.

Vitamin D is known as the basic hormone that controls bone metabolism by providing calcium and phosphorus balance (14). Since 90-95% of vitamin D is synthesized in the skin with the effect of sunlight, its deficiency can be seen frequently in diseases with skin involvement. In addition, gastrointestinal absorption also affects vitamin D levels (11). In some recent studies, it has been stated that vitamin D replacement may be effective in preventing disease activation and progression in rheumatoid arthritis patients (15,16). Similarly, it has been shown that there is a correlation between disease activity and acute phase reactant serum concentrations and vitamin D serum levels (17).

The relationship between vitamin D and SSc is a controversial issue, and it is still unclear whether vitamin D is a cause, an accelerating factor, or a consequence of SSc. Serum 25-(OH) D acts as a negative acute phase reactant with effects for acute and chronic inflammatory diseases, and decreases in vitamin D levels are observed as a result of the error (18). In our study, we did not find a significant correlation between 25-(OH) D and ESR and CRP.

Due to its immunomodulatory and antifibrotic effects, vitamin D is thought to have an important role in the pathogenesis and treatment process of SSc (10,18). Insufficient vitamin D status in scleroderma patients appears to be associated with skin or mucosal thickening resulting in inadequate uptake and absorption (19,20). In our results, we found that SSc patients had significantly lower vitamin D levels compared to the healthy group.

Skin involvement is an indicator of disease activity, severity, and prognosis. Extensive skin fibrosis, as well as excessive and excessive skin thickening, and severe visceral involvement, are associated with a poor prognosis. In a retrospective cohort study, Arnson et al. found a negative correlation between vitamin D concentrations and age ($p<0.05$), while many other studies were unable to demonstrate any correlation between serum vitamin D and age, gender, body mass index (BMI), and therapy in SSc (21). In our study, when the relationship between age, acute phase reactants, disease duration, and smoking was examined, no significant correlation was found between vitamin D levels.

In the studies by Giuggioli et al it was suggested that the most important cause of vitamin D deficiency in scleroderma patients is fibrosis of the skin, which contributes to active vitamin D synthesis (22). We could not find a significant correlation between vitamin D level and mRSS.

In a study, when the potential relationship between vitamin D levels and the clinical phenotype of SSc was examined more closely, no significant difference was found in 25 (OH) vitamin D levels in most studies, regardless of disease subtype (23). However, An et al lower serum vitamin D levels were found in SSc compared to healthy controls and in dSSc compared to lSSc. It is reported that patients with low vitamin D levels have the more severe diseases than those with optimal vitamin D levels. There was no difference between subgroups in clinical features such as Rodnan score, gastrointestinal ulcer, pulmonary involvement, or systolic arterial pressure among SSc patients with vitamin D deficiency (24).

The link between abnormal serum vitamin D and serological specificities in SSc is still under investigation. In contrast, Gambichler et al. It showed that there was no significant relationship between vitamin D and antinuclear

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autoantibodies (25). In our study, antibody titer and staining patterns were also examined, but no significant correlation was found between ANA positivity and vitamin D level.

Some studies have focused on statistically significant relationships between vitamin D and parathyroid hormone (PTH), not only in healthy individuals but also in SSc patients. Furthermore, Hax et al demonstrated that 25 (OH) vitamin D levels s are inversely correlated with PTH (26). In this study, it was found to be negatively correlated in the SSc group as we expected.

Pulmonary involvement in scleroderma is an important cause of morbidity and mortality. Especially in the diffuse form, the development of lung fibrosis seriously affects the functional status of the patient. In a study in the literature, serum levels of vitamin D were found to be inversely correlated with disease activity, especially lung involvement in scleroderma (21,27). In some studies, it has been stated that vitamin D is also effective on the transdifferentiation of lung epithelial cells to myofibroblasts. In some studies, it has been shown that lung involvement is more severe in patients with vitamin D deficiency. More severe lung disease in SSc patients with low vitamin D levels may provide a plausible explanation (28,29).

In our study, we had 23 patients with a ground-glass appearance when viewed with HRCT for pulmonary involvement. It was seen in 17 (56.6%) patients in the dSSc group, and there was a significantly higher rate of involvement compared to the lSSc group. In the evaluation of respiratory function, although FVC decreased in the diffuse SSc group, its mean value was 81.40±9.84. There was a significant difference between the two groups in DLCO (p=0.023). However, we could not find a significant correlation between FVC, DLCO and 25 (OH) vitamin D levels in this study.
Vacca et al emphasized a significant negative correlation between vitamin D and the European Disease Activity Score (22). Lower levels of vitamin D are usually seen in active disease. Therefore, lower vitamin D levels are frequently seen in SSc, an inflammatory disease, and higher doses are needed for replacement therapy, especially in patients with high inflammatory activity or severe disease (30,31). In this study, there was no significant correlation between the EScSG activity index and vitamin D level.

Systemic scleroderma is a rare disease, but vitamin D levels are often low due to severe organ involvement. In this study, we analyzed the clinical and laboratory status of our patients in many ways by comparing them with healthy controls.

LIMITATION

A limitation is that it is a retrospective study. Another point is that scleroderma is a rare rheumatologic disease and the number of patients followed up in our outpatient clinic was lower than in other rheumatologic patient groups. There is a need for a larger sample to determine the frequency of vitamin D deficiency and a prospective study to evaluate its relationship with disease severity.

CONCLUSION

In our study, we showed that patients with scleroderma exhibit lower levels of vitamin D compared to healthy controls. When patients with diffuse SSc and patients with limited SSc were compared, there was no significant difference between vitamin levels. There was no significant correlation between skin involvement, respiratory functions, disease activity and 25 (OH) vitamin D levels.

Patients with scleroderma often have low 25 (OH) vitamin D levels due to skin and gastrointestinal involvement, so they require higher doses instead of standart-dose treatments. We wanted to emphasize the importance of being careful in terms of vitamin D replacement and making the necessary replacement by measuring 25 (OH) vitamin D levels at regular intervals.

Patient Consent for Publication: Writen informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.
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