# RELATIONSHIP BETWEEN VITAMIN D LEVEL AND SYSTEMIC LUPUS ERYTHEMATOSIS DISEASE ACTIVITY

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**Abstract:** *Vitamin D status was determined in patients diagnosed with systemic lupus erythematosus (SLE) with nephritis and SLE patients without nephritis. Vitamin D deficiency and insufficiency was observed to a greater extent in patients with SLE/LN, compared with SLE without LN.*

**Key words**: *systemic lupus erythematosus, lupus nephritis, vitamin D deficiency.*

**Annotatsiya:** *Tizimli qizil toshma lyupus nefritli (TQT/LN) va lyupus nefritsiz bemorlarda, xamda sog'lom odamlardan iborat nazorat guruxida vitamin D xolati aniqlandi. Vitamin D defitsiti va yetishmovchiligi TQT/LN bo'lgan bemorlarda, LNga chalinmagan bemorlarga nisbatan ko'proq kuzatildi.*

**Kalit so'zlar:** *tizimli qizil yuguruk, lyupus nefrit, vitamin D yetishmovchiligi*

**Аннотация :** *Статус витамина D был определен у пациентов которым был поставлен диагноз системная красная волчанка (СКВ) с нефритом. Дефицит и недостаточность витамина Д наблюдался в большей степени у больных с СКВ/ВН по сравнению при СКВ без нефрита.*

**Ключевые слова:** *системная красная волчанка, люпус нефрит, дефицит витамина D.*

## INTRODUCTION

Vitamin D in addition to its classic function, the human body vitamin deficiency D also associated with many chronic diseases (5,6), These include immune diseases such as multiple sclerosis, rheumatoid arthritis, type 1 diabetes, scleroderma, systemic lupus erythematosus cardiovascular diseases such as coronary heart disease, (7,8). One Meta analysis suggests that lower and higher levels of 25-(OH)- D are associated with increased risk of disease mortality, and that ultraviolet radiation may affect many of the processes associated with vitamin D production in the body(2). As more and more research has been done on vitamin D in recent years, it has been found that it is more and more relevant to many diseases, especially in the field of immune diseases.

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by loss of tolerance to nuclear antigens, impaired activation of T- and B-lymphocytes, followed by polyclonal activation of circulating B-lymphocytes producing

autoreactive autoantibodies, the formation of immune complexes that lead to damage to various tissues and organs (1). This is a complex immunological process involving various cytokines, chemokines, signaling molecules, and receptors. Patients with SLE are dominated by low serum VD levels, ranging from 16% (7) to 95% (8), which may be due to several factors such as photosensitivity, sunscreen use, kidney damage, chronic glucocorticoid use, or antimalarial therapy (9). Lupus nephritis (LN) is a paradigm (model) of immune complex inflammation, the development mechanism of which reflects the pathogenesis of SLE in general. The basis of the disease is polyclonal hyperactivity of the B-cell system, manifested by uncontrolled production of antibodies, and/or defects in T-cell self-regulation, leading to disruption of cell apoptosis and the recognition process with loss of immune tolerance to self antigens, primarily nuclear ones (2). Active LN may be the initial manifestation in approximately 30% of SLE patients (15), and 10–30% of SLE patients may develop end stage renal disease (ESRD) 10 years after the onset of LN (16). Kidney damage disrupts 1-hydroxylation, which is necessary for the development of the active form of VD. Therefore, kidney damage is the strongest predictor of TD <10 ng/mL (17).

In this study, we aimed to compare the relationship between VL levels in patients with SLE with LN and those without SLE without VL and to determine the relationship between VL levels, laboratory and clinical findings in these patients.

**MATERIALS AND METHODS**

The study included 30 patients with SLE without LN (SLE/without LN) and 30 SLE with LN (SLE/LN) collected at the TMA clinic in the departments of rheumatology and nephrology from March 2022 to December 2022. All patients with SLE met at least 4 of the 11 American College of Rheumatology (ACR) criteria since 1997 for the diagnosis of SLE (18). In this study, the LL criteria described by the ACR (18) were adopted: Persistent proteinuria >0.5 g/day or >3+ urinalysis, or cellular casts (erythrocytes, hemoglobin, granular, tubular, or mixed). And also, 30 healthy people of the control group were included in the study. The following variables were recorded: age, sex, duration of SLE, photosensitivity, skin changes, active arthritis, LN activity, and medication. All patients received basic therapy, while none of the patients received VD and calcium supplements. All patients submitted blood and urine samples for complete urinalysis on the same day of clinical evaluation. All patients underwent the following laboratory tests: complete urinalysis, complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum creatinine, the presence of antinuclear autoantibodies (ANA) and anti-ds-DNA, Interleukin 6, 4 and TNF. Urine samples were obtained to evaluate the 24-hour urinary protein content and the presence of urinary casts. Disease activity in a SLE patient was assessed using the Modified SLE 2000 Disease Activity Index (SLE-DAI). VD status was determined by measuring the serum concentration of 25-hydroxyvitamin (25(OH)D), which is the major circulating form of VD. VD deficiency was defined as serum 25(OH)VD <30 ng/mL and above 15 ng/mL,

while VD deficiency was defined as serum 25(OH)VD <15 ng/mL. All statistical analyzes were performed using SPSS for Windows version 20.0. Continuous data were expressed as mean ± standard deviation (SD) and categorical data were expressed as numbers and percentages. Correlations between serum 25(OH)VD levels and continuous data were assessed using a correlation coefficient test.

**RESULTS**

The study included 30 patients with SLE/without LN, 30 patients with SLE/LN and 30 healthy controls. The SLE/no LN group included 29 women (96.6%) and 1 man (3.4%); their age ranged from 24 to 54 years with a mean ± SD of 37.2 ± 9.1 years, and their disease duration ranged from 2 to 18 years with a mean ± SD of 9.0 ± 4.3 years. The SLE/LN group included 27 women (90.0%) and 3 men (10.0%); their age ranged from 26 to 53 years with a mean ± SD of 39.7 ± 8.8 years, and their disease duration ranged from 1 to 15 years with a mean ± SD of 7.6 ± 3.7 years. The control group included 27 women (90.0%) and 3 men (10.0%); their age ranged from 25 to 53 years with a mean ± SD of 41.3 ± 7.5 years. There were no significant differences between the studied groups in terms of age and sex composition.

Comparison of serum 25(OH)VD levels between groups

The mean serum 25(OH)VD level in the SLE/LN group was 16.2 ± 5.3 ng/ml compared with 29.2 ± 8.5 ng/ml in the SLE/no LN group. This difference was significant (p=0.015). The mean serum 25(OH)VD level was also significantly lower in the SLE/LN group compared to the control group (16.2 ± 5.3 vs. 36.5 ± 14.1 ng/mL, p<0.001). In addition, in the SLE/non-LN group, the mean serum 25(OH)VD level was significantly lower than in the control group (29.2 ± 8.5 vs. 36.5 ± 14.1 ng/mL, p = 0.031) (Fig. 1).

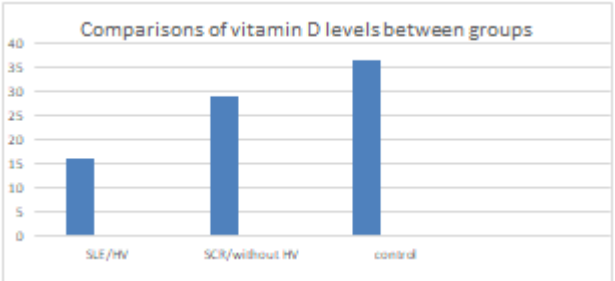


**Figure 1**. Comparison of serum 25(OH)VD levels (ng/mL) among patients with SLE/LN, SLE/without LN, and controls.

In terms of VD status among groups, the highest frequency of VD deficiency was found in the SLE/VL group, followed by the SLE/no VL group, while it was lowest in the control group. Likewise, the frequency of VD insufficiency is highest in the SLE/LN group and lowest in the control group. These differences were significant (p=0.013) (Table 1).

**Table 1**. Comparison of serum 25(OH)VD status between groups.

| | SLE/VL group | | SLE/no VL group | | Control group | | p |
|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | |
| Deficit | 8 | 26.7 | 6 | 20 | 4 | 13.3 | 0.011 |
| Failure | 20 | 66.7 | 16 | 63.3 | 13 | 4 3.3 | 0.015 |
| Ordinary | 3 | 6.7 | 5 | 16.7 | 13 | 4 3.3 | 0.013 |

Comparison of SLE/LN and SLE/non-LN groups

Table 2 compares clinical and laboratory data between SLE/LN and SLE/no LN groups. The incidence of clinical manifestations and drug use did not differ significantly between the SLE/VL and SLE/LN-free groups. None of the patients in the SLE/Non-LN group had proteinuria, hematuria, or urinary casts, while 56.7%, 36.7%, and 23.3% of patients in the SLE/VL group had proteinuria, hematuria, and urinary cylinders, respectively ($p<0.001$). The SLE/VL group was more likely to have low C3 ($p=0.037$), low C4 ($p=0.035$), and anti-dsDNA positivity ($p=0.018$) than the SLE/LN group.

| | SLE/VL group | | SLE/no VL group | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Fatigue | 24 | 80 | 22 | 73.3 | 0.541 |
| Mucosal ulcer | 11 | 36.7 | 9 | 30 | 0.584 |
| Rash | 27 | 90 | 25 | 83.3 | 0.447 |
| Light sensitivity | 27 | 90 | 25 | 83.3 | 0.447 |
| alopecia | 14 | 46.7 | 9 | 30.3 | 0.184 |
| Arthritis | 24 | 80 | 19 | 63.3 | 0.152 |
| Pleurity | 9 | 30 | 5 | 16.7 | 0.222 |
| Pericarditis | 4 | 13.3 | 3 | 10 | 0.687 |
| Proteinuria | 17 | 56.7 | 0 | 0% | <0,001 |
| Hematuria | 11 | 36.7 | 0 | 0% | <0,001 |
| Anti-dsDNA | 22 | 73.3 | 14 | 46.70% | 0.018 |

**Table 2.** Comparison of frequency of clinical and laboratory markers between patient with SLE/LN Patients with SLE/without LN.

Correlation of the level of 25(OH)VD in blood serum with clinical and laboratory data.

In the SLE/LN group and in the SLE/LN-free group, serum 25(OH)VD was inversely correlated with SLE-DAI (p=0.012 and p=0.037, respectively), with ESR (p=0.016 and 0.049, respectively), and with serum creatinine level (p=0.015) only in the SLE/LN group, while the serum 25(OH)VD level does not have a significant relationship with the age of the patients, the duration of SLE (Table 3).

| | SLE/VL group | | SLE/no VL group | |
|---|---|---|---|---|
| | p | n | p | n |
| **Age** | 0.136 | 0.473 | 0.308 | 0.098 |
| **SLE duration** | -0.11 | 0.543 | -0.146 | 0.442 |
| **SLE-DAI score** | -0.453 | 0.012 | -0.382 | 0.037 |
| **ESR** | -0.436 | 0.016 | -0.363 | 0.049 |
| **SRP** | 0.103 | 0.584 | 0.106 | 0.574 |
| **Serum creatinine** | -0.441 | 0.015 | -0.187 | 0.322 |

**Table 3** Correlation of serum 25(OH)VD levels with clinical and laboratory data in patients with SLE/LN and patients with SLE/without LN.

**Discussions:** The main findings of the present study are that (a) VD is more common in SLE/LN patients than in SLE/non-LN patients, and VD is more common in both groups than in controls, (b) VD levels serum levels were inversely correlated with SLE-DAI score, (c) low serum VD was significantly associated with fatigue and photosensitivity in SLE patients, and (d) in SLE/LN patients, low vitamin D was associated with proteinuria and anti-dsDNA. Among the SLE patients who participated in the present study, 88.3% of patients had a low level of VD in the blood serum, while 23.3% had VD deficiency and 65% of patients had insufficiency. Abaza et al reported a prevalence of vitamin D deficiency and insufficiency of 73% and 23% among SLE patients in Egypt, respectively. Another study reported that the overall prevalence of VD insufficiency and VD deficiency among patients with SLE was 69% and 39%, respectively. In addition, Korach et al. found lower serum VD levels in SLE patients compared to controls. These results generally confirm that low serum vitamin D predominates among SLE patients. Moreover, our results are consistent with the results of studies conducted in other countries, at different geographic locations and latitudes. The prevalence of vitamin D deficiency in SLE patients was 55% in Brazilians, 66.7% in Canadians (20), 81.9% in Hungarians (16) and 98.8% in SLE patients from Saudi Arabia. In Saudi Arabia, 55% of the control group had skin manifestation deficiency, which can be explained by their traditional clothing, which greatly reduces the likelihood of sun exposure.

Furthermore, consistent with our findings, previous studies have shown that mean serum vitamin D in SLE patients was significantly lower than in healthy controls (2, 12). The results of our study showed that the SLE/LN group had the highest incidence of VD deficiency and insufficiency, followed by the SLE/LN group, while the control

group had the lowest frequency. Similarly, when serum vitamin D was expressed in ng/mL, our results showed that the SLE/LN group had significantly lower serum vitamin D than those in the SLE/non-LN group, as well as compared to healthy controls. In addition, patients in the SLE/non-LN group had significantly lower mean serum vitamin D levels than healthy controls. Consistent with our results, a strong association between vitamin D deficiency and LN has been reported (20), and patients with SLE/LN have a higher prevalence of vitamin D deficiency (17). Our results showed that serum VP levels were inversely correlated with SLE-DAI scores in the SLE/LN group as well as in the SLE/LN-free group. In addition, mean serum VD levels were significantly lower in patients with active SLE than in those with inactive disease (20). The study did not find a significant association between serum VD levels and the duration of SLE, which is supported by many other studies (15,19) indicating that VD status is more affected by how the disease manifests itself clinically than by the duration of the disease. VD is inversely related to proteinuria and anti-dsDNA in the SLE/LN patient group. The results of the present study revealed a significant association between low serum VD levels and anti-dsDNA antibodies. In support of our results, other studies have reported a strong inverse relationship between VD and anti-dsDNA antibodies (10, 13). Studies have shown that the presence of proteinuria and photosensitivity is also associated with lower serum VD levels in the regression analysis test. Consistent with these findings, kidney injury (OR=13.3; $p<0.001$) followed by photosensitivity (OR=12.9; $p<0.001$) was found to be the strongest predictor of low VP (17). In addition, according to our study, serum creatinine was found to be the strongest predictor of low serum VD in a regression analysis test (20). To confirm the results of the present study, it is recommended to study the relationship between VD and LN in a larger number of patients.

**CONCLUSION**

Vitamin D deficiency and insufficiency predominate in patients with SLE and are more common in patients with SLE-LN. Low serum vitamin D levels are significantly correlated with higher disease activity and ESR. Low serum VD levels are strongly associated with the presence of fatigue and photosensitivity. The strongest factors determining the level of VD in the blood serum of patients with SLE were the presence of LN and photosensitivity.

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