ORIGINAL ARTICLE

Rheumatology Quarterly

DOI: 10.4274/qrheumatol.galenos.2024.13008
Rheumatology Quarterly 2024;2(2):72-9

EVALUATION OF THE RELATIONSHIP BETWEEN SERUM VITAMIN D LEVEL AND CLINICAL ACTIVATION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

Kezban Armağan Alptürker[1], Bilge Ekinci[2], Serhat Hayme[3]

[1]Demokrasi University Buca Seyfi Demirsoy Training and Research Hospital, Clinic of Rheumatology, İzmir Turkey
[2]Erzincan Binali Yıldırım University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Erzincan, Turkey
[3]Erzincan Binali Yıldırım University Faculty of Medicine, Department of Biostatistics, Erzincan, Turkey

Abstract

Aim: In this study, we aimed to analyze the clinical activity relationship between serum vitamin D levels, which are also steroid hormones, and to investigate the correlation between clinical and laboratory data and possible relationships.

Material and Methods: A total of 126 adult patients who met the 2019 systemic lupus erythematosus (SLE) classification criteria and the 2010 rheumatoid arthritis (RA) classification criteria and were treated in the outpatient clinics of Rheumatology and Physical Medicine and Rehabilitation were included in the study. Ten patients were excluded because their data were not suitable for the study. In all patients. Erythrocyte sedimentation rate, C-reactive protein level, vitamin D level, pain assessment with Visual Analog Scale, and Health Assessment Questionnaire (HAQ) were used to assess functional ability and health status in daily life.

Results: Eighty-four patients (72.4%) who participated in the study had RA and 32 patients (27.6%) had SLE. In the SLE group, 27 (84.4%) patients were female, and there was no difference between the two groups in terms of gender. The mean age was 39.32±6.64 years in the SLE group and 50.76±9.07 years in the RA group. While the 25-hydroxyvitamin D [25-(OH)D] level in the SLE group was 10.53±3.52, the vitamin D level in the RA group was 14.20±5.28, and the difference between the two groups was significant ($p<0.0001$). In the RA group, a significant negative correlation was found between the HAQ level and 25-(OH)D measured in terms of clinical activation ($p=0.001$).

Conclusion: In this cross-sectional study, 25-(OH)D levels were lower in patients with SLE, one of the major autoimmune diseases, than in patients in the RA group. A negative correlation of the 25-(OH)D level with HAQ was found in RA patients. Monitoring vitamin D levels and raising them to an optimal level are clinically important in autoimmune diseases.

Keywords: Rheumatoid arthritis, systemic lupus erythematosus, 25-hydroxyvitamin D, disease activation

Address for Correspondence: Kezban Armağan Alptürker, Demokrasi University Buca Seyfi Demirsoy Training and Research Hospital, Clinic of Rheumatology, İzmir Turkey
Phone: +90 232 452 52 52 **E-mail:** kezban887@gmail.com **ORCID ID:** orcid.org/0000-0001-7380-6097
Received: 22.05.2024 **Accepted:** 01.06.2024

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disease often affecting women of reproductive age that causes tissue damage in a number of target organs after the development of pathogenic autoantibodies and immune complexes. SLE is characterized by antibodies against nuclear and cytoplasmic antigens. Excessive production of pathogenic autoantibodies by B cells, dysregulation of cytokines, which results in damage to tissues and organs, and abnormal conductivity of T cell receptors also contribute to SLE autoimmunity (1).

As a chronic, inflammatory, multi-systemic disease, rheumatoid arthritis (RA) particularly involves small joints. The etiology of the disease is unknown; however, genetic factors, infectious agents, gender, hormonal factors, and lifestyle factors are considered contributing factors (2).

The presence of hormonal factors is thought to contribute to both RA and SLE, which are autoimmune diseases. Particularly in SLE, estradiol, progesterone, and prolactin, and some pituitary hormones, play a role in regulating the immune system (3). 25-hydroxyvitamin D [25-(OH)D] is a prohormone that is primarily involved in calcium metabolism and has a variety of biological effects, such as antimicrobial activity and modulation of cellular differentiation. Inhibition of autoantibody production by vitamin D leads to suppression of dendritic cell-associated pathways and inhibition of T cell activation (4).

In some studies, vitamin D deficiency has been reported to act not only as a predisposing factor for the development of RA and SLE but also to enhance disease severity and activity (5). There is a higher prevalence of vitamin D deficiency in patients with systemic lupus than in the healthy population. There are some specific risk factors associated with this disease. Less sun exposure due to photosensitivity observed in these patients decreases vitamin D synthesis from the skin. Furthermore, the hydroxylation step of vitamin D is impaired in lupus nephritis, resulting in inadequate conversion to the active form (4,6). Chronic use of commonly used corticosteroids also adversely affects vitamin D metabolism (7).

A number of studies indicate that 25-(OH)D levels are negatively associated with disease activity and mortality risk in RA, but the mechanism for this association has not yet been fully explored (8).

In the literature, there has been little research on the relationship between vitamin D levels and clinical activation in patients with RA and SLE. We conducted this study to investigate the relationship between 25-(OH)D levels and the activity of autoimmune diseases using laboratory data that can be easily obtained from peripheral blood samples.

MATERIAL AND METHODS

This study was planned as a single-center, cross-sectional study to determine the relationship between serum vitamin D levels and disease activity in individuals with RA and SLE.

Sample and Population

There were 84 participants in the study, aged 18 to 65, who applied to Erzincan Binali Yıldırım University, Mengücek Gazi Training and Research Hospital Physical Medicine and Rehabilitation and Rheumatology outpatient clinics between February 2023 and May 2023, who had been diagnosed with RA by a physician depending on the American College of Rheumatology (ACR) and/or American College of Rheumatology-European League Against Rheumatism (ACR-EULAR) 2010 criteria and had been diagnosed with RA for at least a year, as well as 32 individuals who were diagnosed with SLE based on EULAR/ACR-2019 classification criteria. Due to seasonal variation in vitamin levels, the values between February and May were considered.

The exclusion criteria included those who received vitamin D3 replacement within the previous 6 months, pregnant patients, those with severe neurologic impairments that limit perception, and individuals with dysfunction such as uncooperation. Ten patients were excluded because their data were not suitable for the study. These patients were excluded from the study because pregnancy was detected after the examinations in three SLE patients, two SLE patients experienced activation due to discontinuation of their medications and therefore the current treatment was changed, and the other five patients' past vitamin D3 intake was later discovered from their E-nabız records.

Ethical Principles of the Study

Ethics committee approval (date: 08.12.2022; approval number: 2022-7/10) for the implementation of the study was obtained from the Faculty of Medicine Clinical Research Ethics Committee of Binali Yıldırım University.

Data Collection Tools and Data Analysis

The participants were questioned by face-to-face interview using the Patient Information Form prepared by the authors after obtaining verbal and written consent regarding their sociodemographic characteristics, health status, disease activity, sleep quality, fatigue severity, pain levels, and physical activity characteristics. In addition to demographic and clinical laboratory findings, age at diagnosis, disease duration, treatment, and prognosis (age, gender, smoking, diagnosis,

diagnosis duration, treatment and follow-up, acute phase response, hematologic findings, organ involvement findings, disease activation scoring, comorbidity and drug history, antibody levels, and follow-up) were measured and recorded.

All blood samples were drawn from the antecubital vein in the morning. All parameters were studied in the laboratory of the Mengücek Gazi Training and Research Hospital.

Regarding hematological findings, the parameters of complete blood count, erythrocyte sedimentation rate, C-reactive protein (CRP), rheumatoid factor, and anti-cyclic citrullinated peptide were measured (ARCHITECT, refrigerated centrifugation at 400 rpm for at least 15 minutes with thawed samples) and recorded. To evaluate renal involvement caused by SLE, complete urinalysis and 24 hours urinalysis were conducted on the patients. Anti-recurrent antibodies (ANA) and anti-dsDNA levels were determined by ELIZA (Alegria, ORGANTEC Diagnostica, Mainz, Germany), with moderate and high values being considered positive. A nephelometric technique was used to determine the levels of serum complement (C3, C4) (normal values for C3: 85-200 mg/dL, for C4: 20-50 mg/dL).

Using the Agilent Technologies 6460 Triple Quad liquid chromatography (LC)/mass spectrometry (MS) device, high-performance liquid chromatography (HPLC), and MS methods, serum vitamin 25-(OH)D and blood samples collected in EDTA tubes were analyzed. The 25-(OH)D concentration in serum and blood samples collected in an ethylenediamine tetraacetic acid (EDTA) tube was analyzed using an Agilent Technologies 6460 Triple Quad LC/MS device, HPLC, and MS. The reference values for vitamin 25-(OH)D were evaluated according to the device, and vitamin D levels were classified as sufficient at 30 ng/mL, insufficient at 20-30 ng/mL, deficient at 20 ng/mL, and severe at 10 ng/mL (9).

A visual analog scale (VAS) was used to determine participants' pain levels; a Disease Activity Score (DAS-28-CRP) was used to assess RA disease activity; and a Health Assessment Questionnaire (HAQ) was used to assess functional capacity and health status in daily life. Clinical findings regarding SLE, organ involvement, and other follow-up parameters, as well as SLE disease activation scores, were evaluated using the Disease Activity Index (SLEDAI).

VAS

The VAS pain score was evaluated as "no pain" (score=0) and "worst pain possible" (score=10) and divided into three groups according to the pain intensity scale of the World Health Organization: if the score was <3, it was considered mild pain, 3-6 as mild-moderate pain, and >6 as moderate-severe pain (10).

HAQ

This questionnaire consisted of 20 questions and eight activities. The score obtained from each activity was determined according to the highest score obtained from the questions in that activity. The total score was calculated by taking the sum of the scores obtained from the eight activities and dividing by 8, and was evaluated with a score between 0 and 3. Higher scores indicate an increased level of functional dependence (11).

DAS-28 Score Calculation Form

The DAS-28 score was used to assess disease activation in RA. It was calculated using the swollen joint count, tender joint count (over 28 joints), VAS, and CRP (mg/dL) data. A special type of calculator was used for this calculation. As a result of the calculation, values of 2.6 and below were considered "remission" , values between 2.6 and 3.2 as "low level of disease activity", values between 3.2 and 5.1 as "moderate level of disease activity", and values of 5.1 and above as "high level of disease activity" (12).

SLEDAI

In the case of SLE, activity classification was based on the SLEDAI score. Whenever there was no activity, the score was accepted as zero. A score of 1-5 was considered mild activity, 6-10 was moderate activity, 1-19 was high activity, and ≥20 was very high activity. Laboratory parameters included in the DAS were obtained from the patient's examinations in the last month (13).

Statistical Analysis

The analysis was performed using the SPSS 22.0 software package. Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as percentages. The normal distribution of the continuous variables was tested using the Kolmogorov-Smirnov test. For the continuous variables, an independent sample t-test or Mann Whitney U test was used. Correlations between the data were tested using Spearman's and Pearson correlation analysis. The chi-square test was used to compare categorical values. For all tests, a two-way p-value of 0.05 for the patients was considered significant. The relationship between variables in the patients group was analyzed using Spearman's correlation analysis (r-value).

RESULTS

A comparison of the demographic and laboratory characteristics of the 126 individuals participating in the study is presented in Table 1.

There were 84 individuals (72.4%) with RA and 32 individuals (27.6%) with SLE. The SLE group consisted of 27 (84.4%) female

Table 1. Comparison of demographic and laboratory characteristics of the RA and SLE groups

Variables	RA (n=84, 72.4%)	SLE (n=32, 27.6%)	p-value
Age (year), (min.-max.)	50.76±9.07 (28-67)	39.32±6.64 (21-52)	**0.001***
Gender, female (n, %)	58 (69.0%)	27 (84.4%)	0.095**
Age of disease onset (years) (mean ± SD)	41.05±9.11	30.03 ±6.85	**0.001****
Disease duration (months) (mean ± SD)	135.36±69.62	126.36±49.32	0.414*
Current smokers (n, %)	28 (33.3%)	10 (31.3%)	0.831**
Hbg, (g/dL)	12.58±1.07	11.73±0.76	**0.001***
MPV	9.59±0.59	9.73±0.74	0.322*
WBC, µL	6.96±7.97	4.08±0.77	**<0.001***
Serum creatinine (mg/dL)	0.76±0.13	0.94±0.28	**0.001***
CRP mean ± SD (mg/dL)	9.52±6.80	8.77±6.96	0.258*
ESH mean ± SD (mm/hour)	26.17±10.18	31.87±13.42	**0.018***
25-(OH) vitamin D (<29.9 ng/mL) (min.-max.)	14.20±5.28 (2.90-25.2)	10.53±3.52 (4.20-23.30)	**0.001***
RF positivity, n (%)	61 (72.6%)	4 (12.5%)	**<0.001****
Anti-CCP positivity, n (%)	35 (41.7%)	2 (6.3%)	**<0.001****
ANA positivity, n (%)	39 (46.4%)	32 (100%)	**<0.001****

*Mann-Whitney U test in an independent sample, **chi square test. In the table, the values are presented as median (minimum-maximum) or number (%), mean ± SD: Mean ± standard deviation (was considered significant at p<0.05), RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, min.: Minimum, max.: Maximum, Std : Standard, n: Number, Hbg: Hemoglobin, MPV: Mean plateau volume, WBC: White blood cell, CRP: C-reactive protein, ESH: Erythrocyte sedimentation rate, 25-(OH) vitamin D :25-hydroxyvitamin D, ESR: Erythrocyte sedimentation rate, RF: Rheumatoid factor, Anti-CCP: Anticyclic citrullinated peptide, ANA: Antinuclear antibody, SD: Standard deviation

patients, and there was no gender difference between the groups. The mean age was 39.32±6.64 years in the SLE group and 50.76±9.07 years in the RA group, which was significantly younger in the SLE group than in the RA group.

The 25-(OH)D level in the SLE group was 10.53±3.52, which was significantly lower than the 25-(OH)D level in the RA group (14.20±5.28) (p<0.0001). In the SLE group, 4 patients (12.5%) had 25-(OH)D vitamin deficiency, 13 patients (40.6%) had 25-(OH)D vitamin deficiency, and 15 patients (46.8%) had severe 25-(OH)D vitamin deficiency. In the RA group, 25-(OH)D was <20 ng/mL in 56 (66.6%) patients.

All patients in the SLE group were ANA-positive. In the RA group, ANA positivity was determined in 39 (46.4%) patients. Anti-dsDNA, C3, and C4 levels were measured in the SLE group. The anti-dsDNA level was found to be higher than the normal reference range (n=>20 IU/L) in 8 patients (25%) in the SLE group. Serum complement (C3, C4) levels of the patients were measured using the nephelometric method (normal values were C3: 85-200 mg/dL, C4: 20-50 mg/dL). C3 complement levels (n=75-135 mg/dL) were found to be lower than normal reference ranges in 12 (37.5%) patients.

A comparison of the treatments between the patient groups is presented in Table 2. While there was no statistical difference

Table 2. Comparison of treatments between the patient groups

Current treatment	RA (n=84, 72.4%)	SLE (n=32, 27.6%)	p*
Corticosteroid, n (%)	62 (73.8%)	24 (75.0%)	0.205
HCQ, n (%)	9 (10.7%)	24 (75.0%)	<0.0001
MTX , n (%)	38 (45.2%)	6 (18.8%)	<0.0001
Anti-TNF-α, n (%)	27 (32.1%)	-	

*chi square test, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, HCQ: Hydroxychloroquine, MTX: Methotrexate, anti-TNF-α: Anti-tumor necrosis factor alfa treatment, n: Number

in terms of the number of patients treated with steroids in both groups, the difference was significant in terms of disease-modifying antirheumatic drugs (DMARDs) treatments (p<0.0001). However, the duration of steroid treatment was longer in the SLE group (8.62±2.6 months) than in the RA group (5.28±1.61), but there was no statistically significant difference, as cumulatively similar doses.

When the treatments of the patients were analyzed, hydroxychloroquine was prescribed to 24 patients (75%) in the SLE group, whereas methotrexate was prescribed to 38 patients (45.2%) in the RA group. The number of patients who used anti-

tumor necrosis factors (TNFs) because of resistant disease despite DMARD treatment was 27 (32.1%) in the RA group. As anti-TNF, adalimumab treatment was administered to 12 (14.2%) patients, golimumab treatment was administered to eight (9.5%) patients, etanercept treatment was administered to four (4.7%) patients, and certolizumab treatment was administered to three (3.5%) patients.

A comparison of disease activation between the groups is presented in Table 3. The difference between VAS and HAQ values between both groups was not significant (p>0.05). The DAS-28 CRP score was 4.21±0.84 in the RA group. In the DAS-28 evaluation, 48 individuals (57.1%) were found to have a moderate level of disease activity. In the SLE group, the SLEDAI was determined to be 6.84±4.54. Six (18.7%) individuals with SLE had a moderate level of activity (SLEDAI 6-10).

When the patients were analyzed in terms of organ involvement, 7 patients (8.3%) in the RA group had interstitial lung disease; therefore, 4 patients (4.7%) were treated with Rituximab (RTX) and 3 patients (3.5%) were administered with a Janus kinase inhibitor (tofacitinib). In the SLE group, 3 patients (9.3%) were treated with Azathioprine, 3 patients (9.3%) with mikofenolat mofetil, and 3 patients (9.3%) with RTX because of renal proteinuria.

Table 3. Comparison of disease activation parameters between the patient groups

	RA (n=84, 72.4%)	SLE (n=32, 27.6%)	p
VAS (unit), (mean ± SD)	5.98±0.99	6.37±1.03	0.068
HAQ, (mean ± SD)	1.27±0.29	1.30±0.26	0.074
DAS-28 CRP score (min.-max.)	4.21±0.84 (2.96-6.84)	-	
SLEDAI (min.-max.)	-	6.84±4.54 (1-20)	

RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, SD: Standard deviation, min.: Minimum, max.: Maximum, VAS: Visual analog scale, HAQ: Health Assessment Questionnaire, DAS-28: Disease Activity Score of 28 joints, CRP: C-reactive protein, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index

Table 4. Correlation between the 25-(OH)D vitamin and disease activation parameters in the RA group

Variables	r	p*
Disease duration	-0.112	0.086
CRP	0.043	0.695
ESH	0.132	0.230
DAS-28 CRP	-0.101	0.369
VAS	-0.160	0.147
HAQ	-0.361	**0.001**

*Pearson correlation analysis. 25-(OH) vitamin D :25-hydroxyvitamin D, RA: Rheumatoid arthritis, CRP: C-reactive protein, ESH: Erythrocyte sedimentation rate, DAS-28: Disease Activity Score 28 joints, VAS: Visual analog scale, HAQ: Health Assessment Questionnaire

In Table 4, the correlation between 25-(OH)D and disease activation parameters in the RA group is presented. When the correlation of serum 25-(OH)D levels with parameters was examined, a negative correlation was found with disease duration, DAS-28, and VAS, but it was not significant. The negative correlation between HAQ level and 25-(OH)D was significant (p=0.001).

The correlation between 25-(OH)D vitamin and disease activation parameters in the SLE group is presented in Table 5. When the correlation of serum 25-(OH)D level with the parameters was analyzed, the negative correlation with SLE disease duration was found to be significant (p=0.015). Its negative correlation with SLEDAI, HAQ, sedimentation, and dsDNA levels was determined, but it was not statistically significant (p>0.05).

DISCUSSION

In this study, we examined the correlation between 25-(OH)D levels in peripheral blood samples and disease activation in patients with RA and SLE.

There was no difference between the two groups in terms of gender, with most females in both groups. The SLE group (mean age: 39.32±6.64 years) consisted of younger individuals than the RA patients (mean age: 50.76±9.07 years), as expected.

Sedimentation and CRP levels, which were routinely measured during clinical follow-up, were associated with disease activation

Table 5. Correlation between the 25-(OH)D and disease activation parameters in the SLE group

Variables	r	p*
Disease duration	-0.226	**0.015**
CRP	0.420	0.820
ESH	-0.025	0.892
C3 levels	0.294	0.191
Anti-dsDNA levels	-0.232	0.210
SLEDAI	-0.152	0.408
VAS	0.290	0.873
HAQ	-0.050	0.807

*Pearson correlation analysis. 25-(OH) vitamin D :25-hydroxyvitamin D, SLE: Systemic lupus erythematosus, CRP: C-reactive protein, ESH: Erythrocyte sedimentation rate, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, VAS: Visual analog scale, HAQ: Health Assessment Questionnaire

and prognosis. Patients with active lupus, in contrast to those with RA, had high sedimentation levels as a characteristic finding of the disease (14). According to this study, sedimentation was higher in the SLE group (31.87±13.42), and the difference was statistically significant (p=0.018).

Studies in the literature have revealed that 25-(OH)D deficiency is highly prevalent in patients suffering from autoimmune rheumatic diseases. In our country, many studies have been conducted on this subject, and in the study of Çalışkan Uçkun et al., (15) it was found that 25-(OH)D levels were significantly lower in individuals with RA than in healthy controls, and 73% of individuals with RA were reported to have vitamin D deficiency, similar to our study. This study was cross-sectional, and vitamin D levels were measured in patients who had not been administered 25-(OH)D3 within the past 6 months. In this study, the 25-(OH)D level was found to be 14.20±5.28 in the RA group, and the vitamin D level was <20 ng/mL in 66.6%.

According to a study involving patients with systemic sclerosis, which is an autoimmune disease characterized by skin involvement, 25-(OH)D levels were 11.35±4.09 ng/dL, a value significantly lower than those of healthy controls (16). The presence of skin involvement in lupus patients was also considered as a disadvantage.

Because it is negatively related to vitamin D levels, the cause of this condition is not entirely understood. In the general population and in patients with SLE, female gender is a classic risk factor for D hypovitaminosis. These differences have been attributed to lower body surface area and androgen-related differences in vitamin D-binding protein levels (4,17). This study found that the female gender predominated in both groups, and there was no gender difference between the groups. There was a significantly higher proportion of females in the group suffering from SLE (84.4%).

As reported in the literature, 25-(OH)D levels were lower in the SLE group than in the RA group in this study. The lower 25-(OH)D levels in patients with lupus compared with RA were attributed to intestinal malabsorption, higher corticosteroid levels, renal involvement and proteinuria, different polymorphisms of 25-(OH)D receptors in patients with lupus, and greater sun protection (7,18).

In the study conducted by Bogaczewicz et al. (19) in 2012 on 49 patients with SLE and a control group (49 people), 25-(OH)D deficiency was found in 90.9% of the group with SLE, whereas 25-(OH)D deficiency or insufficiency was observed in 55.5% of the control group. The level of vitamin D was found to be lower and statistically significant in patients with SLE than in the control group (p=0.0005) (19). There was no control group in this study, but 25-(OH)D levels were quite low in the SLE group, with 25-(OH)D deficiency being detected in 13 patients (40.6%) and severe 25-(OH)D deficiency being detected in 15 patients (46.8%). Based on a literature review, some studies found a correlation between vitamin D and RA activity and flare-up frequency, especially in developing countries, whereas other studies found no correlation (8,20).

Although there was a lack of consistency in studies on 25-(OH)D levels and disease activity in SLE, both of the largest studies to date revealed a significant correlation between high disease activity and low 25-(OH)D levels. These studies also identified that improving vitamin D status among patients with SLE could alleviate other common symptoms such as fatigue and cognitive impairment (21).

As part of a prospective follow-up study for 1 year, vitamin D3 supplementation was administered to patients with SLE, and it was observed that disease activity measured by SLEDAI-2K improved, and parallel with this, serum anti-dsDNA levels decreased both at 6 and 12 months from onset (4,18). According to our study, a negative correlation was observed between serum 25-(OH)D levels and clinical activation, but the results were not statistically significant (p>0.05). Quality of life may be negatively affected by low levels of the 25-(OH)D. In the RA group, there was a negative correlation between 25-(OH)D, DAS-28, and VAS, but this correlation was not significant. The negative correlation between the HAQ level and 25-(OH)D was significant (p=0.001).

Vitamin D was found to act as a negative acute phase reactant, thus explaining its decrease in levels during acute inflammatory processes, and its deficiency was associated with an increase in inflammatory cytokines such as interferon alpha and interferon gama and a high autoantibody titer (22). These cytokines play an important role in SLE pathogenesis. An inverse relationship was found between vitamin D levels and disease activity and anti-dsDNA titers in Cutolo et al. (23). However, some studies have found a contrary correlation. It was believed that ethnicity-related genetic differences in vitamin D receptors were responsible for these differences in study results (23).

In our study, a negative correlation was found between 25-(OH)D level and dsDNA, but this result was not statistically significant (p>0.05). Nevertheless, the negative correlation with vitamin D levels should be considered as a parameter that should be evaluated in patients with lupus nephritis.

Serum 25(OH)D levels decrease with decreased glomerular filtration rate in patients with chronic kidney disease (24). In our study, the creatinine value was significantly higher in the SLE group than in the RA group (p=0.001), and 12 patients (37.5%)

in the SLE group were on advanced treatment for proteinuria. When compared with the RA group, the 25-(OH)D level was also significantly lower.

Some studies in the literature have reported that 25-(OH)D serum values in SLE patients were significantly lower than those in RA patients with the same geographical location, D3 supplementation, and other risk factors (7,22,25). Because vitamin D synthesis occurs through the skin and these patients had skin involvement, 25-(OH)D deficiency should be considered more profound in SLE patients.

CONCLUSION

This study suggests that vitamin D levels should be monitored in patients with autoimmune diseases and that this can serve as an effective follow-up parameter for patients with RA in terms of quality of life and clinical activation. By using a treatment as safe, cheap, and widely available as vitamin D in these patients, we believe that morbidity and mortality related to vitamin D deficiency can also be reduced. It is necessary to conduct further large-scale, prospective, and long-term follow-up studies to determine the optimal range of serum 25(OH)D levels for reducing clinical activation and morbidity.

The study was planned cross-sectionally. No healthy control group could be included in addition to the patient groups. A prospective study with a long-term follow-up and including a control group will contribute more to the literature.

Ethics

Ethics Committee Approval: Ethics committee approval (date: 08.12.2022; approval number: 2022-7/10) for the implementation of the study was obtained from the Faculty of Medicine Clinical Research Ethics Committee of Binali Yıldırım University.

Informed Consent: The participants were questioned by face-to-face interview using the Patient Information Form prepared by the authors after obtaining verbal and written consent regarding their sociodemographic characteristics, health status, disease activity, sleep quality, fatigue severity, pain levels, and physical activity characteristics.

Authorship Contributions

Surgical and Medical Practices: K.A.A., B.E., S.E., Concept: K.A.A., Design: K.A.A., Data Collection or Processing: K.A.A., B.E., Analysis or Interpretation: K.A.A., S.E., Literature Search: K.A.A., B.E., Writing: K.A.A.

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

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Ameer MA, Chaudhry H, Mushtaq J, et al. An overview of systemic lupus erythematosus (SLE) pathogenesis, classification, and management. Cureus. 2022;14:e30330.
2. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: a review. JAMA. 2018;320:1360-72.
3. Lee J, Shin EK, Lee SY, et al. Oestrogen up-regulates interleukin-21 production by CD4(+) T lymphocytes in patients with systemic lupus erythematosus. Immunology. 2014;142:573-80.
4. Magro R, Saliba C, Camilleri Let al. Vitamin D supplementation in systemic lupus erythematosus: relationship to disease activity, fatigue and the interferon signature gene expression. BMC Rheumatol. 2021;5:53.
5. Szodoray P, Nakken B, Gaal J, et al. The complex role of vitamin D in autoimmune diseases. Scand J Immunol. 2008;68:261-9.
6. Kamen DL. Vitamin D in lupus-new kid on the block? Bull NYU Hosp Jt Dis. 2010;68:218-22.
7. Maryam S, Atabati E, Yalda R. Comparison of vitamin D serum values between rheumatoid arthritis and lupus populations: an observational study. Open Rheumatol J. 2018;12:65-9.
8. Sahebari M, Mirfeizi Z, Rezaieyazdi Z, et al. 25(OH) vitamin D serum values and rheumatoid arthritis disease activity (DA S28 ESR). Caspian J Intern Med. 2014;5:148-55.
9. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011;96:1911-30.
10. Miller MD, Ferris DG. Measurement of subjective phenomena in primary care research: the Visual Analogue Scale. Fam Pract Res J. 1993;13:15-24.
11. Küçükdeveci AA, Sahin H, Ataman S, et al. Issues in cross-cultural validity: example from the adaptation, reliability, and validity testing of a Turkish version of the Stanford Health Assessment Questionnaire. Arthritis Rheum 2004;51:14-9.
12. Prevoo ML, van 't Hof MA, Kuper HH, et al. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38:44-8.
13. Aydın SG, Esen BA. Sistemik lupus eritematozus' da hastalık aktivitesinin değerlendirilmesi ve aktivite indeksleri. RAED Dergisi. 2018;10:6.
14. Pan L, Lu MP, Wang JH, et al. Immunological pathogenesis and treatment of systemic lupus erythematosus. World J Pediatr. 2020;16:19-30.
15. Çalışkan Uçkun A, Yurdakul FG, Kılıçarslan A, et al. Impact of vitamin D on rheumatoid arthritis: real or just patient's perception?. Arch Clin Exp Med. 2018;3:127-31.
16. Armagan K, Soysal Gündüz Ö. Evaluation of the frequency of vitamin D deficiency and its relationship with disease involvement in patients with systemic sclerosis. Maltepe tıp derg. 2023;15:10-6.

17. Mithal A, Wahl DA, Bonjour JP, et al. Global vitamin D status and determinants of hypovitaminosis D. Osteoporos Int. 2009;20:1807-20.

18. Kavadichanda C, Singh P, Maurya S, et al. Clinical and serological association of plasma 25-hydroxyvitamin D (25(OH)D) levels in lupus and the short-term effects of oral vitamin D supplementation. Arthritis Res Ther. 2023;25:2.

19. Bogaczewicz J, Sysa-Jedrzejowska A, Arkuszewska C, et al. Vitamin D status in systemic lupus erythematosus patients and its association with selected clinical and laboratory parameters. Lupus. 2012;21:477-84.

20. Bragazzi NL, Watad A, Neumann SG, et al. Vitamin D and rheumatoid arthritis: an ongoing mystery. Curr Opin Rheumatol. 2017;29:378-88.

21. Amital H, Szekanecz Z, Szücs G, et al. Serum concentrations of 25-OH vitamin D in patients with systemic lupus erythematosus (SLE) are inversely related to disease activity: is it time to routinely supplement patients with SLE with vitamin D? Ann Rheum Dis. 2010;69:1155-7.

22. Squance ML, Reeves GE, Tran HA. Vitamin D Levels Are Associated with Expression of SLE, but Not Flare Frequency. Int J Rheumatol. 2014;2014:362834.

23. Cutolo M, Paolino S, Sulli A, et al. Vitamin D, steroid hormones, and autoimmunity. Ann N Y Acad Sci. 2014;1317:39-46.

24. Ureña-Torres P, Metzger M, Haymann JP, et al. Association of kidney function, vitamin D deficiency, and circulating markers of mineral and bone disorders in CKD. Am J Kidney Dis. 2011;58:544-53.

25. Costenbader KH, Feskanich D, Holmes M, et al. Vitamin D intake and risks of systemic lupus erythematosus and rheumatoid arthritis in women. Ann Rheum Dis. 2008;67:530-5.