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THE INFLUENCE OF VITAMIN D ON LUPUS NEPHRITIS ACTIVITY

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ABSTRACT

The aim of our study was to determine the serum vitamin D levels in patients with lupus nephritis and its association with clinical and laboratory parameters of the disease. Vitamin D levels were studied in patients with systemic lupus erythematosus (SLE) with nephritis, as well as in 20 healthy individuals in the control group. In addition to general clinical examinations, all patients underwent immunological analysis, and the results were compared with vitamin D levels. According to the obtained data, IL-6 and TNF-alpha levels were significantly higher in patients with active lupus nephritis compared to the control group and the group of patients with minimal disease activity. Additionally, IL-4 levels were also elevated in the first group. High IL-6 and TNF-alpha levels were more frequently observed in the group of patients with active lupus nephritis and showed an inverse correlation with vitamin D levels. These findings confirm the strong association between disease activity and vitamin D levels, indicating the need for vitamin D level correction in SLE patients depending on the degree of disease activity.

Key words: systemic lupus erythematosus, lupus nephritis, vitamin D, interleukin.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the excessive production of autoantibodies against nuclear components, leading to immune inflammation and damage to internal organs and tissues [11, 19]. The prevalence of SLE varies according to different sources, ranging from 4 to 250 cases per 100,000 people [11, 2, 1, 5]. Over the past decade, the increasing detection of latent cases and improved treatment efficacy have enhanced the quality of life for SLE patients [2, 8, 10, 14]. Kidney involvement in SLE, known as lupus nephritis (LN), is one of the most common and severe complications, significantly worsening disease prognosis. The state of the kidneys

serves as a critical indicator for assessing disease progression and prognosis. Lupus nephritis is an immune complex-mediated inflammation that plays a key role in the pathogenesis of SLE [14]. It is characterized by excessive activation of B lymphocytes, which are crucial for humoral immunity, leading to the production of autoantibodies against cytoplasmic and nuclear proteins. Recent studies suggest that vitamin D plays a crucial role in modulating immune system activity. It helps regulate T and B cell functions, potentially preventing autoimmune processes. In lupus nephritis, the immune system is pathologically overactive, resulting in kidney damage. Additionally, vitamin D has anti-inflammatory properties, reducing inflammatory modulators such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which may help lower inflammation in lupus nephritis. Another important function of vitamin D is its protective effect on kidney tissue. It limits mesangial cell proliferation and prevents kidney fibrosis. These findings suggest that correcting vitamin D levels in the blood may play a significant role in the development and progression of lupus nephritis. Recent data indicate that vitamin D deficiency is present in two-thirds of SLE patients, with severe deficiency observed in one out of five patients [14]. Sunlight exposure is known to trigger SLE, leading patients to avoid direct sun exposure, which could explain the high prevalence of vitamin D deficiency among them. Moreover, factors such as renal failure, prolonged use of medications (e.g., glucocorticoids and anticonvulsants), and other conditions contribute to hypovitaminosis D in SLE patients [15-16]. A study by D.L. Kamens et al., involving 123 SLE patients and 140 controls, demonstrated significantly higher vitamin D deficiency among SLE patients [17]. The study revealed that 67% of SLE patients had vitamin D deficiency, with African Americans showing lower levels (16 ng/mL) compared to Caucasians (31 ng/mL). Critically low vitamin D levels (<10 ng/mL) were found in 22 patients, who also exhibited increased photosensitivity and kidney involvement. Similar findings were observed in patients with long-standing SLE [18, 19].

MATERIALS AND METHODS

This study was conducted at the Department of Therapeutic Disciplines No. 2, Tashkent State Dental Institute, in collaboration with the Republican Specialized Scientific and Practical Medical Center for Nephrology and Kidney Transplantation. A total of 108 patients with lupus nephritis secondary to SLE were selected and underwent comprehensive clinical and laboratory examinations. Based on lupus nephritis activity, patients were divided into two groups: active lupus nephritis

(Group 1, n=53) and minimally active lupus nephritis (Group 2, n=55). Additionally, 20 healthy individuals were included as the control group.

RESULTS

The study included 53 patients with active lupus nephritis (Group 1), 55 patients with minimally active lupus nephritis (Group 2), and 20 healthy individuals (Group 3). In Group 1, 4 (7.5%) were male and 49 (92.5%) were female, whereas in Group 2, 5 (9%) were male and 50 (91%) were female.

1-table. Analysis of Patient Gender, Disease Duration, and Activity Between Groups

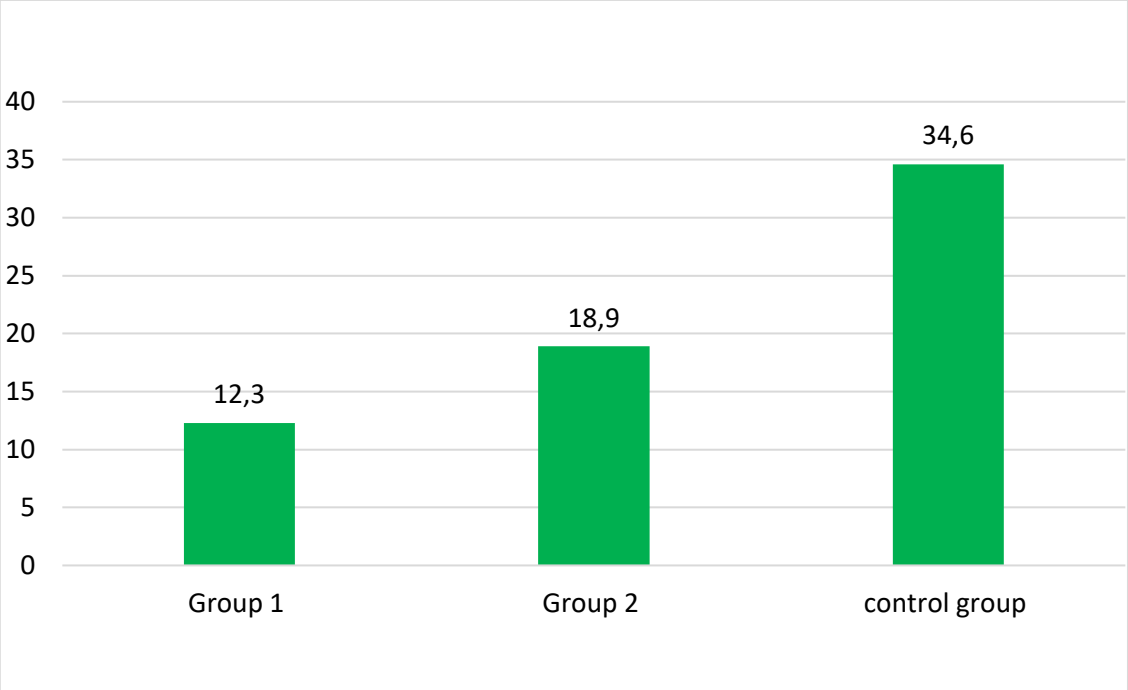
Indicator		1st group (n=53)	2nd group (n=55)
Age (years)		32.16 ± 6.41	33.54 ± 11.64
Gender	**Female (F)**	4 (7.5%)	5 (9%)
	Male (M)	49 (92.5%)	50 (91%)
Disease duration (years)		8.22 ± 5.3	7.73 ± 5.02
Activity level	**I**	18 (34%)	22 (40%)
	II	24 (45%)	26 (49%)
	III	11 (20.7%)	7 (11%)
Course of disease	**Acute (A)**	3 (5.6%)	-
	Subacute (S)	32 (60.3%)	23 (42.8%)
	Chronic (C)	24 (45.2%)	26 (47.2%)
SLEDAI score	**3-12 (inactive)**	31 (58.5%)	37 (67.2%)
	>12 (active)	22 (41.5%)	18 (32.7%)

The control group consisted of 9 males and 11 females. The mean disease duration was 8.22 ± 5.3 years in Group 1 and 7.73 ± 5.02 years in Group 2. In the 1st group, 18 patients (34%) had grade I TQT activity, while 24 patients (45%) and 11 patients (20.7%) had grade II and III activity, respectively. In the 2nd group, these

indicators were 22 patients (40%), 26 patients (49%), and 7 patients (11%), respectively. Regarding the course of systemic lupus erythematosus, in the 1st group, the disease was acute in 3 patients (5.6%), subacute in 32 patients (60.3%), and chronic in 24 patients (45.2%). In the 2nd group, only subacute (23 patients, 42.8%) and chronic (26 patients, 47.2%) forms of the disease were observed. According to the SLEDAI scale, in the 1st group, 58.5% of cases were assessed as inactive, while 41.5% were active. In the 2nd group, 67.2% of cases were inactive, whereas 32.7% were active (Table 1).

In addition to general clinical tests, the main objectives of our study were to examine the level of vitamin D in the blood and the status of interleukins (IL-6, IL-4, ONO-alpha). According to the results of the study, the status of vitamin D in the blood in the groups was as follows.

Comparison of blood vitamin D levels (ng/mL) in patients with SLE/active LN, SLE/minimal active LN and control groups



Vitamin D levels varied significantly among the groups. The control group had the highest mean vitamin D level (34.6 ± 2.4 ng/mL), while the lowest levels were observed in Group 1 (12.3 ± 1.5 ng/mL), which was significantly lower than in Group 2 (18.9 ± 2.1 ng/mL) ($p<0.001$). Vitamin D levels were categorized as follows: normal (≥30 ng/mL), deficiency (20-29 ng/mL), and severe deficiency (<20 ng/mL). Accordingly, when comparing the groups, a significant difference was found between them, $p=0.05$ (Table 2).

Table-2. Comparison of blood vitamin D status between groups, (n = 128).

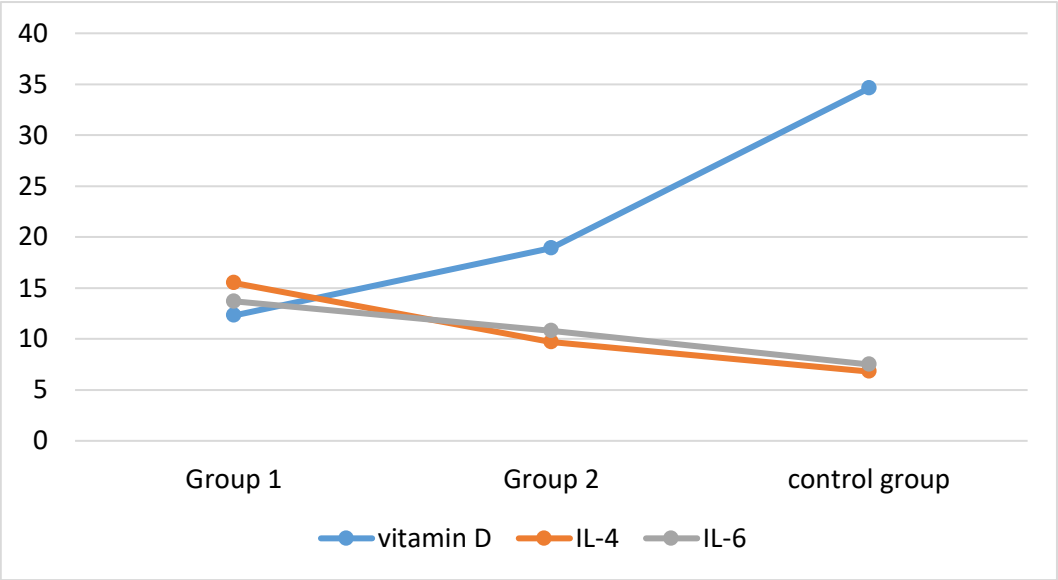
vitamin D	Control gr (n =20)	1-group (n =53)	2-group (n =55)	Xi2 P=0,05 (1-2)	Xi2 P=0,05 (1-3)	Xi2 P=0,05 (2-3)
	1	*2*	*3*			
normal (≥30ng/ml)	14 (70%)	2 (3,7%)	9 (16,3%)	37.21	19.84	4.83
shortage (>20ng/ml)	6 (30%)	27 (50,9%)	30 (54,5%)	19.25	12.24	0.14
D deficiency (<20 ng/ml)	-	24 (45,2%)	16 (29,2%)	-	-	3.03

According to the analysis results, the number of patients with normal vitamin D levels in the blood was significantly lower in Groups 1 and 2 compared to the control group. Specifically, in the control group, 70% of patients had normal vitamin D levels, whereas this indicator was 3.7% in Group 1 and 16.3% in Group 2. There was also a significant difference between Groups 1 and 2, with the lowest percentage observed in the group of patients with active lupus nephritis. The percentage of individuals with vitamin D insufficiency was 30% in the control group, while it was significantly higher in Groups 1 and 2, reaching 50.9% and 54.5%, respectively. Vitamin D deficiency was not observed in the control group, whereas it was the highest in Group 1 at 45.2%, followed by Group 2 at 29.2%. Since IL-6, IL-4, and ONO-alpha are markers of kidney damage in systemic lupus erythematosus, immunological parameters in the groups were analyzed as follows. According to the results of immunological analysis, all parameters were higher in groups 1 and 2 than in the control group, with a significant difference between the studied groups. Accordingly, the amount of IL-4 in patients in group 1 was higher than in group 2 and the control group by 16.51±1.32 ($p<0.001$).

3-table. Comparison of immunological assay results between groups (n = 128).

Indicators	**Control gr (n =20)**	**1-group (n =53)**	**2-group (n =55)**	**Xi2 P=0,05 (1-2)**	**Xi2 P=0,05 (1-3)**	**Xi2 P=0,05 (2-3)**
IL-4, Pg/ml	6.85±1.25	16.51±2.32	9.76±1.34	0,001	0,001	0,05
IL-6, Pg/ml	4.53±1.32	23.69±1.21	10.87±0.68	0,001	0,001	0,05
TFN-ǎ	4.32±1.24	10.35±1.25	8.53±0.58	0,001	0,001	0,05

Cytokine analysis revealed significant differences in inflammatory markers among the groups. IL-6 levels were highest in Group 1 (23.69 ± 1.21 pg/mL) compared to Group 2 (10.87 ± 0.68 pg/mL) and the control group (4.53 ± 1.32 pg/mL) ($p<0.001$). Similarly, TNF-α levels were significantly elevated in Group 1 (10.35 ± 1.25 pg/mL) compared to Group 2 (8.53 ± 0.58 pg/mL) and the control group (4.32 ± 1.24 pg/mL). IL-4 levels followed a similar pattern, with the highest levels in Group 1 (16.51 ± 2.32 pg/mL), followed by Group 2 (9.76 ± 1.34 pg/mL) and the control group (6.85 ± 1.25 pg/mL) ($p<0.001$). A strong inverse correlation was observed between vitamin D levels and IL-6, as well as IL-4 levels, with the correlation being more pronounced for IL-6.



According to the analysis results, the maximum values of the indicators were as follows: In Group 1, the maximum IL-4 level was 17.31, while in Group 2, it was 10.12. The maximum IL-6 level in Groups 1 and 2 was 25.71 and 12.34, respectively. Additionally, the study revealed an inverse correlation between IL-6 levels and vitamin D levels. A similar relationship was observed between vitamin D and IL-4 levels, although it was less pronounced (Figure 2).

CONCLUSION

Regarding the results of the immunological analysis conducted during the study, IL-6 and TNF-alpha levels were significantly higher in patients with active lupus nephritis compared to the control group and the group of patients with minimally active LN. IL-4 levels were also elevated in Group 1. Higher IL-6 and TNF-alpha levels were more frequently observed in the group of patients with active

LN, and these indicators showed an inverse correlation with vitamin D levels. These findings suggest an intrinsic relationship between disease activity and vitamin D levels, confirming the necessity of vitamin D correction in patients with different activity levels of SLE.

REFERENCES

1. AA Xasanov, FT Xusanxodjaeva, NZ Muxiddinova vitamin d i immunitet journal of innovations in scientific and educational research 7 (5), 144-151
2. Adorini, L., & Penna, G. (2008). Control of autoimmune diseases by the vitamin D endocrine system. Nature clinical practice. Rheumatology, 4(8), 404–412. https://doi.org/10.1038/ncprheum0855
3. Borchers, A. T., et al. (2010). The geoepidemiology of systemic lupus erythematosus. Autoimmunity reviews, 9(5), A277–A287. https://doi.org/10.1016/j.autrev.2009.12.008
4. BX Bobomurodovich, ShL Xusanovna, XF Tulkunovna surunkali buyrak kasalligini II-III bosqichida antiagregant terapiya fonida buyrak funksional zaxirasini baholash Oriental Renaissance: Innovative, educational, natural and social sciences
5. Chew, C., et al. (2021). Lower vitamin D is associated with metabolic syndrome and insulin resistance in systemic lupus: data from an international inception cohort. Rheumatology (Oxford, England), 60(10), 4737–4747. https://doi.org/10.1093/rheumatology/keab090
6. Dankers, W., et al. (2017). Vitamin D in Autoimmunity: Molecular Mechanisms and Therapeutic Potential. Frontiers in immunology, 7, 697. https://doi.org/10.3389/fimmu.2016.00697
7. FT Xusanxodjaeva SOVREMENNIY PODXOD K VITAMINU D I SISTEMNOY KRASNOY VOLChANKE Meditsina i innovasii 8 (4), 144-154
8. FT Xusanxodjaeva, AA Xasanov, MS Ismailova Vliyaniya vitamina d na sostoyanie pochek u bolnix s skv lyupus nefritom Novosti obrazovaniya: issledovanie v XXI veke 1 (11), 267-278
9. FT Xusanxodjaeva, FE Salyamova, DT Axmadalieva, GA Kabilova Noviy podxod k lecheniyu infeksiy mochevix putey u bolnix saxarnim diabetom 2 tipa putem dobavleniya vitamina d Uzbek Scholar Journal 10, 407-417
10. FT Xusanxodjaeva, FE Salyamova, NZ Muxitdinova Optimizatsiya lecheniya infeksiy mochevix putey u bolnix saxarnim diabetom 2 tipa putem dobavleniya vitamina D Interdiscipline innovation and scientific research conference 1 (3), 10-20

11. FT Xusanxodjaeva, KM Daminova Lyupus nefrit rivojlanishning patogenetik mexanizmlari MedUnion 2 (1), 261-270

12. FT Xusanxodjaeva, KM Daminova, AA Xasanov Sivorotochniy vitamin D u pasientov s sistemnoy krasnoy volchankoy i yego svyaz s lyupus nefritom Meditsina i innovasii 10 (2), 114-125

13. Ginsberg, C., et al. (2020). Differential effects of phosphate binders on vitamin D metabolism in chronic kidney disease. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 35(4), 616–623. https://doi.org/10.1093/ndt/gfaa010

14. Hassanalilou, T., et al. (2017). Role of vitamin D deficiency in systemic lupus erythematosus incidence and aggravation. Auto- immunity highlights, 9(1), 1. https://doi.org/10.1007/s13317-017-0101-x

15. Heidari, B., et al. (2019). Vitamin D Deficiency and Rheumatoid Arthritis: Epidemiological, Immunological, Clinical and Therapeutic Aspects. Mediterranean journal of rheumatology, 30(2), 94–102. https://doi.org/10.31138/mjr.30.2.94

16. MA Sabirov, FE Salyamova, FT Xusanxodjaeva Narushenie Serdechnogo Ritma U Bolnix S Xronicheskoy Bolezn Pochek Vst Kak Prediktor Serdechno-Sosudistogo Risk Central Asian Journal of Medical and Natural Science 3 (2), 193-196

17. Mathieu C. (2015). Vitamin D and diabetes: Where do we stand?. Diabetes research and clinical practice, 108(2), 201–209. https://doi.org/10.1016/j.diabres.2015.01.036

18. MB Bobokulov, NR Babadjanova, FT Xusanxodjaeva, FE Salyamova, Otsenka morfofunksionalnogo sostoyaniya transplantanta v period posle transplantatsii pochki Uzbek Scholar Journal 10, 418-427

19. SF Erkinovna, XF Tulkunovna, MN Zoxiriddinovna, MS Iskandarovich, Structural and functional features of the myocardium against the background of renal replacement therapy International Journal of Medical Sciences And Clinical Research 2 (11), 01-07

20. Shankar, A. S., et al. (2021). Vitamin D metabolism in human kidney organoids. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 37(1), 190–193. https://doi.org/10.1093/ndt/gfab264

21. XF Tulkunovna, DK Maratovna relationship between vitamin d level and systemic lupus erythematosis disease activity innovative developments and research in education 2 (24), 57-65