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Study of Vitamin D in Patients with Systemic Lupus Erythematosus and Its Association with Lupus Nephritis

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is considered an autoimmune disease that can affect many organs in the body with various clinical manifestations and different severity levels.

Objective: This work aimed to assess the level of vitamin D in the serum of patients with and without lupus nephritis and its association with disease activity, clinical and laboratory findings.

Methods: This cross-sectional study included 150 participants divided into 3 groups: Group 1 (LN group) included 50 SLE cases with lupus nephritis, group II (SLE group) contained 50 SLE cases without lupus nephritis and group III (control group) consisted of 50 healthy and sex-matched subjects. All cases were subjected to assessment of the disease activity by SLE Disease Activity Index 2000 (SLEDAI), renal SLE Disease Activity Index (rSLEDAI) and laboratory investigations [complete blood count (CBC), C- reactive protein (CRP), ESR, anti-ds-DNA, ANA, C3 and C4 concentration, urine analysis, 24-hours' protein in the urine, serum creatinine and serum 25(OH) vitamin D level].

Results: There was a significant difference between the 3 studied groups regarding 25(OH) D where the lowest level was in the LN group (p-value < 0.001). In LN and SLE groups there was a significant relation between serum 25(OH) D titre and SLEDAI (p-value.36, 0.011 respectively). Also, regression analysis test revealed that there was a significant association between 25 (OH) D and HB, WBCs, PLT, Anti-ds DNA, C3, C4, SLEDAI, and renal SLEDAI in LN and SLE groups. Low vitamin D titre showed high frequency in patients with SLE and was more frequent in SLE with lupus nephritis in all grades of low vitamin D titre (Insufficient, Deficient and sever).

Conclusions: There was a significant relation between low vitamin D titre and high and very high disease activity in patients with lupus nephritis.

Keywords: Vitamin D, Systemic lupus erythematosus, Lupus nephritis, Disease activity.

INTRODUCTION

Systemic lupus erythematosus is an autoimmune disease that affects many organs in the body, it has many clinical manifestations (cutaneous, cardiac, neurologic, hematologic, and renal). SLE can also range in intensity from minor to serious (mild, moderate, and severe). Lupus Erythematosus Disease Activity Index (SLEDAI) is the gold standard for assessing disease activity worldwide [1].

It is thought that SLE may be due to variable causes, including genetics, environmental, and hormonal, which all work together to cause this illness. Several studies have shown that SLE has a positive family history [2].

Among the most serious organ symptoms of SLE is lupus nephritis (LN), a type of glomerulonephritis. Lupus nephritis is histologically classified into five distinct classes that represent different manifestations and severities of renal involvement. End-stage kidney disease (ESKD) occurs in 10% of LN cases within 10 years. Renal involvement can interfere with 1-hydroxylation which is essential to make an active form of VD [3].

Vitamin D (VD) is the principal factor that maintains calcium homeostasis. The presence of VD has been linked to improved intestinal calcium intake and renal calcium reabsorption. Further, 1, 25 dihydroxycholecalciferol [1, 25OHD3], the biologically active form of VD, can mediate the immune system. Vitamin D receptor (VDR), a ligand-activated transcription factor that regulates gene expression in the context of immune modulation. In the last decade, there evidence that linked low levels of 25 (OH) D3 (VD3) to an increased risk of many diseases, including diabetes, cardiovascular diseases, dermatological diseases, different forms of cancer, and autoimmune diseases [4].

Studies have linked VD deficiency to SLE, suggesting that it may play a role in the disease's pathogenesis and pathology. Avoiding sunlight, using sunglasses, renal inadequacy, and using medications like glucocorticoids, anticonvulsants, antimalarials, and calcineurin inhibitors 6 are all potential causes of VD deficiency in SLE cases [5]. This work aimed to assess the level of vitamin D in the serum of patients with and without lupus nephritis and its association with disease activity, clinical and laboratory findings.

PATIENTS AND METHODS

This cross-sectional study included 100 SLE patients older than 18 years, who were labelled as having lupus nephritis according to SLICC classification criteria [6] and 50 healthy age- and sex-matched as control group. They were selected from the Outpatient Clinic of Rheumatology, Rehabilitation and Physical Medicine Department of Tanta University Hospitals.

Exclusion criteria: Patients with kidney disease due to causes other than SLE, ESRD with or without dialysis,

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granulomatous disorders, malignancy, and other autoimmune diseases. Also, patients on medications for osteoporosis except for calcium supplements and on VD supplementation or medications that can alter VD metabolism.

The participants were divided into 3 groups: Group I: 50 SLE cases with LN, group II: 50 SLE cases without LN and group III: 50 healthy age- and sex-matched subjects as control group. All were subjected to complete history taking, complete clinical examination, assessment of the disease activity, and laboratory investigation [complete blood count (CBC), C- reactive protein (CRP), ESR, anti-ds-DNA, ANA, C3 and C4 concentration, urine analysis, 24-hours' protein in urine, serum creatinine and serum 25OH vitamin D level.).

Assessment of the disease activity:

The disease activity was assessed according to SLEDAI. The SLEDAI is a global index that evaluates disease activity. It includes 24 items collecting specific manifestations in 9 organ systems: neurological, musculoskeletal, renal, mucocutaneous, general, heart, respiratory, vascular, and hematological. The SLEDAI classifies levels of exercise as follows: no activity (SLEDAI = 0), light activity (SLEDAI = 1-5), moderate activity (SLEDAI =6-10), high activity (SLEDAI =11-19), and very high activity (SLEDAI =20).

To evaluate the severity of kidney disease, researchers used the rSLEDAI. The four factors linked to the kidney were hematuria, pyuria, proteinuria, and urinary casts, which make up the total. The kidney SLEDAI scale includes a 0 (no evidence of renal disease) to a 16 (severe renal disease). To be diagnosed with active lupus nephritis, a case must have a rSLEDAI score of 4 or higher [7].

Measuring VD:

The serum vitamin D level (25, OH VD) was evaluated with an ELISA kit. Estimated levels of insufficient VD were below 30 ng/ml, deficient at below 20 ng/ml, and severely deficient below 12 ng/ml.

Ethical approval: Tanta University Hospitals' Ethical Council approved the study's procedures on March 2021. The participants provided their written consents after being fully informed of the risks involved (approval code: 34489/2/21) in accordance with Helsinki.

Statistical analysis

Statistical analysis was done by SPSS version 27 (IBM©, Armonk, NY, USA). Histograms and the Shapiro-Wilks test were used to determine if the data followed a normal distribution. Parametric quantitative data were summarised and analysed using the ANOVA (F) test and post hoc test for means and standard deviations (Tukey). The Kruskall-Wallis test and the Mann-Whitney U test were used to make group comparisons from the quantitative non-parametric data given as the median and IQR. The Chi-square test was used to analyse qualitative factors given in frequency and percentage (%) formats. The cutoff for statistical significance was a two-tailed P value of less than 0.05. To determine which clinical or laboratory symptoms of SLE are most strongly correlating with blood 25-OH-VD level, we performed a linear regression analysis in the current research. The threshold for statistical significance was $p \leq 0.05$.

RESULTS

There is a significant difference between 3 groups according to 25OHD level (Table 1).

Table (1): Comparison among the three studied groups according to various parameters

		LN (n = 50)	SLE (n = 50)	Controlled (n = 50)	P value	
Age (years)		32.36 ± 8.94	32.28 ± 7.95	35.48 ± 14.8	0.255	
Sex	**Male**	6 (12%)	7 (14%)	11 (22%)	0.352	
	Female	44 (88%)	43 (86%)	39 (78%)		
Marital	**Single**	17 (34%)	13 (26%)	15 (30%)	0.683	
	Married	33 (66%)	37 (74%)	35 (70%)		
25OHD	**Normal (>30)**	0 (0%)	0 (0%)	13 (26%)	<0.001*	P1<0.001*
	Insufficient (20 - 30)	6 (12%)	21 (42%)	15 (30%)		P2<0.001*
	12 – 20 (Deficient)	17 (34%)	24 (48%)	21 (42%)		P3<0.001*
	Severe (<12)	27 (54%)	5 (10%)	1 (2%)		
25OHD		12.86 ± 4.56	18.12 ± 6.15	32.54 ± 10.98	<0.001*	P1<0.001*
						P2<0.001*
						P3<0.001*

Data presented as a mean ± SD or frequency (%). SD: Standard deviation, LN: Lupus nephritis, SLE: Systemic lupus erythematosus, 25OHD: 25-hydroxyvitamin D, p1: p-value for comparing between LN and SLE, p2: p-value for comparing between LN and Controlled, p3: p-value for comparing between SLE and Controlled, *: Statistically significant at $p \leq 0.05$

There was no significant difference between the 2 groups as regards clinical manifestations except for malar rash and oral ulcer (Table 2).

Table (2): Comparison between the LN and SLN groups according to various parameters

		LN (n = 50)	SLE (n = 50)	P value
Special habits	**No smoker**	45 (90%)	44 (88%)	0.749
	Smoker	5 (10%)	6 (12%)	
Onset (years)		7.64 ± 3.8	5.94 ± 3.12	0.017*
Fatigue		39 (78%)	38 (76%)	0.812
Fever		31 (62%)	26 (52%)	0.419
Alopecia		17 (34%)	9 (18%)	0.110
Malar rash		45 (90%)	34 (68%)	0.014*
Ulcer		44 (88%)	30 (60%)	0.003*
Myositis		0 (0.0%)	0 (0.0%)	–
Arthritis		24 (48%)	29 (58%)	0.422
Neuropsychiatric		0 (0.0%)	0 (0.0%)	–
Vacuities		5 (10%)	0 (0%)	0.056
Renal		50 (100.0%)	0 (0.0%)	---
Serositis		0 (0.0%)	0 (0.0%)	–
Hb (mg/dL)		10.34 ± 1.7	10.13 ± 2.06	0.575
RBCs (x 10^6/ µL)		3.75 ± 0.79	3.61 ± 0.68	0.369
WBCs (x 10^6/ µL)		7.67 ± 1.64	6.64 ± 1.61	0.106
PLT (x 10^3/ µL)		333.52 ± 31.14	363.46 ± 73.48	0.333
ESR		67.1 ± 6.22	56.1 ± 3.94	0.076
CRP (mg/L)		7.66 ± 1.15	6.26 ± 1.44	0.015*
Creatinine (mg/L)		2.33 ± 0.07	1.18 ± 0.26	<0.001*
Proteinuria		2065.58 ± 178.9	244.7 ± 17.83	
		(n =49)	**(n = 45)**	
ANA		6.93 ± 2.3	6.22 ± 2.25	0.135
		(n = 50)	**(n = 38)**	
Anti-dsDNA		125.5 ± 7.19	118.03 ± 6.1	0.460
C4		94.68 ± 3.49	103.98 ± 5.91	0.277
C3		18.36 ± 4.64	15.46 ± 3.63	0.098
Urinary cast		47 (94%)	0 (0.0%)	<0.001*
Crystals in urine		5 (10%)	0 (0%)	0.056
Pus HPF in urine		14.42 ± 6.94	10.02 ± 5.73	0.001*
RBCs in urine		8.86 ± 5.51	3.76 ± 2.59	<0.001*
SLEDAI		19.1 ± 5.26	6.34 ± 4.42	<0.001*
rSLEDAI		7.2 ± 2.76	0 ± 0	---
Renal biopsy		35 (70%)	0 (0%)	---
		(n = 15)	**(n = 0)**	
Class	**2**	3 (20%)	–	----
	3	1 (6.67%)	–	
	4	6 (40%)	–	
	5	5 (33.33%)	–	

Data is presented as mean ± SD or frequency (%), LN: Lupus nephritis, SLE: Systemic lupus erythematosus, Hb: hemoglobin, RBCs: red blood cells, WBCs: white blood cells, PLT: platelets, ESR: Erythrocyte sedimentation rate, CRP: C-Reactive Protein, ANA: Antinuclear antibody, C4: Complement component 4, C3: Complement component 3, HPF: High power field, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, rSLEDAI: Renal SLEDAI, SD: Standard deviation, *: Statistically significant at $p \leq 0.05$

A significant positive correlation between 25OHD and hemoglobin (Hb), red blood cells (RBCs), white blood cells (WBCs), and platelets was detected. A significant negative correlation between 25OHD and proteinuria, rSLEDAI and SLEDAI was detected. Serum VD level was significantly reduced in cases with consumed C3 and C4 and cases with positive anti-ds DNA in LN and SLE groups (Table 3).

Table (3): Correlation between 25OHD and various parameters in each group

	25OHD			
	LN		SLE	
	r	p	r	p
Age (years)	0.126	0.385	0.086	0.551
Onset (years)	- 0.194	.176	0.094	0.518
Hb	0.565	< 0.001*	0.419	0.002*
RBCs	0.355	0.011*	0.388	0.005*
WBCs	0.493	<0.001*	0.481	<0.001*
PLT	0.374	0.007*	0.310	0.029*
ESR	0.155	0.282	0.057	0.694
CRP	0.179	0.214	-0.134	0.353
Creatinine	0.071	0.626	0.133	0.356
Proteinuria	-0.410	0.003*	0.071	0.622
ANA	0.117	0.424	-0.045	0.770
Anti-dsDNA	- 0.322	0.023*	-0.615	<0.001*
C3	0.460	<0.001*	0.482	<0.001*
C4	0.398	0.004*	0.284	0.046*
Pus HPF in urine	0.008	0.959	-0.107	0.459
RBCs in urine	0.052	0.718	-0.150	0.297
SLEDAI	-0.419	0.002*	-0.463	<0.001*
rSLEDAI	-0.495	<0.001*	--	--

LN: Lupus nephritis, SLE: Systemic lupus erythematosus, 25OHD: 25-hydroxyvitamin D, Hb: hemoglobin, RBCs: red blood cells, WBCs: white blood cells, PLT: platelets, ESR: Erythrocyte sedimentation rate, CRP: C-Reactive Protein, ANA: Antinuclear antibody, Anti-dsDNA: Anti-double stranded DNA, C4: Complement component 4, C3: Complement component 3, HPF: High power field, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, rSLEDAI: Renal SLEDAI,*: Statistically significant at $p \leq 0.05$

Serum VD level was significantly decreased in cases with fatigue in LN and SLE group (Table 4).

Table (4): Relation between 25OHD and various parameters in LN group and SLE group (n = 50)

		25OHD	P value
Sex	**Male**	15.25± 4.1	0.173
	Female	12.53± 4.5	
Marital	**Single**	14.4± 4.8	0.083
	Married	12.05 ± 4.2	
Special habits	**No smoker**	12.8±4.6	0.966
	Smoker	12.9 ± 4.6	
Fatigue		11.17±3.4	<0.001*
Fever		12.9 ± 4.6	0.942
Alopecia		14.3 ± 4.9	0.100
Malar rash		12.8 ± 4.6	0.953
Ulcer		12.9 ± 4.5	0.676
Arthritis		13.7±5.0	0.203
Vacuities		12.2±3.5	0.723
Urinary cast	**Negative**	18.2±3.8	<0.001*
	Positive	11.8 ± 3.9	
Crystals in urine	**Negative**	12.6 ± 3.3	0.130
	Positive	17.6 ±3.3	
Renal biopsy	**0**	13.5 ± 4.4	0.545
	1	12.6 ± 4.6	
Different parameters in SLE group			
Sex	**Male**	16.14 ± 5.4	0.365
	Female	18.4±6.3	
Marital	**Single**	19.38±5.5	0.395
	Married	17.7 ± 6.4	
Special habits	**No smoker**	17.7 ± 6.1	0.254
	Smoker	20.8 ± 5.9	
Fatigue		16.5 ± 5.8	<0.001*
Fever		15.4 ± 5.7	<0.001*
Alopecia		17.8±8.5	0.856
Malar rash		18.12±6.4	0.997
Ulcer		18.13 ± 6.4	0.985
Arthritis		18.24 ± 6.5	0.872

Data is presented as mean ± SD, LN: Lupus nephritis, SLE: Systemic lupus erythematosus, 25OHD: 25-hydroxyvitamin D, p: p-value for comparing between the studied categories, *: Statistically significant at $p \leq 0.05$

In the present study, we noticed that there was a significant inverse relation between a low titre of 25OHD and SLEDAI activity, in LN and SLE groups there was a significant relation between a low titre of 25OHD and very high SLEDAI activity and high SLEDAI activity respectively (Table 5).

Table (5): Relation between SLEDAI and 25 OHD in LN and in SLE (n = 50)

	SLEDAI				**P value**
	High (n = 24)		**Very High (n = 26)**		
25OHD	14.25 ± 3.91		11.57 ± 2.87		0.036*
In SLE					
	Inactive (n = 3)	**Mild (n = 24)**	**Moderate (n = 8)**	**High (n = 15)**	
25OHD	18 ± 3.61	20.88± 5.53	16.75± 3.16	14.47± 3.76	0.011*
	P1=0.838, P2=0.988, P3=0.754, P4=0.289, P5=0.006*, P6=0.791				

Data is presented as mean ± SD, LN: Lupus nephritis, SLE: Systemic lupus erythematosus, 25OHD: 25-hydroxyvitamin D, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, *: Statistically significant at $p \leq 0.05$, P1: P value between Inactive and mild, P2: P value between Inactive and Moderate, P3: P value between Inactive and High, P4: P value between mild and Moderate, P5: P value between mild and high, P6: P value between moderate and high

In LN and SLE groups, linear regression analysis revealed that there was a significant link between low titre of 25OHD and Hb, WBCs, PLT, nati-ds DNA, C3, C4, SLEDAI, rSLEDAI, but inversely correlated with SLEDAI and rSLEDAI (Table 6).

Table (6): Linear regression test for the parameters affecting 25OHD in LN (n = 35)

	linear regression test	
	p	**SE (95%C. I)**
Hb	<0.001*	3.34 (-9.56: 3.89)
WBCs	<0.001*	0.16 (0.30: 0.93)
PLT	0.007*	0.004 (0.003: 0.022)
Anti-dsDNA	0.022*	0.01 (-0.58: -0.004)
C3	<0.001*	0.07 (0.12: 0.43)
C4	0.004*	0.019 (0.019: 0.099)
SLEDAI	0.002*	0.11 (-0.59: -0.13)
rSLEDAI	<0.001*	0.20 (-1.2: -0.40)
in SLE		
Hb	0.002	0.39 (0.46: 2.04)
WBCs	<0.001*	0.29 (0.53: 1.73)
PLT	0.028*	0.004 (0.001: 0.02)
Anti-dsDNA	<0.001*	0.017 (-0.11: 0.045)
C3	<0.001*	0.08 (0.14: 0.47)
C4	0.045*	0.016(0.001: 0.06)
SLEDAI	<0.001*	0.18 (-1.002: -0.29)

LN: Lupus nephritis, SLE: Systemic lupus erythematosus, Hb: hemoglobin, RBCs: red blood cells, WBCs: white blood cells, PLT: platelets, ESR: Erythrocyte sedimentation rate, CRP: C-Reactive Protein, ANA: Antinuclear antibody, C4: Complement component 4, C3: Complement component 3, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index, rSLEDAI: Renal SLEDAI, SE: standard error, C.I: Confidence interval, #: All variables with $p<0.05$ was included in linear regression test, *: Statistically significant at $p \leq 0.05$,

DISCUSSION

SLE is a chronic inflammatory multisystem illness that causes a broad variety of symptoms and is defined by prototypical abnormalities of the immune response, [8] and this was clear with our research as there is a significant difference between 2 groups as regards clinical manifestations except for malar rash and oral ulcer (p-value 0.014, 0.003 respectively). Our results are matched with **Elessawi *et al.*** [9], **Elsaid *et al.*** [10] and **Kwon *et al.*** [11] who observed that there is an insignificant difference regarding fatigue, mucocutaneous, alopecia, musculoskeletal, myositis and arthritis between SLE with nephritis and SLE without nephritis. Mucocutaneous had the highest prevalence among the two studied groups, this is similar to what was reported by **Niazy *et al.*** [12] and **Abdel Galil *et al.*** [13], and in our research fatigue and arthritis came the second most common manifestations represented 75-90% of the cases.

The strongest predictor of VD status in people is the measurement of circulating 25-OH-VD, which represents VD reserves accumulated from both food consumption and ultraviolet light exposure. Current study indicated that VD deficiency was broadly common in instances of active SLE and LN in Egypt, despite the country's year-round sunshine. This agrees with the findings of **Elsaid *et al.*** [14] that VD deficiency and insufficiency in LN can reach 93.4% in Egyptian cases.

In the present research, there was a significant difference between the 3 groups regarding 25-OH-D level, which is concurrent with **Mahmoud *et al.*** [15] who documented that vit D was evidently decreased in SLE/LN compared to SLE/ no LN and control group. Contrary to our research, **García-Carrasco *et al.*** [16] did not find a statistically significant difference between LN and SLE groups regarding VD concentrations but they did not give a clear explanation for their results.

In the present research, regarding VD status among the groups, the highest frequency of VD (severe and deficiency) was categorised in the LN and SLE groups respectively, while they were least in the control group. Also, VD insufficiency category was highest in the SLE and was least in SLE with LN (42% versus 12% respectively). These differences were significant. The lowest value was in the LN group (p-value <0.001), which may be due to that kidneys are playing a vital role in making vitamin D useful to the body. In chronic kidney disease, it was founded that vitamin D levels were below the normal range, or even severely low. This can occur due to injury in kidneys making them not efficient to convert vitamin D to its active form [17]. In the same line with our findings, **Gaik *et al.*** [18] studied Associations between VD state and SLE symptoms, cardiovascular risk factors, autoantibodies and disease activity. Their retrospective research included 216 SLE cases. Among the various clinical manifestations of SLE, only LN showed a statistically significant link with VD status. 50 (23.1%) cases with lupus nephritis had vit D deficiency, 120 (55.6%) vit D insufficiency and only 46 (21.3%) had Adequate vit D concentration. In addition to its antiproliferative effects, VD regulates cell cycle development, making it an essential player in the pathogenesis of SLE. VD may play a novel role in the treatment of SLE if its link with disease activity and lupus nephritis (LN) can be determined [19].

In the present research, there was a significant positive correlation between 25-OH-D and HB, RBCs, WBCs, and Platelet. There was a significant negative correlation between 25-OH-D and proteinuria, renal SLEDAI and SLEDAI. There was a significant correlation between 25-OH-D level and creatinine, pus, RBCs in urine, ESR and CRP in LN group. In SLE our research revealed a significant positive correlation between 25-OH-D and HB, RBCs, WBC and Platelet. There was a significant negative correlation between 25-OH-D and SLEDAI. There was a significant correlation between 25-OH-D level and age, duration, creatinine, proteinuria, pus and RBCs in urine and CRP in SLE cases. Our results are supported by **Mahmoud *et al.*** [15] who revealed that vit D was evidently positively correlated with HB and PLT in SLE cases.

Regarding clinical manifestation in the present research, serum vit D level was significantly decreased in cases with fatigue and musculoskeletal disorders in LN group. Also, decreased with fatigue in SLE cases. Our results come in line with **Correa-Rodríguez *et al.*** [20] and **Isalam *et al.*** [21] who found that fatigue has been frequently reported to be correlating with inadequate serum level of VD in SLE cases. This can be explained by that VD is a powerful modulator of skeletal muscle physiology. So, one way that VD affects muscle development and differentiation, especially in fast-twitch fibres, by increasing the expression of genes involved in these processes (type II). Muscle samples of people with a VD deficit also reveal increased interfibrillar spaces, infiltration of fat, fibrosis, and glycogen, all of which are characteristic of muscular dystrophies. [22]

In the present research, serum VD level was significantly lower in cases with consumed C3 & C4 and cases with positive anti-ds DNA in LN and SLE groups. Our results are compatible with **Athanassiou *et al.*** [23] who studied VD in cases with SLE and they found that C3 and C4 levels were found to be positively correlated with 25-OHD3. They said that the kidneys and liver play crucial roles in VD biosynthesis. Because C3 and C4 complement deficiencies are associated with hepatic and renal disorders, complement component level can be used as a proxy for the health of these organs. In the endoplasmic reticulum and mitochondria of hepatocytes, vitamin D3 is hydroxylated to 25-OH-D, and then in the epithelial cells of the proximal convoluted tubule of the kidney, it is triggered once more by the 1-hydroxylase system to 1,25-(OH)2D3. Additionally, pathological diseases correlating with C3 or C4 amounts may also impede VD activation and reabsorption [24]. This is

consistent with the VD's inhibitory effects on B-cell activities that a negative link has been shown to exist between VD3 level and titres of autoantibodies such as anti-dsDNA [25].

In LN and SLE groups, linear regression analysis revealed that there is a significant link between low titre of vit D (OH D 25) and HB, WBCs, PLT, Anti-ds DNA, C3, C4, SLEDAI, renal SLEDAI, but inversely correlated with SLEDAI and renal SLEDAI. Possible explanations include VD's immune-supporting properties. Sufficient VD supplementation has been proposed to improve the function of VD receptor-expressing immune cells like macrophages, dendritic cells, B cells, and T cells. [26]

Hemoglobin content (r = - 0.04, p = 0.003), mean corpuscular hemoglobin (r = - 0.11, p 0.001), and red blood cell count (r = - 0.04, p = 0.002) were all evidently and inversely correlated with 25-OH-D level. In a population-based group of teenagers, there was a substantial correlation between serum VD level and several indices of red blood cell maturation, which is inconsistent with VD's role as a growth factor [27]. In the research by **Zhou *et al.*** [26] who noted that linear regression analysis showed that 25-OH-D could evidently impact the renal outcome in these cases with biopsy proven DN [HR, per SD 25-OH-D 0.261, 95% CI 0.155-0.441, p<0.001]. However, **Lin *et al.*** [28] linear analysis demonstrated that serum 25-OH-D status was not evidently correlating with the level of white blood cell (p = 0.987), hemoglobin (p=0.428), platelet (p =0.389), creatinine (p =0.775), and anti-dsDNA (p =0.243), or daily and cumulative steroid dosages within 1 month before the examination (p= 0.794 and p = 0.328, respectively)

In the present study, we noticed that there was a significant inverse relation between a low titre of 25-OH-D and SLEDAI activity, in LN and SLE groups there was a significant relation between a low titre of HO-D and very high SLEDAI activity and high SLEDAI activity respectively. Consistent with other SLEDAI-based cross-sectional investigations, such as those done by **Borba *et al.*** [29] (P = 0.0005) and **Yeap et al.** [30] (P = 0.033), the latter found that SLEDAI was linked with low VD level and high cytokine level such as IL-6 and TNF. Several other studies corroborated our finding, though their methods of measuring activity differed from SLEDAI's. For example, **Amital *et al.*** [31] found a negative correlation between VD level and SLE disease activity and questioned whether or not VD supplements should be given routinely to people with SLE. This correlation can be explained by VD's inhibitory impact on Th1 immunity and autoantibody formation, which was discovered in preliminary research. Also, it was found that VD reduces pro-inflammatory cytokine secretion by B cells and suppresses cytokine-mediated B-cell activation by working on T-helper cells [32].

Individuals with systemic lupus erythematosus who had severe VD deficiency had considerably more SLE flares and nephritis [33]. The observed significant negative correlation between SLE activity and VD level in our research could be predicted because the underlying inflammation in lupus enhances the catabolic process of VD.

In our research, there was a significant relation between low VD and pus in urine (p-value <0.001) and this is in agreement with **Deng *et al.*** [34] who found that a lack of VD was linked to a marked rise in the probability of contracting a UTI. It is unclear how VD shortage contributes to UTI recurrence. Different urine host defence proteins like the Tamm-Horsfall protein, lactoferrin, and lipocalin can help ward off infections. Epithelial cells in the urinary system generate the antibacterial molecule cathelicidin LL-37 in response to infections. Innate defence antibacterial peptides, such as cathelicidin LL-37, may be stimulated by vitamin D [35].

CONCLUSION

Vitamin D deficiency and insufficiency showed high frequency in cases with SLE and were more frequent in SLE with lupus nephritis. Low serum VD had a significant negative correlation with disease activity, renal disease activity, ESR and ds DNA and positively correlated with C3 & C4. Low serum VD was significantly correlated with the presence of fatigue and musculoskeletal disorders.

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