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The Effect of Vitamin D Level on Systemic Lupus Erythematosus in Saudi Patients at a Tertiary Care Center

El efecto del nivel de vitamina D sobre el lupus eritematoso sistémico en pacientes saudíes en un centro de atención terciaria

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ABSTRACT

Objective: To assess the prevalence of insufficiency and deficiency of vitamin D, the correlation between vitamin D and disease activity and clinical parameters, and the effect of vitamin D supplementation on SLE activity. **Methods:** This retrospective study was carried out on 68 Saudi patients aged 15–57 and both sexes who received SLE treatment and met at least four of the 1997-revised classification criteria for SLE as outlined by the American College of Rheumatology. The Abcam ELISA kit catalog ab213966 was employed to quantify serum 25-hydroxycholecalciferol vitamin D (25(OH)D). **Results:** Post-treatment, SLEDAI score, ESR, bilirubin, and ALP significantly decreased, while RBCs, albumin, vitamin D, and Ca significantly increased. The prevalence of vitamin D insufficiency (45.6%) and deficiency (26.5%) pretreatment decreased to 13.2% and 7.4%, respectively, post-treatment. Pretreatment, vitamin D showed a significant inverse correlation with WBCs, ESR, ALP, and SLEDAI score, and a positive correlation with albumin and Ca. Post-treatment, vitamin D maintained a significant inverse correlation with bilirubin, ESR, ALP, and SLEDAI score and a positive correlation with albumin and Ca. Conclusions: Vitamin D correlated with bilirubin,

ESR, ALP, albumin, and Ca. Deficiency is linked to high SLE activity; supplementation reduces it.

Keywords
vitamin D; systemic lupus erythematosus; disease activity.

RESUMEN
Objetivo: Evaluar la prevalencia de insuficiencia y deficiencia de vitamina D, la correlación entre la vitamina D y la actividad de la enfermedad y los parámetros clínicos, y el efecto de la suplementación con vitamina D en la actividad del lupus eritematoso sistémico (LES). **Métodos:** Este estudio retrospectivo se realizó en 68 pacientes saudíes de 15 a 57 años, de ambos sexos, que recibieron tratamiento para LES y cumplieron al menos 4 de los criterios de clasificación revisados en 1997. Se empleó el kit ELISA Abcam, catálogo ab213966, para cuantificar la concentración sérica de 25-hidroxicolecalciferol (vitamina D, 25(OH)D). **Resultados:** Tras el tratamiento, la puntuación SLEDAI, la VSG, la bilirrubina y la fosfatasa alcalina (FA) disminuyeron significativamente; mientras que los glóbulos rojos, la albúmina, la vitamina D y el calcio aumentaron significativamente. La prevalencia de insuficiencia (45,6 %) y deficiencia (26,5 %) de vitamina D antes del tratamiento disminuyó al 13,2 % y al 7,4 %, respectivamente, después del tratamiento. Antes del tratamiento, la vitamina D mostró una correlación inversa significativa con los leucocitos, la VSG, la FA y la puntuación SLEDAI, y una correlación positiva con la albúmina y el calcio. Después del tratamiento, la vitamina D mantuvo una correlación inversa significativa con la bilirrubina, la VSG, la FA y la puntuación SLEDAI, y una correlación positiva con la albúmina y el calcio. **Conclusiones:** La vitamina D se correlacionó con la bilirrubina, la VSG, la FA, la albúmina y el calcio. La deficiencia se asocia a una alta actividad del LES; la suplementación la reduce.

Palabras clave
vitamina D; lupus eritematoso sistémico; actividad de la enfermedad.

Introduction

53.9% of Egyptian women and 26% of Egyptian men are estimated to have osteopenia, the prevalence of osteoporosis in Egypt has been estimated at 28.4% in women and 21.9% in men (1). Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by dysregulated immune responses and systemic inflammation, leading to multi-organ damage (2–4). In Saudi Arabia, its prevalence is estimated at 19.28 per 100,000 individuals, with rising incidence over recent decades (5,6).

Vitamin D insufficiency is highly prevalent in SLE and may contribute to disease pathogenesis through immunomodulatory effects (7). Immune cells (B cells, T cells, antigen-presenting cells) express vitamin D receptors, enabling active vitamin D metabolites to suppress inflammatory pathways and promote tolerance (8,9). Critically, vitamin D acts as a negative acute-phase reactant: inflammation suppresses its serum levels, while immunosuppressive therapy often increases them independent of supplementation (10,11). This complicates the interpretation of low vitamin D status in active SLE.

While observational studies associate vitamin D deficiency with higher SLE disease activity, organ damage, and mortality (12-14), causal relationships remain unproven. Notably, evidence that vitamin D supplementation improves clinical outcomes (e.g., reduced flares, damage accrual, or mortality) is lacking (7,15). This represents a significant knowledge gap, as vitamin D insufficiency persists as an independent predictor of morbidity despite conventional therapy (13,14).

Therefore, this study aimed to determine the prevalence of vitamin D deficiency and insufficiency in an SLE cohort, examine relationships between circulating 25-hydroxyvitamin D, disease activity indices, and key clinical parameters, and evaluate the effects of vitamin D supplementation on immunological markers and clinical outcomes in patients with SLE.

Methods

Study Design and Setting

A retrospective cohort study was conducted at the rheumatology clinic of King Fahad Medical City Hospital in collaboration with Nourah Bint Abdulrahman University from 2016 to 2023. Ethical approval was obtained from the institutional review board (Approval Code: H-01-R-059), and the study was performed in accordance with the Declaration of Helsinki and the National Committee of Bioethics guidelines

of Saudi Arabia. Written informed consent was obtained from all participants.

Participants

The study population comprised Saudi patients aged 15 years and older of both sexes who fulfilled at least four of the 1997 American College of Rheumatology revised classification criteria for SLE (16) and were receiving treatment at the KMFC rheumatology clinic during the study period. Patients with suspected malignancy and pregnant or lactating women were excluded from the analysis.

Sample size calculation

Sample size calculation was performed using G*Power 3.1.9.2 software (Universität Kiel, Germany). We conducted a pilot study with five patients to estimate pre- and post-treatment SLEDAI scores (mean ± SD: 22.6 ± 11.8 vs. 12.6 ± 9.37). A sample size of 62 patients was calculated (effect size: 0.938, $\alpha = 0.05$, power = 95%). Accounting for a 10% dropout rate, 68 patients were enrolled.

Data collection

Clinical data were retrospectively extracted from electronic health records using a standardized data collection form. Variables collected included demographic characteristics, clinical presentation patterns, reproductive health status, disease complications and comorbidities, diagnostic investigations, and laboratory parameters at baseline and follow-up visits.

Laboratory assessments

Laboratory evaluations were conducted at pretreatment baseline and six months post-treatment initiation. Assessments included complete blood count, hepatic and renal function tests, erythrocyte sedimentation rate, C-reactive protein, urinary total protein, serum calcium levels, and 25-hydroxyvitamin D (25(OH)D) concentrations.

Serum 25-hydroxycholecalciferol vitamin D levels were quantified using the Abcam ELISA kit (catalog ab213966). Vitamin D status was categorized according to established thresholds: deficiency was defined as concentrations below 20 ng/mL, insufficiency as levels below 30 ng/mL, and normal vitamin D status as concentrations between 30 and 50 ng/mL (17). Disease activity was evaluated using the SLE Disease Activity Index (SLEDAI) score (18).

Vitamin D supplementation protocol

Patients diagnosed with vitamin D insufficiency received vitamin D3 supplementation at 8000 IU daily for four weeks, followed by maintenance therapy at 2000 IU daily. Those with vitamin D deficiency were administered 8000 IU of vitamin D3 daily for eight weeks, and subsequently continued on 2000 IU daily maintenance therapy according to established clinical guidelines. All patients received generic cholecalciferol. Post-treatment laboratory assessment was performed 6 months after initiating supplementation.

Outcome measures

The primary outcome measure was improvement in SLEDAI score following vitamin D supplementation. Secondary outcomes included the prevalence of vitamin D insufficiency and deficiency in the study population and correlation analyses between vitamin D levels and SLEDAI scores, as well as other SLE-associated clinical parameters.

Statistical analysis

Statistical analyses were performed using SPSS version 26 (IBM Inc., Chicago, IL, USA). Data distribution normality was assessed through the Shapiro-Wilk test and histogram

visualization. Repeated measures analysis of variance was employed to analyze and compare means and standard deviations of continuous parametric variables. Categorical variables were analyzed using chi-square tests and presented as frequencies and percentages. Correlations between normally distributed continuous variables were examined using Pearson product-moment correlation coefficients. Statistical significance was defined as a two-tailed *p*-value ≤ 0.05.

Results

The mean ±SD of age was 33.5±10.46. Most participants (86.8%) were females. Out of 68 participants, 50% were married, 41.18% were single, and 8.82% were divorced. Most participants (32.4%) completed a bachelor's, and 51.47% worked remotely. Only 25% exhibited a family history of connective tissue disorder, and 4.4% disclosed a history of smoking (Table 1).

Table 1.
Demographic data of the patients studied

Characteristics		Mean	SD
Age		33.5	10.46
		Frequency	**%**
Gender	Male	9	13.2
	Female	59	86.8
Marital status	Single	28	41.18
	Married	34	50
	Divorced	6	8.82
Education	Primary	12	17.6
	Secondary	16	23.5
	Bachelor	22	32.4
	None	3	4.4
Occupation	Employed	15	22.06
	Home worker	35	51.47
	Student	18	26.47
Family history of connective tissue disorder		17	25
Smoking		4	5.88

Data is presented as frequency %.

Table 2 shows that most participants (98.53%) had illness duration over six months. Fever (2.94%) and weight loss (5.9%) were uncommon. Oral ulcers appeared in 11.76%, nasal ulcers and shortness of breath in 11.8%, and photosensitivity in 60.29%. Malar rash (19.2%) and alopecia (60.3%) were frequent, while arthritis (10.29%) and arthralgia (27.94%) were the main joint issues. Menstrual irregularities affected 36.8%, with 22.1% reporting amenorrhea. OCP use was 13.24%, and 23.53% experienced pregnancy post-diagnosis, with 22.06% reporting abortions.

Table 2.
Clinical characteristics and reproductive health of the studied patients

Clinical characteristics		Frequency	%
Disease duration	Less than 6 months	1	1.47
	More than 6 months	67	98.53
Fever		2	2.94
Weight loss		4	5.9
Eye symptoms		30	44.12
Sjögren syndrome		2	2.9
Oral ulcer		8	11.76
Nasal ulcer		8	11.8
Shortness of breath		8	11.8
Malar rash		13	19.12
Other skin rash		12	17.6
Photosensitivity		41	60.29
Alopecia	Diffuse	9	13.24
	Patchy	32	47.06
Arthralgia		19	27.94
Arthritis		7	10.29
Abdominal tenderness		5	7.35
Diarrhea		3	4.41
Menstrual period	Regular	28	41.2
	Irregular	10	14.7
	Amenorrhea	15	22.1
OCP		9	13.24
Pregnancy after diagnosis		16	23.53
Abortions		15	22.06

OCP: Oral contraceptive pills.

Pericarditis and pleuritic pain were found in 5.9% of patients, and pulmonary hypertension in 7.35%. IHD affected 7.4%, Raynaud's phenomenon 22.06%, and DVT 8.8%. Colitis occurred in 4.41%, lymphadenopathy in 13.24%, and organomegaly in 8.82%. Dialysis was needed in 2.9%. Stroke affected 14.71%, mobility issues 19.12%, neuropathy 27.94%, and psychological symptoms 13.24% (Table 3).

Table 3.
Comorbidities of the studied patients

Disorders		Frequency	%
Pleuritis		4	5.9
Pericarditis		4	5.9
Pulmonary HTN		5	7.35
HTN		27	39.71
IHD		5	7.4
Raynaud's phenomenon		15	22.06
DVT		6	8.8
Colitis		3	4.41
Organomegaly		6	8.82
Lymphadenopathy		9	13.24
Renal replacement therapy	Dialysis	2	2.9
	Transplant	2	2.9
Vascular necrosis		9	13.24
Myositis		4	5.88
Movement disorder		13	19.12
Seizure		9	13.24
Stroke		10	14.71
Transverse myelitis		0	0
Neuropathy		22	32.35
Psychosis		13	19.12
Depression		9	13.24
Hypothyroidism		11	16.18
DM		6	8.82
Cancer		6	8.82
Infection		8	11.76

HTN: hypertension; IHD: ischemic heart disease; DVT: deep vein thrombosis; DM: Diabetes mellitus.

RBCs, albumin, vitamin D, and Ca were markedly more elevated post than pretreatment ($p < 0.05$). ESR, bilirubin, and ALP were substantially lower post than pretreatment ($p < 0.05$). Hemoglobin, RDW, WBCs, platelets, CRP, ALT, AST, Creatinine, urea, and random protein in urine were insignificantly different between pretreatment and post-treatment (Table 4).

Table 4.
Laboratory parameters of the patients studied

	Pre	Post	*p*-value
Hemoglobin (g/dl)	11 ± 1.78	11.2 ± 1.93	0.502
RBCs (× 1012/L)	4.2 ± 0.82	4.5 ± 0.69	0.015*
RDW (%)	15.3 ± 3.92	15.9 ± 4.12	0.461
WBCs (× 109/L)	6.6 ± 3.15	20.7 ± 82.88	0.166
Platelets (× 109/L)	287.3 ± 130.76	261.9 ± 114.44	0.051
ESR (mm/hr)	42.1 ± 34.84	32.7 ± 20.9	0.037*
CRP (mg/dL)	16.8 ± 43.99	14.9 ± 29.89	0.669
ALT (U/L)	29.7 ± 24.48	43.3 ± 93.78	0.272
AST (U/L)	27.1 ± 20.91	27.3 ± 16.9	0.925
Albumin (g/dL)	33.5 ± 7.74	36.5 ± 8.02	0.008*
Bilirubin (mg/dL)	6.6 ± 7.26	4.5 ± 3.37	0.006*
ALP (U/L)	89.5 ± 89.56	65.9 ± 37.62	0.03*
Creatinine (µmol/L)	88.1 ± 95.49	84.4 ± 88.71	0.564
Urea (mg/dl)	6.3 ± 5.79	6.3 ± 6.68	0.935
Random protein in urine	0.5 ± 0.71	0.4 ± 0.64	0.879
Ca (mg/dL)	2.2 ± 0.33	2.7 ± 0.35	<0.001*
Vitamin D (ng/mL)	33.05 (19.37–51.6)	60.05 (37.25–79.35)	<0.001*

* Significant *p*-value <0.05. RBCs: red blood cell count; RDW: red cell distribution width; WBCs: white blood cells; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; ALT: alanine aminotransferase; AST: Aspartate aminotransferase; ALP: alkaline phosphatase; Ca: calcium.

The prevalence of vitamin D insufficiency was 31 (45.6%), and deficiency was 18 (26.5%) pretreatment, and became 9 (13.2%) and 5 (7.4%), respectively, post-treatment. Vitamin D insufficiency and deficiency percentage were substantially decreased post than pretreatment ($p < 0.05$). SLEDAI score was considerably lower post than pretreatment ($p < 0.001$) (Table 5).

Table 5.
Vitamin D insufficiency and deficiency and SLEDAI score of the patients studied

		Pre	Post	*p* value
Vitamin D	Insufficiency	31 (45.6%)	9 (13.2%)	**<0.001***
		17.9 ± 5.7	20.3 ± 6.54	0.056
	Deficiency	18 (26.5%)	5 (7.4%)	**0.005***
		14 ± 3.96	15.4 ± 3.26	0.347
	Patients convert from Insufficiency to Deficiency	2 (2.94%)		
	Patients convert from normal to Deficiency	1 (1.47%)		
	Patients convert from normal to Insufficiency	1 (1.47%)		
SLEDAI score		15.4 ± 11.27	9 ± 7.86	**<0.001***

* Significant p-value <0.05. SLEDAI: Systemic Lupus Erythematosus Disease Activity Index.

In the pretreatment phase, vitamin D showed a substantial inverse correlation with (WBCs, ESR, ALP, and SLEDAI score) and a positive correlation with (albumin and Ca). Post-treatment, vitamin D showed a substantial inverse correlation with (bilirubin, ESR, ALP, and SLEDAI score) and a substantial positive correlation with (albumin and Ca) (Table 6).

Table 6.
Correlation between vitamin D levels and laboratory parameters of the studied patients

	Pre		Post	
	r	*p*	r	*p*
Hemoglobin	0.049	0.690	−0.104	0.401
RBCs	−0.024	0.849	−0.169	0.168
RDW	−0.054	0.662	0.001	0.997
WBCs	−0.238	**0.050***	0.010	0.937
Platelets	−0.081	0.517	−0.093	0.462
ESR	−0.24	**0.049***	−0.307	**0.011***
CRP	0.022	0.863	−0.065	0.611
ALT	0.060	0.637	−0.126	0.329
AST	0.142	0.354	0.154	0.325
Albumin	0.349	**0.003***	0.380	**0.001***
Bilirubin	−0.078	0.531	−0.300	**0.015***
Creatinine	−0.172	0.156	−0.009	0.946
Random protein in urine	−0.130	0.431	−0.196	0.183
Urea	−0.193	0.118	−0.020	0.873
ALP	−0.319	**0.010***	−0.351	**0.005***
Ca	0.385	**0.001***	0.321	**0.007***
SLEDAI score	−0.410	**<0.001***	−0.354	**0.003***

* Significant p-value <0.05. r: Pearson coefficient; RBCs: red blood cell count; RDW: red cell distribution width; WBCs: white blood cells; ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; Ca: calcium.

Discussion

Vitamin D, a steroid hormone activated in the liver and kidneys, regulates calcium metabolism (15), suppresses Th1, enhances Tregs (19,20), affects dendritic cells and IFN genes in SLE (21,22), with deficiency common from photoprotection, renal issues, and medications (23).

The study results revealed that RBCs, albumin, vitamin D, and Ca were significantly higher post than pre. ESR, bilirubin, and ALP were substantially lower post than pre. Vitamin D insufficiency and deficiency percentage were considerably lower post-treatment than pretreatment. SLEDAI score showed a substantial decrease after post-treatment in contrast to pretreatment. In the pretreatment phase, a substantial inverse correlation was observed between vitamin D and (WBCs, ESR, ALP, and SLEDAI score), while we observed a positive correlation between vitamin D and (albumin and Ca). Additionally, a substantial negative correlation was observed between vitamin D and (bilirubin, ESR, ALP, and SLEDAI score) following treatment. Conversely, a substantial positive correlation was identified between albumin, calcium, and vitamin D.

Vitamin D is essential for the immune system, as it regulates the production of antibodies, inhibits IL-2, and the proliferation of lymphocytes (24). Vitamin D3 has been found to prevent autoimmune diseases like SLE; however, its deficiency potentially leads to SLE etiology and aggravation (25). High vitamin D3 levels have been shown to lower the disease risk by 62%. Moreover, in vitro studies have shown that vitamin D3 can prevent dendritic cell differentiation, modulate T cell phenotype and function, and prevent the production of cytokines and the proliferation of T cells (26). This suggests that vitamin D status correlates with SLE disease activity through immunomodulatory mechanisms, including dendritic cell regulation and T-cell function (27). Fibromyalgia and fibromyalgianess are increased in SLE patients, and regular exercise can help improve fatigue, cognitive dysfunction, and pain from fibromyalgia (28).

Vitamin D deficiency can exacerbate SLE symptoms and increase autoantibody generation. At the same time, its immunomodulatory effects help mitigate immunological abnormalities in SLE patients, making it a risk associated with SLE disease development (29). Vitamin D is a safe and cost-effective intervention for patients with SLE, offering immune-inflammatory-modulatory benefits. It has the potential to enhance musculoskeletal and cardiovascular symptoms, preserve immune health, and prevent the excess

morbidity and mortality that are associated with vitamin D deficiency (30).

In agreement with our result, Kamen et al. (31) discovered a high percentage of patients with SLE suffer from vitamin D deficiency, with substantially reduced levels of serum 25-hydroxyvitamin D. This deficiency was particularly prevalent in African Americans and individuals with photosensitivity. Similarly, Borba et al. (32) discovered that patients with high SLE activity had lower levels of vitamin D3 in comparison to controls and low-activity patients. Moreover, Bonakdar et al. (33) and Islam et al. (34) noted that at the time of diagnosis, the majority of SLE patients exhibit vitamin D deficiency, which is correlated with an increased clinical activity. Furthermore, Mahmoud et al. (35) demonstrated that the correlation between vitamin D and (ESR and ALP) was inverse, while Ca and serum albumin exhibited a positive correlation with vitamin D. However, no correlation was observed between vitamin D and WBCs in patients with SLE. The correlation between vitamin D and (ESR and ALP) was inverse, while Ca and serum albumin exhibited a positive correlation with vitamin D. However, no relationship was observed between vitamin D and WBCs in patients with SLE. Also, Acosta Colman et al. (36) showed that there was an inverse relationship between vitamin D concentrations and SLE disease activity.

Our trial has several limitations, including a relatively limited sample size and single-center design, which limits generalizability to broader populations. The retrospective nature of the study prevented standardized follow-up intervals and comprehensive documentation of concurrent medications that could influence both vitamin D metabolism and SLE activity. Detailed information on concurrent SLE treatments, including immunosuppressive medications, corticosteroids, and other therapeutic interventions, was not systematically available, limiting our ability to isolate the independent effects of vitamin D supplementation. Additionally, data on patient adherence to supplementation protocols, baseline dietary vitamin D intake, and sun exposure patterns were not collected, which could have influenced the observed outcomes. Further prospective, controlled trials with standardized treatment protocols are needed to establish definitive guidelines for vitamin D supplementation in SLE management and to confirm the causal relationship between vitamin D status and disease activity improvement.

Conclusions

The prevalence of vitamin D insufficiency was 31 (45.6%), and deficiency was 18 (26.5%) pretreatment, and became 9 (13.2%) and 5 (7.4%), respectively, post-treatment. The results indicated a substantial correlation between vitamin D levels and (bilirubin, ESR, ALP, albumin, and Ca). Vitamin D deficiency showed an inverse correlation with SLE activity before treatment, while vitamin D supplementation correlated with reduced SLE activity.

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