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Vitamin D3 Serum Level Relationship with Severity and Activity of Lupus Disease

Elham Rajaei[1], Karim Mola[2*], Mehrdad Dargahi-Malamir[3] and Sahar Hatami[4]

[1]Department of Rheumatology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[2]Department of Internal Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[3]Department of Internal Medicine, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[4]Internal Group, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: The importance of vitamin D and its inhibitory effects has been proven in many autoimmune diseases. The present study was conducted to determine the relationship between serum levels of vitamin D3 and the severity and activity of lupus disease.
Materials and Methods: In a descriptive-analytical study, serum levels of vitamin D3 were measured in 100 patients with lupus and 100 non-infected individuals as a control group with matching age and sex. The deficiency and insufficient level of vitamin D was calculated based on 10 and 30 ng/mL, respectively. The medical history of all patients was checked out, and the disease activity was evaluated based on SLEDAI criteria. Finally, the collected data were analysed by SPSS software.
Result: In the present study 96 women and 4 men with lupus participated. The mean level of

**Corresponding author: E-mail: medresearchers@gmail.com;*

vitamin D3 in the lupus patients group was significantly higher than the control group (42.44 ± 16.87 ng/mL vs. 81.69 ± 13.30 ng/mL; p=0.012). Also, 79% of patients with lupus and 87% of patients in the control group had deficiency and insufficient vitamin D levels. There was no significant relationship between vitamin D3 level and severity of disease (SLEDAI) (P = 0.362). But there was a significant relationship between the duration of the disease and serum levels of vitamin D3 (P = 0.045).

Conclusion: Given that vitamin D deficiency in the control group and SLE patients are of common difficulties, but vitamin D levels in patients with SLE did not correlate with the disease activity.

Keywords: Vitamin D level; systemic lupus erythematosus; disease activity (SLEDAI).

1. INTRODUCTION

Vitamin D is a group of soluble lipid steroids that synthesised in vitamin D2 and in vitamin D3, mainly in the skin after ultraviolet light. In the liver, it is converted to calcidiol, and then transformed to the calcitriol with inherent metabolism activity of the kidneys. Calcitriol induces its effects with the help of vitamin D receptors that are present in the nucleus of target tissue cells. Stability of calcium levels and bone density is one of the known effects of vitamin D [1,2].

Laboratory experiments have shown that vitamin D3 leads to chemotaxis exacerbations and activates macrophage phagocytosis, inhibiting the production of IL-17 and also with the reduction in production and differentiation of B cells these features result in reduced production and insufficient immunoglobulins and autoantibodies. In addition, studies have shown that the use of VDR agonists leads to the stimulation of NKT cells, which ultimately results in a reduction in Th1 responsiveness. Calcitriol also leads to an increase in apoptosis and dendritic cell suppress [3,4]. Each of the vitamin D-induced immune pathways has profound consequences for patients with SLE [5]. Systemic Lupus Erythematosus (SLE) is an autoimmune disorder and one of the most common vascular collagen diseases. The incidence of this disease ranges from 20 to 150 per 100,000 people, and the incidence ratio of this in young women of fertility age is 9 to 1 [6].

Microvascular inflammation of multiple organs with the production of autoantibodies is the main inherent properties and a key feature of this disease. Although all the mechanisms and factors involved in the incidence of SLE have not been fully disclosed yet, the role of genetic, racial, hormonal, autoimmune, some environmental factors and infections has been proven. The role of vitamin D3 Immunomodulatory in patients with lupus has also been proven in many studies [2,7]. In many recent studies, among environmental factors, the role of vitamin D3 in autoimmunity have been reported [8,9].

Considering the relationship between vitamin D deficiency and severity of SLE disease ant its activity, also considering a gap of knowledge in this regard with few studies done, the present study was conducted to determine the relationship between serum levels of vitamin D3 and the severity and activity of lupus disease.

2. MATERIALS AND METHODS

This present cross-sectional study was performed in one year period on lupus and healthy subjects (as controls) referred to a private clinic in Ahvaz in 2016. The sample size of this study was calculated according to previous study [10]. Inclusion criteria were diagnosed patients with SLE according to ACR2012 criteria and age of less than 75 years old. Also, exclusion criteria were over 5 years of disease duration, pregnancy, acute infectious diseases, an association of disease with a musculoskeletal disease which was simultaneous and effective on the severity of the symptoms of the patient. Cases for the control group were also selected from the general population and referrals to the neurologist's clinic at an adjacent office. Control group cases reveal no clue of rheumatologic disease. Samples of this group were non-random selected and available sampling and age and sex synchronisation with the group of patients with lupus erythematosus.

In this study, all cases (including the case group of lupus patients and non-lupus group) were sampled in a seasonal period. A score higher than or equal to 6 is considered as criteria for

disease activity [11]. Also, the level of activity is evaluated in 3 scales: poor activity: score 1-5, average activity: 6-12 points, intense activity: score 13-20. It should be noted that the severity of the disease was calculated online by providing the necessary factors and variables. Finally, after collecting data, serum levels of vitamin D3 and SLEDAI index were entered into SPSS software and analyzed. Serum levels of vitamin D3 was measured by ELISA method in verified standard laboratory. The mean serum level of vitamin D3 in lupus patients was compared with those in the non-lupus group. Also, the association between the deficiency and inadequate serum vitamin D3 level with the time of diagnosis, the severity of lupus disease based on SLEDAI index, taking cortex, and anti-malarial use were investigated.

To measure the significance of differences and to compare quantitative and qualitative variables, t-test and Chi-square test were used respectively. Finally, to determine the association between vitamin D3 level according to Likert variables, severity and activity of lupus disease, One-way analysis of variance (ANOVA) with Post Hoc Tukey's test and Spearman correlation test was used. The significance level in the tests was considered to be 0.05.

3. RESULTS

In this study, the relationship between vitamin D3 levels and lupus disease, severity and activity of the disease, and other variables were investigated. One hundred patients with lupus and 100 healthy individuals as control group were studied. Serum levels of vitamin D3 were measured for all individuals. In this study, 96 women and 4 men with lupus were participated. The mean age of lupus patients was 36.07 ± 10.16 years (range 11-61 years). The results of the statistical analysis did not show a significant difference between age and sex between the two groups (P>0.05). The mean duration of lupus involvement was 2.11 ± 1.29 years (range 1 to 5 years). The mean level of vitamin D3 in the lupus patient group was 24.44 ± 16.87 (range 5-103) and in the control group was 81.69 ± 13.30 ng/ml (range 5 to 65), and so, significant statistical difference were observed between the two groups (P = 0.012). Also, 79% of patients with lupus and 87% of patients in the control group had a deficiency and insufficient vitamin D level (Fig. 1).

In the present study, there was no significant relationship between gender and serum levels of vitamin D3 (P=0.694). Also, the results of this study showed that there was no significant relationship between age and serum level of vitamin D3 (P= 0.803).

In this study, there was a significant relationship between the duration of the disease and serum levels of vitamin D3 (P = 0.045), so that the mean duration of the disease in patients with vitamin D3 deficiency was higher than those with a sufficient level of vitamin D3. In this research, there was no significant relationship between BMI and vitamin D3 levels in patients with lupus (P = 0.849).

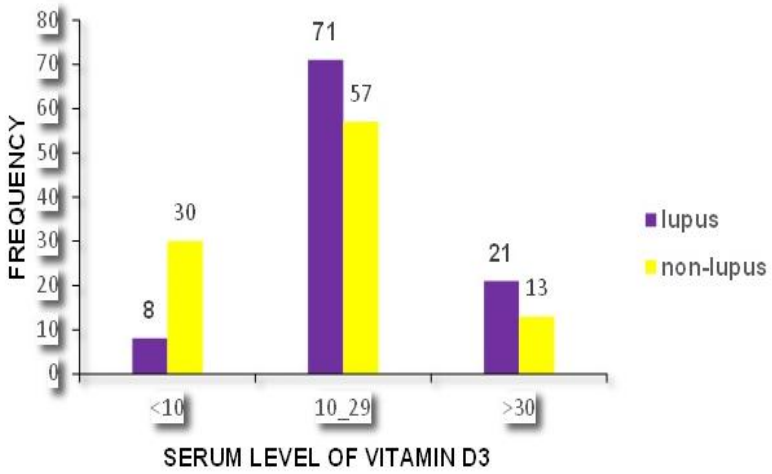

Fig. 1. Comparison of serum levels of vitamin D3 in the two groups

The results of this study showed no significant relationship between smoking, anti-malaria use and vitamin D3 levels (P<0.05). The mean of the SLEDAI index was calculated to be between 31.22 ± 7.63 in lupus patients (range 1 to 45). The index was more than 13 in most people (52%) and only 12% of the patients had a lower than 6 (mild disease) index. The vitamin D3 level was higher in people with severe disease activity than in other subjects (Table 1) but the results showed no significant relationship between vitamin D3 and severity of disease (SLEDAI) (P = 0.362) (Fig. 2).

4. DISCUSSION

Many studies have shown that the prevalence of vitamin D deficiency is high in SLE patients, but its relation with the severity and activity of the disease is a matter of discuss. In this regard there is controversy among literatures. Therefore, the present study was conducted to determine the relationship between serum level of vitamin D3 and the severity and activity of lupus disease.

In this study, the results showed vitamin D deficiency in 8% and inadequate levels of vitamin D in 71% of patients with lupus. Also, vitamin D deficiency was significantly higher in the control group than in patients with lupus. These results indicate a high prevalence of vitamin D deficiency in the general population. These findings is similar to the results explained by Fragoso et al. [10] which reveals that modern life activities cause a lack of sunlight which lead to the reduction in the synthesis of vitamin D.

In contrast with the results of this study, Emam et al. [12] in a study indicated that vitamin D levels in lupus patients was significantly lower than individuals in the control group. They also represented that 85% of patients with lupus and 60% of the control group had vitamin D deficiency/insufficiency (>30 ng/ml). In addition, results of Fragoso et al. showed that deficiency and insufficiency of vitamin D3 levels were found in 57.7% of patients with lupus and 39% in the control group. Also, there was a significant difference between the levels of vitamin D3 in the group with lupus (29.2 ng/mL) and the control group (33.12 ng/mL) [10]. These findings were in contrast with the findings of the present study.

The results of the study of de Souza et al. (2014), unlike the present study, showed that the prevalence of vitamin D3 deficiency was higher in people with lupus (55%) than in the normal population (8%) [13].

Table 1. Relationship between vitamin D3 level and severity of lupus

	Severity of disease activity	Frequency percent	VitD Value(ng/ml) Standard Deviation±Mean	p-value
Index SLEDAI	Low (1-5)	12	20.25±15.45	0.362
	Mean (6-12)	36	20.58±11.27	
	Sever (higher than 13)	52	28.08±9.63	

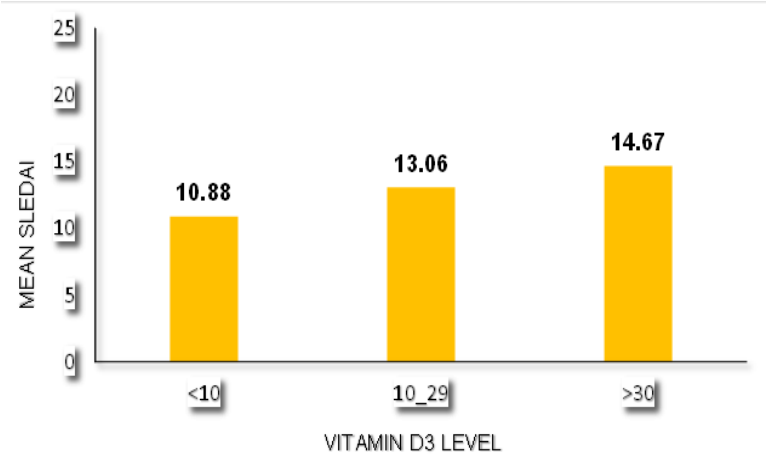

Fig. 2. The mean of SLEDAI index according to vitamin D3 level in lupus patients

The results of this study were not consistent with the findings of the Damanhouri study [14]; this study was performed on 165 SLE patients and 124 healthy people as control and showed that vitamin D deficiency was significantly higher in SLE than in control group (98.8% versus 55%).

In another study, Handono et al. [15] showed that 20.37% of 45 women with SLE had normal levels of vitamin D, 24.7% had inadequate levels and 55.56% had vitamin D deficiency.

The results of Attar and Siddiqui (2013) also showed that there was no significant relationship between serum level of vitamin D and disease activity score (SLEDAI-2K) [16].

The reason for the difference in the results of the studies can be related to the low number of samples, the very low activity of the disease [17], and the heterogeneity of treatment, especially HCQ [9]. The study of Ruiz-Irastorza et al. [18] showed that light sensitivity and light protection are respectively predictors of inadequate and deficiency of vitamin D. They reported that both lupus and healthy people who were allergic to light and consistently used sun protection were at risk for vitamin D3 deficiency.

The relationship between low levels of vitamin D and high SLEDAI scores in some studies has shown that vitamin D can help to prevent the progression of SLE. However, all studies reporting this relationship were cross-sectional, and therefore, considering hierarchy of evidence, it is not certain that the vitamin D status affects the severity of the disease or not.

In the present study, there was a significant relationship between the level of vitamin D3 and the duration of the disease. These results indicate that the short disease duration reduces the likelihood of affecting the level of vitamin D on the activity of the disease, so it can be concluded that vitamin D deficiency is caused by the disease and does not cause disease activity. Also, there was no significant relationship between age, BMI, smoking and anti-malarial drugs (hydroxychloroquine) and vitamin D3 levels. Also, because all patients used corticosteroids in the study, it was not possible to investigate the relationship between their use and vitamin D levels. Hydroxychloroquine (HCQ) is an important drug for SLE patients, and has been associated with high bone mineral density in SLE patients, and HCC seemed to have an effect on calcium and bone metabolism [19]. This drug can prevent the conversion of 25(PH)D to $1.25(OH)_2D$, thereby reducing the level of the most active form of vitamin D [20], but the precise mechanism of this operation was unknown.

Finally, the strength points and advantages of this study can be seen in the presence of control group and uniformity of patients in terms of treatment. The study also encountered some constraints: Since this study was a cross-sectional study, it is not suitable to study casualty, so the main cause of vitamin D deficiency was not investigated. Exposure to sunlight, the use of sunscreens, and the use of vitamin supplements are affecting variables on the level of vitamin D but were not investigated in this study. Cross-sectional measurement of serum levels of vitamin D and no follow up to study the severity of the disease over time can be considered as limitations.

5. CONCLUSION

The results of this study showed that vitamin D deficiency was not only prevalent in patients with lupus, but even more in the healthy individuals as a control group. It indicates the necessity of treatment with vitamin D3 supplements in patients with lupus as well as general population.

In patients with lupus, there was no significant relationship between the level of vitamin D and the severity of the disease, so the results reveals that vitamin D deficiency is not a risk factor in the severity and development of SLE disease. In contrast, results demonstrated that the duration of the disease was associated with the reduction of vitamin D levels in SLE patients.

Considering controversies of results of similar studies, also with limitation of this study – such as study type and sample size- a definitive and accurate conclusion about the relationship of vitamin D and the severity and activity of lupus disease requires further prospective studies with larger study population.

CONSENT

As per international standard or university standard written participant consent has been collected and preserved by the authors.

ETHICAL APPROVAL

The registration number of this thesis is 1827, the approved code is U_95111, and the approved date was 24 June 2017.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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