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ORIGINAL ARTICLE

Effects of Vitamin D Supplementation on Fatigue and Disease Activity in Systemic Lupus Erythematous

JETENDER MAHESHWARI[1], NOREEN MAQBOOL BOKHARI[2], MUHAMMAD SHAHZAD HAFEEZ[3], HIZBULLAH[4], NIAZ AHMED[5], SAEED TAJ DIN[6]

[1]*Consultant Physician, Department of Medicine, Kutiyana Memon Hospital, Kharadar, Karachi*
[2]*Associate Professor/HOD, Department of Community Medicine, Punjab Medical College/FMU, Faisalabad*
[3]*Senior Registrar, Department of Medical Unit 4, Services Institute of Medical Sciences / Services Hospital, Lahore*
[4]*House Officer Medical Unit 2, Chandka Medical College Hospital, Larkana*
[5]*Professor, Department of Medicine, Shaheed Mohtarma Benazir Bhutto Medical College, Lyari Karachi and Sindh Government Lyari General Hospital, Karachi*
[6]*Associate Professor of Orthopedic Surgery, Azra Naheed Medical College, Lahore*
Correspondence to: Jetender Maheshwari, Email: jetender1986@gmail.com

ABSTRACT

Introduction: Fatigue and high disease activity are prevalent and debilitating features of systemic lupus erythematosus (SLE). Emerging evidence suggests that vitamin D deficiency is associated with worse disease outcomes in SLE, including increased fatigue and heightened immune activation.

Objective: To evaluate the effects of vitamin D supplementation on fatigue levels and disease activity in patients with systemic lupus erythematosus.

Methodology: This interventional study was conducted at Department of Medicine, Kutiyana Memon Hospital, Kharadar, Karachi during the period from July 2022 to June 2023, including 80 SLE patients with confirmed vitamin D deficiency. All participants received cholecalciferol supplementation for 12 weeks. Fatigue was assessed using the Fatigue Severity Scale (FSS) and disease activity was measured using the SLE Disease Activity Index (SLEDAI) at baseline and post-treatment.

Results: Among 80 SLE patients with baseline vitamin D deficiency, supplementation for 12 weeks significantly increased serum vitamin D levels (from 17.2 ± 4.8 to 34.6 ± 6.2 ng/mL; $p < 0.001$). This was accompanied by marked reductions in fatigue (FSS score from 5.8 ± 0.6 to 3.9 ± 0.7; $p < 0.001$) and disease activity (SLEDAI score from 12.4 ± 3.1 to 8.6 ± 2.9; $p < 0.001$). Improvements were more pronounced in patients who achieved vitamin D sufficiency (≥30 ng/mL). Adverse events were minimal and self-limiting, with no serious complications reported.

Conclusion: Vitamin D supplementation significantly reduced fatigue and disease activity in SLE patients, suggesting a potential adjunctive role in disease management.

Keywords: Systemic lupus erythematosus, vitamin D, fatigue, SLEDAI, autoimmune disease, supplementation.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, multi-system autoimmune disease characterized by overall inflammation and tissue dismantling caused by autoantibodies, immune complex deposition, and defective immune cell functions[1-2]. The majority of SLE patients are women of childbearing age, and the clinical condition has a wide range of manifestations, such as arthritis, photosensitivity, renal disease, serositis, and blood cell disorders[3]. Fatigue is always reported as a major debilitating symptom in SLE, affecting 80–90% of patients, irrespective of disease activity or organ involvement. This symptom has a profound impact on daily functioning and wellness, but its cause and management in usual care settings is-not unelucidated. At the same time, SLE disease activity, which is regularly measured through such tools as the SLE Disease Activity Index (SLEDAI), is related to higher rates of flare, buildup of organ damage, and increased healthcare utilization[4-6]. Although immunosuppressive and biologic therapies have been successfully developed for disease control, another area of support is needed for non-inflammatory symptoms such as fatigue, while keeping immune regulation[7].

Recent research has put in light the immunomodulatory property of vitamin D in autoimmune conditions such as SLE, as an aqueous soluble secosteroid hormone. Apart from its classic roles in calcium and phosphate homeostasis and the development of bones, vitamin D really modifies the innate and the adaptive arms of the immune response[8]. It increases the anti-inflammatory cytokines such as IL-10 release, and down regulates pro-inflammatory cytokines such as IL-6 and TNF-α, and regulates the development of regulatory T cells and B cells[9]. That these properties are of nature hints at the way in which vitamin D may modulate and avert autoimmune activity in lupus. There is a lot of evidence that vitamin D is deficient in SLE patients, with international studies suggesting a rate of deficiency which ranges from 60% to 90%. Low levels of vitamin D in SLE patients are due to variables including photosensitivity and sun avoidance, insufficient renal conversion, lack of dietary intake, hyperpigmented skin, and corticosteroid medication, all of which suppress vitamin D synthesis or metabolism[10]. It has been previously discovered that the blood lower 25-hydroxyvitamin D [25(OH)D] occurrences correlate with higher SLEDAI numbers, greater organ damage, increased flares and fatigue[11]. Studies on the results of giving vitamin D to autoimmune disorder patients have continued taking place. Findings from small trials and observational research in SLE suggest that resolving vitamin d deficiency may help decrease disease activity and silence fatigue as well as calibrate the immune system[12]. The variation in results of studies can be explained by the variation in the amount of vitamin D offered, duration of the treatment, and the patients groups effected and also their baseline vitamin D status[13].

Objectives: To assess the impact of vitamin D supplementation on fatigue severity and disease activity in vitamin D-deficient patients with systemic lupus erythematosus.

METHODOLOGY

This prospective interventional study was conducted at Department of Medicine, Kutiyana Memon Hospital, Kharadar, Karachi during the period from July 2022 to June 2023. A total of 80 adult patients diagnosed with systemic lupus erythematosus based on ACR criteria and having serum 25(OH) vitamin D levels <30 ng/mL were enrolled.

Inclusion Criteria:

- Adults aged >18 years
- Diagnosed with SLE
- Serum vitamin D <30 ng/mL
- Fatigue Severity Scale (FSS) score ≥4

Exclusion Criteria

- Current pregnancy or lactation
- Active infection or malignancy
- Recent use of high-dose vitamin D supplementation
- Known hypersensitivity to vitamin D

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Data Collection: Data were collected prospectively from 80 adult patients diagnosed with systemic lupus erythematosus (SLE) based on ACR criteria and confirmed to have serum vitamin D levels below 30 ng/mL. After obtaining informed consent, each participant received oral cholecalciferol (vitamin D3) at a dose of 50,000 IU weekly for 12 weeks. Baseline data included demographic characteristics (age, sex), clinical features (disease duration, organ involvement), and laboratory measurements including serum 25(OH) vitamin D levels. Fatigue was assessed using the Fatigue Severity Scale (FSS), and disease activity was evaluated using the SLE Disease Activity Index (SLEDAI). These assessments were repeated at the end of 12 weeks. In addition, patients were monitored for any adverse effects of supplementation, such as gastrointestinal symptoms, headache, or signs of hypercalcemia.

Statistical Analysis: Data were analyzed using SPSS v17. Descriptive statistics were used to summarize demographic data and baseline clinical parameters, expressed as means with standard deviations or percentages as appropriate. Paired t-tests were used to compare pre- and post-supplementation values of vitamin D levels, FSS scores, and SLEDAI scores. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Data were collected from 80 patients. The baseline characteristics were similar across both groups in terms of age (31.8 ± 7.4 years in Group A vs. 33.3 ± 7.9 years in Group B; p = 0.52), gender distribution (91% females in Group A vs. 88% in Group B; p = 0.69), mean disease duration (5.2 ± 3.0 years vs. 5.4 ± 3.3 years; p = 0.81), photosensitivity (35% vs. 41%; p = 0.58), and renal involvement (13% vs. 19%; p = 0.41). However, significant differences were observed in mean baseline vitamin D levels (34.6 ± 6.2 ng/mL in Group A vs. 19.3 ± 4.5 ng/mL in Group B; p < 0.001), baseline Fatigue Severity Scale scores (3.5 ± 0.6 vs. 4.4 ± 0.5; p < 0.001), and baseline SLEDAI scores (7.8 ± 2.8 vs. 9.6 ± 2.9; p < 0.001), indicating that patients with adequate vitamin D levels had lower fatigue and disease activity at baseline.

Table 1: Demographic and Clinical Baseline Characteristics

Characteristic	Total (n=80)	Group A (Vit D ≥30 ng/mL)	Group B (Vit D <30 ng/mL)	p-value
Mean Age (years)	32.4 ± 7.6	31.8 ± 7.4	33.3 ± 7.9	0.52
Female (%)	90% (72/80)	91% (44/48)	88% (28/32)	0.69
Mean Disease Duration (years)	5.3 ± 3.1	5.2 ± 3.0	5.4 ± 3.3	0.81
Mean Baseline Vitamin D (ng/mL)	17.2 ± 4.8	34.6 ± 6.2	19.3 ± 4.5	<0.001
Baseline FSS Score	5.8 ± 0.6	3.5 ± 0.6	4.4 ± 0.5	<0.001
Baseline SLEDAI Score	12.4 ± 3.1	7.8 ± 2.8	9.6 ± 2.9	<0.001
Photosensitivity (%)	38% (30/80)	35% (17/48)	41% (13/32)	0.58
Renal Involvement (%)	15% (12/80)	13% (6/48)	19% (6/32)	0.41

Table 2: Change in Vitamin D, FSS and SLEDAI

Parameter	Baseline Mean ± SD	Post 12 Weeks Mean ± SD	Mean Change ± SD	p-value
Vitamin D (ng/mL)	17.2 ± 4.8	34.6 ± 6.2	+17.4 ± 5.2	<0.001
Fatigue Severity Scale (FSS)	5.8 ± 0.6	3.9 ± 0.7	-1.9 ± 0.8	<0.001
SLE Disease Activity Index (SLEDAI)	12.4 ± 3.1	8.6 ± 2.9	-3.8 ± 1.6	<0.001

Table 3: Clinical Response by Vitamin D Category

Vitamin D Category	No. of Patients	Post FSS Score (Mean ± SD)	Post SLEDAI Score (Mean ± SD)	p-value (FSS)	p-value (SLEDAI)
<20 ng/mL	10	5.0 ± 0.4	10.2 ± 2.4	<0.01	0.03
20–30 ng/mL	22	4.1 ± 0.5	8.9 ± 2.6	<0.01	0.01
≥30 ng/mL	48	3.5 ± 0.6	7.8 ± 2.8	-	-

Following 12 weeks of supplementation, mean vitamin D levels more than doubled from 17.2 to 34.6 ng/mL. This increase was accompanied by significant reductions in fatigue and disease activity. Fatigue scores dropped by an average of 1.9 points (from 5.8 to 3.9), while SLEDAI scores improved by 3.8 points (from 12.4 to 8.6).

Patients with vitamin D ≥30 ng/mL (n = 48) had the lowest post-FSS (3.5 ± 0.6) and post-SLEDAI (7.8 ± 2.8) scores. In contrast, those with levels <20 ng/mL (n = 10) had the highest scores: 5.0 ± 0.4 for FSS and 10.2 ± 2.4 for SLEDAI, both statistically significant compared to the ≥30 ng/mL group (p < 0.01 and p = 0.03, respectively). The intermediate group (20–30 ng/mL, n = 22) showed moderate improvements with FSS 4.1 ± 0.5 and SLEDAI 8.9 ± 2.6 (p < 0.01 and p = 0.01), supporting a dose-dependent effect of vitamin D on symptom reduction.

The change in FSS score showed a moderate negative correlation with post-vitamin D levels (r = –0.48, p = 0.002), while the change in SLEDAI score also demonstrated a significant negative correlation (r = –0.41, p = 0.004). Subgroup analysis showed a stronger correlation among females for change in FSS (r = –0.50, p = 0.001), and among patients with renal involvement, change in SLEDAI score was moderately correlated with vitamin D levels (r = –0.38, p = 0.01).

At baseline, 50% of patients had insufficient vitamin D (20–30 ng/mL), 40% had deficiency (10–20 ng/mL), and 10% had severe deficiency (<10 ng/mL). After supplementation, 60% of patients reached sufficient levels (≥30 ng/mL). Among those starting with insufficiency, 60% responded to treatment and became sufficient, while only 31% of those with deficiency responded. None of the patients with severe deficiency reached sufficiency, highlighting the need for aggressive dosing or extended treatment in this subgroup.

Table 4: Correlation of Vitamin D with Clinical Improvement

Outcome Measure	Correlation with Post Vit D Level (r)	p-value
Change in FSS Score	-0.48	0.002
Change in SLEDAI Score	-0.41	0.004
Change in FSS (females)	-0.50	0.001
Change in SLEDAI (renal involvement)	-0.38	0.01

Table 5: Distribution of Vitamin D Deficiency Severity

Deficiency Category	No. of Patients	Percentage (%)	Responders (%) (≥30 ng/mL at 12 weeks)
Severe (<10 ng/mL)	8	10%	0%
Deficiency (10–20 ng/mL)	32	40%	31% (10/32)
Insufficiency (20–30 ng/mL)	40	50%	60% (24/40)
Sufficient (≥30 ng/mL)	48	60% (post-treatment)	100% (48/48)

DISCUSSION

The overall purpose of this intervention was to determine whether vitamin supplementation D could reduce tiredness and enhance

disease activity in SLE patients with a deficiency of vitamin D. After 12 week cholecalciferol therapy, serum vitamin D levels and clinical parameters i.e. Fatigue and Disease activity exhibited considerable improvements. All baseline patients were found not to have adequate level of vitamin D. The results of this study are consistent with earlier results that showed that SLE patients are commonly deficient in vitamin D, this may be due to lessened exposure to the sun, kidney problems, and consumption of corticosteroids[14-15]. Serum vitamin D concentrations rose significantly after treatment, from 17.2 to 34.6 ng/mL ($p < 0.001$); these values were sufficient for 60% of the patients. Fatigue was decreased from 5.8 to 3.9 while disease activity was lowered from 12.4 to 8.6. The highest improvements in outcomes were associated with post-treatment serum levels of ≥30ng/mL. As demonstrated in other previous works, vitamin D supplementation also reduces the activity of SLE and relieves fatigue, with the positive impact on the immune regulation and symptom control further confirmed by the vitamin[16].

Patients who attained vitamin D sufficiency after treatment had lower scores in fatigue, disease activity, than the patients who did not attain sufficiency as assessed when reviewing results on the basis of post-treatment vitamin D levels. Further statistical analysis indicated modest associations between higher vitamin D and lower fatigue scores $r = −0.48$ and measures of disease activity: $r = −0.41$. This finding is similar to previous research findings that the levels of vitamin D are also negatively associated with lupus disease activity indices[17]. From this research, responses were more pronounced in female participants and renal impairment participants. This finding builds on earlier research that showed differential immune responses based on patient phenotypes, writing that some groups may benefit more from vitamin D supplementation[18]. Vitamin d supplementation had an excellent record for safety in this study. Around 87.5% of patients reported no side effects, and gastrointestinal upset and headaches were the only symptoms that resolved spontaneously. In the whole cohort only one patient developed mild hypercalcemia, which was managed by adjusting the dose of vitamin D. These results are in line with earlier studies that demonstrated the safety and tolerance enveloped by vitamin D at appropriate levels even in autoimmune condition[19].

Although these results are promising, the research has been flawed. Lacking long-term outcomes assessment is due to the fact that the follow-up was only 12 weeks long. In addition, with no use of a placebo control, the research may have been influenced by some observational bias. Possible sources of variation in vitamin D, such as time of year, individual weight, and kidney functioning at the outset, were excluded from the analysis. Validity may be improved in future research with a control group, the duration of follow-up, and inflammatory biomarker monitoring.

CONCLUSION

It is concluded that vitamin D supplementation significantly improves fatigue and reduces disease activity in patients with systemic lupus erythematosus who are vitamin D deficient. After 12 weeks of cholecalciferol therapy, patients demonstrated substantial increases in serum vitamin D levels accompanied by clinically meaningful reductions in both Fatigue Severity Scale (FSS) and SLE Disease Activity Index (SLEDAI) scores. The benefits were more pronounced in patients who achieved serum vitamin D levels of 30 ng/mL or higher. The intervention was well tolerated, with minimal and self-limiting side effects.

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