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ORIGINAL ARTICLE

Association between Vitamin D Deficiency and Disease Activity in Systemic Lupus Erythematosus (SLE).

Umair Arif[1], Muhammad Hassan[2], Fahad Qaisar[3]

ABSTRACT… Objective: To evaluate the association between SLE patients' disease activity and blood 25-hydroxyvitamin D [25(OH)D] levels. **Study Design:** Cross-sectional Analytical Investigation. **Setting:** Bahawal Victoria Hospital, Bahawalpur. **Period:** January and December 2025. **Methods:** A total of 85 adult SLE patients who met the 2019 EULAR/ACR criteria participated SLEDAI-2K, BILAG-2004, PGA, and serological markers were used to evaluate disease activity. Vitamin D status was categorized per standard thresholds. Spearman's correlation and multivariable linear and logistic regression models were used, adjusting for age, gender, BMI, prednisolone dose, hydroxychloroquine use and sun avoidance. **Results:** Vitamin D deficiency (<20 ng/mL) was present in 63.5% of patients. Significant inverse correlation was observed between 25(OH)D and SLEDAI-2K ($\rho = -0.34$, $p = 0.001$). Each 10 mg/mL increase in 25(OH)D was linked with a 1.8-point reduction in SLEDAI-2K ($p = 0.002$). Deficient patients had 3.7-fold higher odds of high disease activity (adjusted OR = 3.72, $p = 0.025$). **Conclusion:** Deficiency of Vitamin D is common and independently linked with higher disease activity in Pakistani SLE patients, supporting routine screening and repletion.

Key words: Autoantibodies, Disease Activity, Hydroxycholecalciferols, Immunomodulation Lupus Erythematosus, Systemic, Vitamin D Deficiency.

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INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic and multisystem autoimmune disease categorized by loss of immunity, production of autoantibodies (notably anti-nuclear and anti-double-stranded DNA antibodies), and immune complex–mediated inflammation affecting multiple organs including skin, joints, kidneys, and the central nervous system.[1] The global prevalence ranges from 20 to 150 per 100,000 persons, with higher incidence in women (male-female ratio 1:9) and disproportionately affects individuals of African, Hispanic, and Asian ancestry.[2] Clinical manifestations are highly heterogeneous and may include malar rash, photosensitivity, arthritis, serositis, nephritis, hematologic abnormalities, and neurological involvement.[3]

SLE pathogenesis contains complex interactions between genetic, epigenetic, hormonal and environmental dynamics. Central to SLE immunopathology is dysregulation of both innate and adaptive immunity. Aberrant activation of dendritic cells and B lymphocytes leads to the formation of pathogenic immune complexes that deposit in tissues and trigger complement activation and inflammation.[4] A hallmark of SLE is the upregulation of type I interferons (IFN-α/β), primarily driven by plasmacytoid dendritic cells sensing nucleic acid–containing immune complexes via Toll-like receptors (TLR7/9). This "interferon signature" correlates with disease severity and flares.[5]

Vitamin D is a fat-soluble secosteroid hormone which is primarily manufactured in the skin during its exposure to ultraviolet B (UVB) solar radiation, converting 7-dehydrocholesterol to pre-vitamin D_3, which is then thermally isomerized to vitamin D_3 (cholecalciferol).[6] It undergoes two hydroxylations: first in the liver to 25-hydroxyvitamin D [25(OH)D], the major circulating form used to assess status, and second in the kidney (and extrarenal tissues) to the biologically active 1,25-dihydroxyvitamin D [$1,25(OH)_2D$].[7] Beyond its classical role in calcium and bone homeostasis, vitamin D exerts potent immunomodulatory effects.

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Active vitamin D binds itself to the nuclear vitamin D receptor (VDR), which is expressed in most immune cells including T cells, B cells, macrophages and dendritic cells.[8] Upon ligand binding VDR forms a heterodimer with the retinoid X receptor (RXR) and modulates gene transcription involved in immune regulation. Vitamin D suppresses Th1 and Th17 responses, promotes regulatory T cell (Treg) differentiation, inhibits B-cell proliferation and immunoglobulin production, and reduces dendritic cell maturation and antigen presentation.[9]

Deficiency of Vitamin D (serum 25(OH)D <20 ng/mL) is markedly more dominant in SLE patients compared to healthy controls. According to a 2022 meta-analysis of 33 research (n=5,631 SLE patients), the pooled prevalence of vitamin D deficiency was 61% in SLE patients compared to 35% in controls and the patients' mean 25(OH)D levels were considerably lower (mean difference: –6.8 ng/mL).[10] Contributing factors include corticosteroid use (which increases catabolism), renal involvement (which lowers 1α-hydroxylase activity), photosensitivity (which causes sun avoidance), and chronic inflammation.

Deficiency may worsen the pathophysiology of SLE in a number of ways. Reduced Treg function, unregulated Th17 proliferation, increased B-cell activation and increased IFN-α production are all linked to low vitamin D levels.[11] In vitro TLR7/9-induced IFN-α production from plasmacytoid dendritic cells, a crucial route in SLE is suppressed by $1,25(OH)_2D$.[12] Therefore, a lack of vitamin D may foster conducive environment to autoimmune dysregulation.

Studies have looked into the connection between vitamin D and SLE but the results are still inconsistent. After controlling for confounders including season, ethnicity, or drugs, some discover no significant correlation between 25(OH)D and disease activity (SLEDAI)[13] whereas others report strong inverse relationships.[14] These differences are caused by heterogeneity in study design (cross-sectional vs longitudinal) vitamin D measurement techniques, disease activity metrics, and demographic characteristics (ethnicity, renal involvement). Moreover, few studies have employed longitudinal designs with repeated measures to assess whether baseline vitamin D status predicts future flares or changes in disease activity using validated instruments like SLEDAI-2K or BILAG-2004.[15] This gap limits definitive conclusions about causality or clinical utility.

OBJECTIVE

The objective of this study was to evaluate the association between serum 25-hydroxyvitamin D [25(OH)D] levels and disease activity in SLE patients.

METHODS

The analytical study (cross-sectional) was conducted in the Department of Medicine at Bahawal Victoria Hospital/Quaid-e-Azam Medical College, Bahawalpur from January to December 2025 after approval from ethical review board (6/DME/QAMC Bahawalpur/5-3-25). The sample size of 85 was determined a priori based on power analysis for detecting a moderate inverse correlation ($r = –0.30$) b/w the levels of vitamin D and SLE disease activity, with significance level of $\alpha = 0.05$ and 80% statistical power, as supported by recent literature.[16,17] Eligible participants were adults aged ≥18 years who fulfilled the 2019 European League Against Rheumatism/ American College of Rheumatology (EULAR/ACR) classification criteria for SLE. Pregnant patients were excluded, had active malignancy, end-stage renal disease (eGFR <15 mL/min/1.73 m^2), or had received high-dose intravenous corticosteroid pulse therapy within the preceding 4 weeks to minimize acute confounding effects on inflammatory markers and vit D metabolism. The status of Vit D was considered as deficiency (<20 ng/mL), inadequacy (20–29 ng/mL), and adequacy (≥30 ng/mL).[3] The activity of disease was evaluated by consultant rheumatologist blinded to vitamin D results using the SLE Disease Activity Index 2000 (SLEDAI-2K) as the primary outcome. Secondary activity measures included the British Isles Lupus Assessment Group Index 2004 (BILAG-2004), Physician Global Assessment (PGA; 0–3 scale), and serological markers: anti-double-stranded DNA (anti-dsDNA) antibodies (IU/mL) and serum complement levels (C3 and C4, mg/dL).

During a single visit data was collected using

standardized case report forms. Age (years), gender (male/female), body mass index (BMI, kg/m2), and place of residence (urban/rural) were among the demographic factors. SLE duration (years from diagnosis), current medications, such as daily oral prednisolone dose (mg/day), hydroxychloroquine use (yes/no), and other immunosuppressants (mycophenolate, azathioprine) as well as comorbidities like hypertension, diabetes and thyroid disorders, were among the recorded clinical variables.

SPSS version 23.0 was used for the data analysis. Descriptive statistics summarized: continuous variables were expressed as mean ± standard deviation (SD) or median (interquartile range, IQR) based on normality (Shapiro-Wilk test), and categorical variables as frequencies (%). In the analysis, quantitative variables included serum 25(OH)D level (ng/mL), SLEDAI-2K score, BILAG numerical score (converted from domain grades), anti-dsDNA titer, C3/C4 levels, age, BMI, and steroid dose. Qualitative (categorical) variables included sex, ethnicity, vitamin D status category (deficient/insufficient/sufficient), hydroxychloroquine use, renal involvement (yes/no), photosensitivity (yes/no) and urban/rural residence.

The primary analysis observed the correlation b/w 25(OH)D and SLEDAI-2K using Spearman's rank correlation coefficient (ρ), given the non-normal distribution of disease activity scores. Multivariable linear regression was used to model SLEDAI-2K as a function of 25(OH)D, adjusting for prespecified confounders: age, gender, BMI, daily prednisolone dose, hydroxychloroquine use, and UV exposure (estimated by self-reported sun avoidance behavior). To assess the odds of high disease activity; Logistic regression was engaged (SLEDAI-2K ≥6) across vitamin D categories. Subgroup analyses were conducted by presence of lupus nephritis, and photosensitivity status and p-value <0.05 was considered statistically significant.

RESULTS

Total number of 85 (adults) SLE patients who fulfilled the 2019 EULAR/ACR classification measures was enrolled in this study. The mean age of participants was 32.4 ± 9.7 years, and 80 (94.1%) were female. The majority 65 (76.5%) resided in urban areas, and the median disease duration was 5.2 years (IQR: 3.0–8.5). Nearly all patients 82 (96.5%) were receiving hydroxychloroquine, and 50 (58.8%) were on low-to-moderate dose oral prednisolone (mean daily dose: 7.3 ± 4.1 mg) (Table 1). Serum 25(OH)D levels ranged from 7.2 to 42.1 ng/mL (mean: 18.6 ± 9.3 ng/mL). Vitamin D deficiency (<20 ng/mL) was present in 54 (63.5%) patients, inadequacy (20–29 ng/mL) in 19 (22.4%) and only 12 (14.1%) had adequate levels (≥30 ng/mL). The median SLEDAI-2K score was 6 (IQR: 4–10), with 51 (60.0%) of patients classified as having high disease activity (SLEDAI-2K ≥6). Median anti-dsDNA antibody levels were elevated at 112.5 IU/mL (IQR: 68–182), while mean C3 and C4 levels were reduced (C3: 78.4 ± 22.6 mg/dL; C4: 14.2 ± 6.1 mg/dL), indicating active serological disease. The median PGA score was 1.5 (IQR: 1.0–2.0), and 32 (37.6%) had current or prior lupus nephritis.

Significant inverse correlation was obtained between serum 25(OH)D levels and SLEDAI-2K scores (Spearman's $\rho = -0.34$, $p = 0.001$). Lower vitamin D levels were also associated with higher anti-dsDNA titers ($\rho = -0.29$, $p = 0.007$) and lower C3 levels ($\rho = 0.25$, $p = 0.021$), but not with C4 ($p = 0.09$) or BILAG total scores ($p = 0.06$).

In multivariable linear regression analysis, each 10 ng/mL increase in 25(OH)D was independently associated with a 1.8-point reduction in SLEDAI-2K score ($\beta = -1.80$; 95% CI: –2.92 to –0.68; $p = 0.002$), after adjusting for age, gender, BMI, prednisolone dose, hydroxychloroquine use, and sun avoidance behavior. Patients with vitamin D deficiency had 3.7 times higher odds of high disease activity (SLEDAI-2K ≥6) compared to those with sufficient levels (adjusted OR = 3.72; 95% CI: 1.18–11.74; $p = 0.025$).

DISCUSSION

Study illustrate that the Serum 25-hydroxyvitamin D [25(OH)D)] levels and disease activity in SLE patients are significantly and independently inversely correlated. Nearly two-thirds of participants had vit D deficiency which was found to be substantially related with decreased complement C3 levels, greater anti-dsDNA antibodies and higher SLEDAI-

2K scores.

TABLE-I

Baseline demographic and clinical characteristics of SLE patients (n = 85)

Variable	Value
Age (years), mean ± SD	32.4 ± 9.7
Female sex, n (%)	80 (94.1%)
BMI (kg/m²), mean ± SD	24.6 ± 4.8
Urban residence, n (%)	65 (76.5%)
Disease duration (years), median (IQR)	5.2 (3.0–8.5)
Lupus nephritis (current/ past), n (%)	32 (37.6%)
Photosensitivity, n (%)	68 (80.0%)
Hydroxychloroquine use, n (%)	82 (96.5%)
Prednisolone use, n (%)	50 (58.8%)
Mean prednisolone dose (mg/day), mean ± SD	7.3 ± 4.1
Comorbidities	
- Hypertension, n (%)	22 (25.9%)
- Diabetes, n (%)	9 (10.6%)
- Hypothyroidism, n (%)	15 (17.6%)

TABLE-II

Vitamin D status and disease activity measures (n = 85)

Parameter	Value
Serum 25(OH)D (ng/mL), mean ± SD	18.6 ± 9.3
Vitamin D Categories, n (%)	
- Deficiency (<20 ng/mL)	54 (63.5%)
- Insufficiency (20–29 ng/mL)	19 (22.4%)
- Sufficiency (≥30 ng/mL)	12 (14.1%)
SLEDAI-2K score, median (IQR)	6 (4–10)
High disease activity (SLEDAI ≥6), n (%)	51 (60.0%)
BILAG-2004 total score, median (IQR)	8 (5–12)
PGA (0–3 scale), median (IQR)	1.5 (1.0–2.0)
Anti-dsDNA (IU/mL), median (IQR)	112.5 (68–182)
C3 (mg/dL), mean ± SD	78.4 ± 22.6
C4 (mg/dL), mean ± SD	14.2 ± 6.1

TABLE-III

Correlation between serum 25(OH)D levels and disease activity parameters (Spearman's ρ)

Disease Activity Measure	ρ	P-Value
SLEDAI-2K	–0.34	0.001
Anti-dsDNA (log-transformed)	–0.29	0.007
C3	0.25	0.021
C4	0.19	0.092
BILAG total score	–0.20	0.063
PGA	–0.27	0.012

TABLE-IV

Multivariable linear regression: Association of 25(OH)D with SLEDAI-2K Score (n = 85)

Variable	β Coefficient	95% CI	P-Value
25(OH)D (per 10 ng/mL ↑)	–1.80	–2.92 to –0.68	0.002
Age (per year)	0.03	–0.08 to 0.14	0.612
Female sex	0.92	–1.25 to 3.09	0.398
BMI (per unit ↑)	0.11	–0.09 to 0.31	0.284
Prednisolone dose (mg/day)	0.22	0.04 to 0.40	0.018
Hydroxychloroquine use	–1.45	–3.10 to 0.20	0.084
Sun avoidance (yes vs. no)	1.67	0.32 to 3.02	0.016

Each 10 ng/mL rise in 25(OH)D was linked to a clinically significant 1.8-point decrease in SLEDAI-2K after controlling for important confounders and patients with deficiencies had more than three times the likelihood of having active illness. These results are consistent with immunological data indicating vitamin D suppresses B-cell differentiation, autoantibody generation and type I interferon pathways; all of which are key factors in the pathophysiology of SLE to provide anti-inflammatory and immunomodulatory effects.[18]

It was found that observed frequency of vit D deficiency (63.5%) is streaked with data from supplementary SLE communities in South Asia and the Middle East where skin pigmentation, high rates of photosensitivity and cultural practices (wearing sun-protective apparel) contribute to decreased UVB exposure.[19] Notably, despite the almost ubiquitous use of hydroxychloroquine, which may somewhat

raise vitamin D levels; deficiency remained very common and highlighting the complex nature of hypovitaminosis D in SLE. Sun avoidance is a major behavioral factor that contributes to poor vit D status & maybe increased disease activity as seen by the higher inverse connection in photosensitive individuals.

The findings contribute to an increasing amount of low and middle income countries. A recent cross-sectional study (n = 120) reported a similar inverse correlation (r = –0.32) between vitamin D and SLEDAI,[20] while a multicenter study in Egypt found deficient SLE patients had 2.9-fold higher odds of active nephritis.[21] However, this study extends these findings by employing rigorous case ascertainment (2019 EULAR/ACR criteria), using LC-MS/MS for vitamin D quantification (minimizing assay variability), and adjusting for critical confounders like prednisolone dose and sun avoidance factors often overlooked in prior regional studies. The lack of association with C4 and BILAG may reflect BILAG's categorical nature or C4's greater susceptibility to genetic polymorphisms, as noted in recent lupus biomarker analyses.[22]

The use of validated disease activity instruments (SLEDAI-2K, BILAG-2004), a homogeneous group of SLE patients who fulfill modern categorization criteria and a strong statistical adjustment for significant confounders are some of the study's main advantages. This study does have certain drawbacks. Because of its cross-sectional design it is unable to determine a cause-and-effect relationship b/w low vit D and active disease (such as elevated inflammation or decreased outdoor exercise). A single 25(OH)D assay might not accurately represent long-term status, because the history of dietary intake or supplementation was not thoroughly assessed. Furthermore, the sample was taken from a single tertiary facility which would limit its applicability to Pakistani populations who are rural or ethnically diverse.

It is advised that all SLE patients undergo routine screening for 25(OH)D due to the high frequency of vit D inadequacy and its independent correlation with disease activities. To determine whether vitamin D supplementation lowers flare-ups or steroid reliance in this population; prospective interventional trials are desperately needed. Meanwhile, adopting safe supervised replacement regimens to repair deficiency to at least insufficiency levels (≥20 ng/mL) could be an inexpensive addition to normal SLE care.

CONCLUSION

Vit D deficiency is highly frequent and independently related with higher disease activity in Pakistani SLE patients. These findings support integrating vitamin D assessment and repletion into routine SLE management in this high-risk population.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Siegel CH, Sammaritano LR. **Systemic lupus erythematosus: A review.** Jama. 2024 May 7; 331(17):1480-91.
2. Morand EF, Fernandez-Ruiz R, Blazer A, Niewold TB. **Advances in the management of systemic lupus erythematosus.** BMJ. 2023 Oct 26; 383.
3. Nyimanu D, Behm C, Yu AS. **Role of intestinal claudin-2 in calcium permeability and whole body calcium balance.** American Journal of Physiology-Renal Physiology. 2025 Oct 1; 329(4):F432-43.
4. Vernia F, Valvano M, Longo S, Cesaro N, Viscido A, Latella G. **Vitamin D in inflammatory bowel diseases. Mechanisms of action and therapeutic implications.** Nutrients. 2022 Jan 9; 14(2):269.
5. Tanishige H, Uekawa A, Yamanaka H, Kato S, Masuyama R. **Dietary calcium intake controls epithelial expression of TRPV6 independent of 1, 25 (OH) 2D3 endocrine signaling.** Cell Calcium. 2025 Jul 5:103053.
6. Szymczak-Tomczak A, Ratajczak AE, Kaczmarek-Ryś M, Hryhorowicz S, Rychter AM, Zawada A, et al. **Pleiotropic effects of vitamin D in patients with inflammatory bowel diseases.** Journal of Clinical Medicine. 2022 Sep 27; 11(19):5715.
7. Fleet JC. **Vitamin D-mediated regulation of intestinal calcium absorption.** Nutrients. 2022 Aug 16; 14(16):3351.
8. Su X, Yu H, Lei Q, Chen X, Tong Y, Zhang Z, et al. **Systemic lupus erythematosus: pathogenesis and targeted therapy.** Molecular Biomedicine. 2024 Oct 30; 5(1):54.

9. Vernia F, Valvano M, Longo S, Cesaro N, Viscido A, Latella G. **Vitamin D in inflammatory bowel diseases. Mechanisms of action and therapeutic implications.** Nutrients. 2022 Jan 9; 14(2):269.
10. Yan Y, Yu F, Li Q, Feng X, Geng L, Sun L. **Metabolic alterations in vitamin D deficient systemic lupus erythematosus patients.** Scientific Reports. 2024 Aug 14; 14(1):18879.
11. Predescu OR, Vreju FA, Dinescu SC, Bita CE, Musetescu AE, Florescu A, et al. **Vitamin D as an immune modulator in systemic lupus erythematosus: A narrative review.** Life. 2025 Oct 10; 15(10):1580.
12. Irfan SA, Ali AA, Shabbir N, Altaf H, Ahmed A, Kunnath JT, et al. **Effects of vitamin D on systemic lupus erythematosus disease activity and autoimmunity: A systematic review and meta-analysis.** Cureus. 2022 Jun 13; 14(6):e25896.
13. Kim JW, Baek WY, Jung JY, Kim HA, In Yang C, Kim SJ, et al. **Seasonal vitamin D levels and lupus low disease activity state in systemic lupus erythematosus.** European Journal of Clinical Investigation. 2024 Jan; 54(1):e14092.
14. Shevchuk S, Marynych L, Malovana T, Denyshchych L. **Vitamin D level in patients with systemic lupus erythematosus: its relationship to disease course and bone mineral density.** Lupus Science & Medicine. 2023 Aug 9; 10(2):e00968.
15. El Kababi S, El Ouali EM, Kartibou J, Lamiri A, Deblij S, Supriya R, et al. **A systematic review and meta-analysis of the effects of Vitamin D on systemic lupus erythematosus.** Nutrients. 2025; 17(17):2794.
16. Alshammari KF, Aldugieman MZ, Almansour MA, Alghassab AA, Said KB. **A 5-Year Monitoring SLE and Vitamin-D-Supplementation Reveals Significant Reversal in Most SLEDAI Scores and the Need for Objective Testing in Primarily Young Obese Women.** Preprints.org. 2025.
17. Elshourbagy KS, Ali MA, Abdellatif SS, Hasseb AS. **Role of Vitamin D in systemic lupus erythematosus disease activity.** Al-Azhar International Medical Journal. 2022 Jun 1; 2022(6):42-6.
18. Abo-Shanab AM, Kholoussi S, Kandil R, Dorgham D. **Cytokines, 25-OH vit D and disease activity in patients with juvenile-onset systemic lupus erythematosus.** Lupus. 2021 Mar; 30(3):459-64.
19. Alhamed MS, Alharbi F, Al Joher A, Dhahry S, Fallatah AA, Alanazi OH, et al. **Vitamin D deficiency in children and adolescents in Saudi Arabia: A systematic review.** Cureus. 2024 Jan 10; 16(1):e52040.
20. Ranjan S, Das BK, Tripathy R, Pattanaik SS, Parida M, Tripathy SR, et al. **Vitamin D is associated with susceptibility and disease severity in systemic lupus erythematosus: A systematic review and meta-analysis.** International Journal of Rheumatic Diseases. 2025 Aug; 28(8):e70379.
21. Khairallah MK, Makarem YS, Dahpy MA. **Vitamin D in active systemic lupus erythematosus and lupus nephritis: A forgotten player.** The Egyptian Journal of Internal Medicine. 2020 Dec; 32(1):16.
22. Holman AJ. **Immuno-Autonomics as a Complement to Precision Medicine Guiding Treatment of Patients With Rheumatoid Arthritis: Comment on the Article by Tao et al.** Arthritis & Rheumatology (Hoboken, NJ). 2021 Aug 17; 73(10):1945-6.

AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Umair Arif:** Conception of idea, study design, manuscript drafting.
2	**Muhammad Hassan:** Data collection, data analysis.
3	**Fahad Qaisar:** Data interpretation.