Does Serum vitamin D affect disease activity, sleep disorders and quality of life in Systemic Lupus Erythematosus patients?

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Abstract

Background: Early detection of vitamin D deficiency in patients with Systemic Lupus Erythematosus (SLE) may prevent or reduce fatigue, sleep and quality of daily life impairment.
Objectives: to assess vitamin D deficiency or insufficiency in SLE patients, and to correlate it with clinical disease activity, sleep and quality of life impairment.
Methods: 80 SLE patients plus 40 healthy volunteers as a control group. Sleep quality assessed by Pittsburgh Sleep Quality Index; disease activity assessed by SLE Disease Activity Index 2000. Functional capacity assessed by health assessment questionnaire. Serum Vit D measured by ELISA.
Results: Serum vitamin D (25-OH D) levels were significantly lower in SLE patients compared to controls (p = 0.02). The lowest vitamin D level was detected in SLE patients with lupus nephritis (p = 0.003).
There was a significant difference in SLEDAI, PSQI, FACIT-F, HAQ and SLE-QoL scores between SLE patients with sufficient and insufficient/deficient vitamin D serum levels (p= 0.028, and 0.001).
a significant negative correlation between serum vitamin D level with clinical disease activity, functional capacity, sleep and quality of life.
Conclusion: Vitamin D may play an important role in the pathogenesis of SLE and could be a promising biomarker of SLE disease activity.
Keywords: Systemic Lupus Erythematosus, vitamin D, Sleep Quality Index (PSQI), vitamin D deficiency, Systemic Lupus Erythematosus Quality of Life (SLEQoL), Lupus nephritis.

BACKGROUND

Systemic Lupus Erythematous (SLE) is a chronic multisystem auto-immune inflammatory disease of unpredictable course and prognosis. It predominantly affects females of reproductive age with a female to male ratio of 9:1. Its prevalence ranges from 20 to 150 per 100,000 individuals worldwide (1).

SLE is characterized by abnormalities of the immune response and variable clinical manifestations target dermatological, musculoskeletal, renal, respiratory, neuropsychiatric and cardiovascular. Active lupus nephritis (LN) occurs in about 30% of SLE patients (2).

The etiology of SLE is still unclear, it involves the interaction of genetic, environmental, hormonal, and immune factors (3). Vitamin D level in SLE has been studied as one of the most important environmental factors. It play an important role in inducing immune tolerance. Its deficiency has been found to be prevalent in patients with autoimmune diseases as rheumatoid arthritis, systemic lupus erthymatosis and inflammatory bowel disease. (4)

Vitamin D is a fat-soluble steroid-derived vitamin; it has an important role in regulating calcium metabolism and bone homeostasis (5).

Vitamin D is resorbed mainly from the skin through ultraviolet light exposure and only a limited amount obtained from diet (6). It is metabolized in the liver to 25-hydroxyvitamin D (25-OH D), which is the best marker reflecting vitamin D level. (25-OH D) is converted in the kidney to 1,25-dihydroxyvitamin D (1,25-OH2 D), which is the most active form of vitamin D. 1,25-OH2 D acts on multiple targets through vitamin D receptors (7).

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Vitamin D (VD) deficiency is a highly prevalent problem in SLE patients, most likely due to photosensitivity, renal impairment and use of glucocorticoids which alter vitamin D metabolism (8). The role of vitamin D in the pathogenesis and progression of autoimmune diseases, as SLE has been investigated with the presence of vitamin D receptors on the surface of several immune cells (as; dendritic cells, macrophages, T and B cells) and many immune cells also synthesize the 1α-hydroxylase enzyme responsible for synthesis of the active form of VD. These findings indicate that VD is involved in immune modulation (9, 10).

Studies report the significant association between vitamin D deficiency and enhanced disease activity and severity of SLE, suggesting the role of low vitamin D levels in disease activity and progression in SLE (11).

Sleep disorders are common in SLE patients, but the underlying mechanisms are obscure including disease activity, cumulative damage, and corticosteroids usage, as well as depression. Vitamin D deficiency association with sleep quality disturbances and psychological health is apparent (12).

Fatigue is one of the most common bothering symptoms in SLE, reported by about 77% of patients. It may impair health-related quality of life, leading to employment disability. Studies show a significant improvement in fatigue with vitamin D supplementation (13). SLE is a chronic disease has the ability to worsen the overall health of patients by limiting their capacity to live well, limit the functional status, productivity and Health Related Quality of Life (HRQOL) and is a major contributor to health care costs (14).

The aim of this study was to assess vitamin D deficiency or insufficiency in SLE patients, and to study its impact on the status of disease activity, functional disability, fatigue, sleep and quality of life impairment.

SUBJECTS AND METHODS

This case-control study was carried out on eighty Systemic Lupus Erythematosus patients fulfilled the Classification criteria of Systemic lupus International Collaborating Clinics (SLICC) (15) selected from the outpatient clinics of Rheumatology, Physical Medicine &Rehabilitation department, Faculty of Medicine, Tanta University Hospitals, and forty apparent healthy volunteers matched in age and sex as controls.

The study was performed according to Helsinki declaration ethical standards, and the protocol for the research has been approved by the Ethical Committee of Faculty of Medicine, Tanta University.

The written informed consent from all the patients and controls for participation in this study was obtained.

Patients with other chronic diseases (autoimmune diseases, inflammatory diseases or systemic diseases), and patients on regular vitamin D supplementation were excluded from the study. Patients who had a change in corticosteroids or immunosuppressive therapy dosage 2 weeks before the study were also excluded.

- **Clinical assessment:**
  - Clinical disease activity assessment was done using Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) (16).
  - Fatigue assessment by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F version 4). It consists of 13 items applied to the preceding week; patient marks one number per item to indicate his response. The level of fatigue is measured on a four-point scale (4 = not at all fatigued to 0 = very much fatigued) (17)
  - Assessment of functional capacity by Health Assessment Questionnaire (HAQ) (18)
  - Sleep quality assessment by Pittsburgh Sleep Quality Index (PSQI). It has 18 items to evaluate the sleep quality within the preceding month. It measures seven components including: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component score is coded from 0 to 3. The total score ranges from 0 to 21, poor sleep quality was defined as PSQI >5.9 (19)
  - -Quality of life assessment by Systemic Lupus Erythematosus Quality of Life (SLEQoL). The questionnaire has 40 items, it covers six domains: physical function, social activity, symptoms, medical treatment, emotions and feelings in the last week before study. Each item score ranges from 1 to 7, higher scores indicate poorer quality of life. The total scores range from 40 to 280. (20)
- **Laboratory investigations:**
  - Routine laboratory investigations (complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum urea & creatinine, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), creatinine clearance, urine analysis, 24-hour urinary protein excretion, serum complement (C3 & C4) levels, antinuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) levels.
  - Assessment of Serum 25-hydroxychloecalciferol vitamin D level by enzyme immunosorbent assay (ELISA) technique: Vitamin D deficiency was defined as serum level <15 ng/mL and insufficiency <30 ng/mL.

Statistical analysis:

Data were analyzed using the SPSS software version 16.0 (20). The normality of data was checked using the Kolmogorov–Smirnov and the Shapiro–Wilk tests. Quantitative variables were expressed as mean ± standard deviation (SD) or range, and categorical variables were reported as number and percentage. Chi-square and independent t-tests were used to test differences for significance. Pearson's correlations were calculated to test correlations between vitamin D level and other variables. Linear regression analysis was computed to test the independent predictors of serum vitamin D levels. A p-value of <0.05 was considered statistically significant.

RESULTS

This study included 80 SLE patients, they were 70 females (87.5%); and 10 males (12.5%); their ages ranged from 20 to 48 years and their disease duration ranged from 6-24 months with a mean of 12.4± 6.3. Forty healthy controls included 36 females (90.0%) and 4 males (10.0%); their ages ranged from 25 to 50 years. There was no significant difference between the studied groups as regards age and sex. (Table 1)

There was a statistically significant difference between SLE patients and controls regarding ESR, CRP, RBCs, ALP, creatinine clearance, protein in 24-h urine, C3, C4, anti-dsDNA, and serum vitamin D. (Table 1)

Table (1): Comparison between SLE patients & control groups:

Variable	SLE group (*n* = 80)	Control (*n* = 40)	*P*-value
Age (ys)	33.1±8.0	36.7 ± 9.8	0.558
Gender (F/M)	(7/1)	(9/1)	0.581
ESR (mm/1st h)	49.54 ± 30.97	5 ± 2.82	**0.03***
CRP (mg/L)	11.21 ± 18.56	4.02 ± 5.7	**0.04***
Hb (g/dl)	10.88 ± 1.62	12.23 ± 1.06	0.45
RBCs (10^3/µl)	3.27 ± 1.69	4.90 ± 1.90	**0.05***
WBCs (10^3/µl)	4.26 ± 2.35	5.60 ± 2.52	0.87
Platelets (10^3/µl)	270.34 ± 124.03	288.33 ± 120.28	0.76
AST (U/L)	23.92 ± 8.79	22.56 ± 9.40	0.72
ALT (U/L)	19.44 ± 3.47	25.11 ± 16.51	0.42
ALP (IU/L)	73.59 ± 53.79	87.33 ± 15.85	**0.04***
Serum albumin (g/dl)	3.50 ± 1.85	4.12 ± 1.01	0.42
Urea (mg/dL)	36.15 ± 12.78	22.40 ± 10.36	0.12
Creatinine (mg/dL)	1.0 ± 0.8	0.80 ± 0.5	0.42
Creatinine Clearance (ml/min)	102.44 ± 47.81	95.24 ± 28.95	**0.05***
24-h protein in urine (mg)	1175.0 ± 288.89	105.04 ± 28.72	**0.04***
C3 (mg/dl)	74.77 ± 22.16	167.04±60.68	**0.01***
C4 (mg/dl)	14.40 ± 9.88	52.06 ± 22.21	**0.000***
Anti-dsDNA (IU/ml)	45.14 ± 11.62	1.34 ± 1.20	**0.04***
Serum Vitamin D (ng/ml)	10.00 ± 7.27	27.10 ± 14.19	**0.02***

*Statistically significant (P-value < 0.05)

ESR: erythrocyte sedimentation rate, CRP: C- reactive protein, Hb: hemoglobin, RBCs: red blood cells, WBCs: white blood cells, AST: aspartate transaminase, ALT: alanine transaminase, ALP: alkaline phosphatase, C3: complement 3, C4: complement 4, Anti-dsDNA: anti- double-stranded DNA.

SLE patients retrospectively divided into patients with Lupus Nephritis (LN) and without LN. LN was defined as active urine sediment, and proteinuria >0.5 g/ day.

The SLE with LN group included 42 females (84.0%) and 8 males (16.0%); their ages ranged from 20 to 48 years and their disease duration ranged from 6-20 months. The SLE without LN group included 27 females (90.0%) and three males (10.0%); their ages ranged from 25 to 45 years and their disease duration ranged from 8 to 24 months, with no significant difference in the disease duration between the SLE both groups. (Table 2)

There was a significant difference between SLE renal positive and negative patients regarding ALP, serum albumin, protein in 24-h urine, RBCs in urine, albumin in urine, C3, C4, and serum vitamin D. (Table 2)

Table (2): Comparison between renal positive and negative SLE patients groups:

Variable	Renal positive (50)	Renal negative (30)	*P* value
Age (ys)	32.7± 8.4	33.5±7.7	0.827
Gender (F/M)	(5.25/1)	(9/1)	0.455
Disease duration (ms)	13.6±6.6	12.4±6.4	0.675
AST (U/L)	25.63 ± 19.23	22.66 ± 8.05	0.73
ALT (U/L)	20.26 ± 23.59	19.75 ± 11.77	0.5
ALP (IU/L)	82.86 ± 64.76	58.31 ± 15.76	**0.04***
Serum albumin (g/dl)	3.03 ± 1.63	4.13 ± 1.41	**0.02***
Urea (mg/dL)	40.32 ± 5.04	26.69 ± 1.88	0.09
Creatinine (mg/dL)	1.2 ± 0.9	0.8 ± 0.6	0.12
24 h protein in urine (mg)	1621.8 ± 1875.6	400.43 ± 58.41	**0.003***
RBCs in urine **negative** **positive**	 22 (44%) 28 (56%)	 30 (100%) 0 (0%)	**0.001***
WBCs in urine **negative** **positive**	 42 (84%) 8 (16%)	 30 (100%) 0 (0%)	0.13
Albumin in urine **negative** **positive**	 22 (44%) 28 (56%)	 30 (100%) 0 (0%)	**0.004***
C3 (mg/dl)	65.83 ± 31.65	83.74 ± 12.67	**0.03***
C4 (mg/dl)	12.0 ± 7.2	15.4 ± 7.4	**0.005***
Anti-dsDNA (IU/ml)	52.22 ± 27.65	29.52 ± 21.34	0.987
Serum Vitamin D (ng/ml)	9.00 ± 5.58	19.01 ± 7.4	**0.003***

*Statistically significant (P-value < 0.05)
AST: aspartate transaminase, ALT: alanine transaminase, ALP: alkaline phosphatase, RBCs: red blood cells, WBCs: white blood cells, C3: complement 3, C4: complement 4, Anti-dsDNA: anti- double-stranded DNA.

Vitamin D inadequacy is a prevalent problem in general population but is more common in SLE patients especially those with lupus nephritis. (Table 3)

Table (3): Comparison between Vitamin D status among the studied participants:

Vitamin D	SLE renal +ve (50)	SLE renal -ve (30)	Control (40)
Normal	5 (10%)	9 (30%)	22 (55%)
Insufficient	15 (30%)	15 (50%)	11(27.5%)
Deficient	30 (60%)	6 (20%)	7(17.5%)

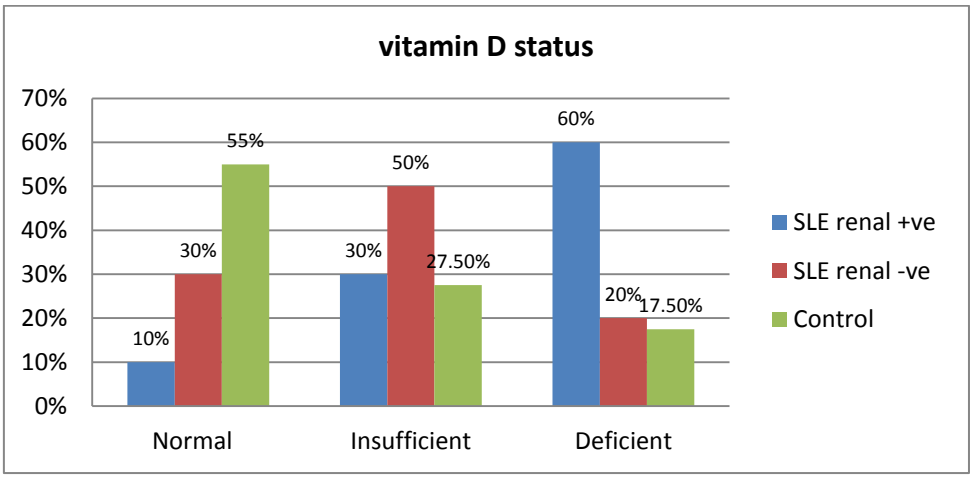

Fig 2: vitamin D status in the studied participants.

There was a statistically significant difference in clinical disease activity, fatigue, functional capacity, sleep and quality of life between SLE patients with adequate and inadequate vitamin D serum levels. (Table 4)

Table (4): Comparison between clinical parameters in SLE patients with adequate and inadequate (Insufficient/Deficient) vitamin D serum levels:

	Vitamin D adequate (14)	Vitamin D inadequate (66)	p-value
SLEDAI-2K	2.45 ± 2.158	3.55 ± 2.998	**0.028***
FACIT-F	45.1 ± 6.9	29.6 ± 6.6	**<0.001***
HAQ	1.538 ± 0.373	2.388 ± 0.320	**0.001***
PSQI	6.800 ± 1.687	13.400 ± 2.459	**0.001***
SLE-QoL	47.200 ± 4.614	76.500 ± 8.196	**0.001***

*Statistically significant (P-value < 0.05)
SLEDAI: systemic lupus erythematosus disease activity index, FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue, HAQ: Health Assessment Questionnaire, PSQI: Pittsburgh Sleep Quality Index, SLE-QoL: Systemic Lupus Erythematosus Quality of Life questionnaire.

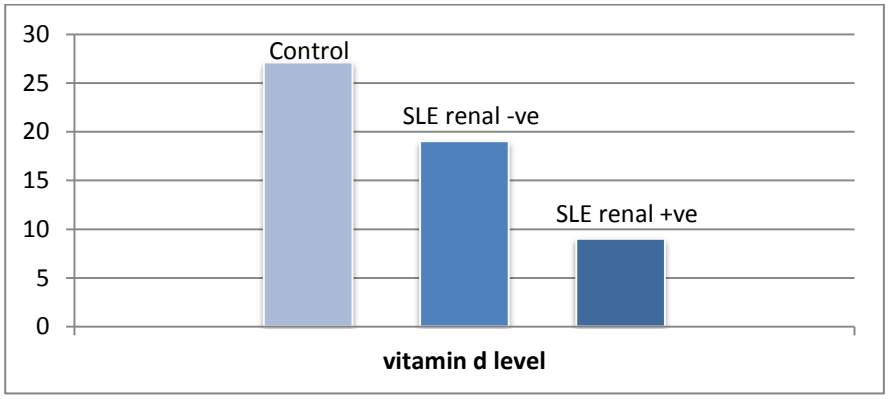

Fig 1: Serum vitamin D levels in the studied participants.

We found a significant negative correlation between serum vitamin D level with clinical disease activity, functional capacity, sleep, quality of life, ESR, CRP, creatinine, and protein in 24-h urine. A significant positive correlation between serum vitamin D level with Chronic Illness Therapy-Fatigue, C3 and C4. While no correlation was found with hemoglobin, creatinine clearance and anti-dsDNA. (Table 5)

Table (5): Correlation of serum vitamin D level versus clinical and laboratory variables of SLE patients:

Variables	Vitamin D level	
	r	p-value
SLEDAI	-0.493	**<0.001***
FACIT-F	0.608	**<0.001***
HAQ	-0.470	**<0.001***
PSQI	-0.32	**0.013***
SLE-QoL	-0.303	**0.018***
ESR (mm/1st h)	-0.311	**0.016***
CRP (mg/L)	-0.480	**<0.001***
Hb (g/dl)	0.181	0.169
Creatinine (mg/dL)	-0.524	**<0.001***
Creatinine Clearance (ml/min)	-0.125	0.344
24 h protein in urine (mg)	-0.299	**0.020***
C3 (mg/dl)	0.294	**0.024***
C4 (mg/dl)	0.350	**0.006***
Anti-dsDNA (IU/ml)	-0.049	0.712

*Statistically significant (P-value < 0.05)
SLEDAI: systemic lupus erythematosus disease activity index, FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue, HAQ: Health Assessment Questionnaire, PSQI: Pittsburgh Sleep Quality Index, SLE-QoL: Systemic Lupus Erythematosus Quality of Life questionnaire, ESR: erythrocyte sedimentation rate, CRP: C- reactive protein, Hb: hemoglobin, C3: complement 3, C4: complement 4, Anti-dsDNA: anti- double-stranded DNA.

Linear regression analysis was done and showed that SLEDAI, FACIT-F, SLE-QoL, Creatinine, protein in 24-h urine, C3, and C4 were independent predictors for serum vitamin D level in SLE patients. (Table 6)

Table (6): Linear regression analysis for the factors predicting the serum vitamin D level in patients with SLE:

Variables	Vitamin D level	
	ß	p-value
SLEDAI	-0.933	**0.032***
FACIT-F	0.649	**0.004***
HAQ	−0.041	0.776
PSQI	-0.129	0.175
SLE-QoL	–0.535	**0.018***
ESR (mm/1st h)	–0.258	0.157
CRP (mg/L)	–0.248	0.154
Hb (g/dl)	0.280	0.085
Creatinine (mg/dL)	−0.06	**0.004***
Creatinine Clearance (ml/min)	− 0.849	0.418
24 h protein in urine (mg)	− 0.297	**0.035***
C3 (mg/dl)	0.443	**0.016***
C4 (mg/dl)	0.688	**0.013***
Anti-dsDNA (IU/ml)	–0.322	0.069

*Statistically significant (P-value < 0.05)

SLEDAI: systemic lupus erythematosus disease activity index, FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue, HAQ: Health Assessment Questionnaire, PSQI: Pittsburgh Sleep Quality Index, SLE-QoL: Systemic Lupus Erythematosus Quality of Life questionnaire, ESR: erythrocyte sedimentation rate, CRP: C- reactive protein, Hb: hemoglobin, C3: complement 3, C4: complement 4, Anti-dsDNA: anti- double-stranded DNA.

DISCUSSION

Systemic Lupus Erythematous (SLE) is a chronic autoimmune disease that affects multiple systems and may lead to life-threatening complications. Renal involvement is one of the most serious complications of SLE (22).

Genetic studies reported associations between vitamin D genetic variation and SLE susceptibility. Higher SLE disease activity also was prevalent in patients with lower serum vitamin D levels. Renal involvement in SLE interferes with vitamin D activation (23).

Growing evidence demonstrated the role vitamin D in sleep regulation. Vitamin D inadequacy can increase risk of sleep disorders and is associated with sleep difficulties and fatigue in SLE (24, 25). SLE affects all aspects of quality of life (QoL) of the patients functioning. Decreased QoL scores have been attributed to SLE progression, chronicity of the disease, vitamin D deficiency and lack of social support (26).

The aim of this study was to evaluate if vitamin D deficiency or insufficiency is a prevalent problem in SLE patients and to assess the correlation between serum vitamin D level in SLE with clinical disease activity, fatigue, sleep, function and quality of life impairment.

In our study there was a significant difference in ESR, CRP, RBCs, creatinine clearance and Anti-dsDNA between SLE patients and controls, with no significant difference between SLE renal positive and negative patients. A significant difference in ALP, protein in 24-h urine, C3, C4 and serum vitamin D level was found between SLE patients and controls, with significant difference between both groups of SLE patients. Serum albumin, RBCs in urine and albumin in urine, showed significant higher level in SLE renal positive and negative patients. As regards hemoglobin, WBCs, Platelets, AST and ALT, there was no significant difference between patients and controls (Table 1, 2)

This was in agreement with other studies found highly statistically significant decreased vitamin D level in Egyptian SLE patients' group versus healthy controls, with the lowest vitamin D level was detected in SLE patients with lupus nephritis in comparison to those without lupus nephritis (27, 28). Khairallah et al. (29) and Mok et al. (3) found that C3 & C4 were significantly higher among SLE without LN group compared to SLE with LN.

Our study reported vitamin D inadequacy in 90% of SLE renal positive (30% insufficiency, 60% deficiency), 70% of SLE renal negative (50% insufficiency, 20% deficiency), and 45% of healthy controls (27.5 % insufficiency, 17.5 % deficiency). (Table 3)

This finding is going with Squance et al. (30), Khairallah et al. (29), Korah et al. (27), Elsaid et al. (31), Abaza et al. (32); they reported vitamin D inadequacy in 43.4-45% of control group, and up to 90-100% of SLE cases. Also, Kamen et al. (33), found vitamin D insufficiency and deficiency in 85% (67% and 17.8% respectively) of their SLE patients.

On the other side, lower rates of vitamin D insufficiency and deficiency have been reported in other studies (34). The difference between results, may be due to vitamin D supplementation in some studies, the different disease durations of each patient, also may be due to the different number of studies' population.

We found a statistically significant difference in SLE disease activity index, fatigue, sleep quality, function and quality of life impairment in SLE patients with adequate and inadequate vitamin D serum level. (Table 4)

This was in agreement with another study that found vitamin D level in active SLE group was statistically lower than in inactive SLE group (28). Another study

reported improvement in fatigue and sleep quality in SLE patients with vitamin D supplementation, while no change in depression, anxiety and functional disability were observed (35). A cross-sectional study of 90 SLE patients found that those with vitamin D deficiency reported higher fatigue scores that those with adequate vitamin D levels (36).

The association found between vitamin D deficiency and quality of life impairment in diabetic, osteoporotic, and osteoarthritic patients (37, 38, 39). However, the available data for quality-of-life association with vitamin D deficiency in SLE were not strong enough to predict the effects of vitamin D in improving the life of SLE patients. The generalized and chronic nature of the disease impacts all aspects of patient's life. Vitamin D deficiency, pain, weakness and fatigue are the most commonly reported symptoms affecting the quality of life in SLE patients (40).

In our study, there was a significant negative correlation between serum vitamin D level with clinical disease activity, functional capacity, sleep, quality of life, ESR, CRP, creatinine, and protein in 24-h urine, with a significant positive correlation between serum vitamin D level with fatigue, C3 and C4. While no correlation was found with hemoglobin, creatinine clearance and Anti-dsDNA. (Table 5)

This was in agreement with other studies documented statistical negative correlation between vitamin D and disease activity index, disease duration, ESR, ANA titre, creatinine, anti-DNA titre and 24 hours urine protein, with a statistical positive correlation between vitamin D and PLTs, C3 & C4 (28, 41, 42, 43). Although Attar and Siddiqui (41) found correlation between vitamin D and C4 only; without C3, they explained this by the fact that in SLE the complement activity is mediated mainly by the classical pathway.

Mahmoud et al. (44) and Bonakdar et al. (45) found a significant correlation between vitamin D deficiencies, lower serum albumin, higher levels of liver enzymes, and higher haemoglobin concentrations. This could be attributed to the different disease duration and the different immunosuppressive drugs and corticosteroids taken by their patients.

Khairallah et al. (29) reported absence of correlation between vitamin D with C3, C4, and anti-dsDNA. Several studies showed no significant association between VD levels with ESR and CRP (29, 46). This controversy between studies may be due to variations in the disease activity, and the drugs used for treatment of SLE and also difference in method of the studies.

Another study reported non-significant association between serum vitamin D status with the levels of white blood cell, hemoglobin, platelet, creatinine, anti-dsDNA, or daily and cumulative steroid dosages within 1 month before the examination (47).

Similar to our results, a study showed that serum vitamin D levels in both inactive and active SLE disease status were significantly but inversely correlated with SLEDAI-2K (47). Gao et al. found that vitamin D deficiency had increased incidence of sleep disorders and poor sleep quality, short sleep duration, and sleepiness. They also provided evidence that serum levels below 20 ng /mL significantly heighten the unhealthy sleep (48). Serum vitamin D level was correlated with physical activity and the PSQI global score (49). Vitamin D insufficiency was associated with fatigue in SLE in some studies (50).

Linear regression analysis was done and showed that clinical disease activity, fatigue, quality of life impairment, serum creatinine, protein in 24-h urine; complement 3 and 4 were independent predictors for serum vitamin D level in SLE patients. (Table 6)

Other studies performed linear regression analysis in SLE, showed that the SLEDAI score and C3 complement are potent predictors for lower serum vitamin D levels (29, 48). Another study computed different models of regression analyses found an association of vitamin D level with the global PSQI scores (49). The increase in the disease activity, as assessed by SLEDAI was significantly associated with more impaired quality of life as assessed by SLEQOL (51).

CONCLUSION

Vitamin D inadequacy is a common problem; it is highly prevalent in SLE patients. There is a strong association between vitamin D levels and SLE disease activity, with various clinical consequences. It influences all aspects of patient's life: physical, psychological and social well-being. Fatigue and quality of life impairment in SLE are multifactorial phenomena involving psychological factors, pain, sleep disorders, lifestyle factors such as reduced physical activity; the disease activity contribution remains controversial.

Further studies and trials are still needed to confirm whether low vitamin D level is a modifiable risk factor for fatigue, sleep disorders and quality of life impairment in SLE patients.

Recommendations:

- Monitoring of vitamin D level in each SLE patient.
- Initiate therapy in individuals with serum vitamin D level < 30 **systemic** ng/mL
- Assessment of fatigue, sleep and quality of life beside measurement of disease activity provides a more comprehensive evaluation of SLE patients and their disease.

List of abbreviations:

SLE: lupus erythematosus.
SLEDAI: Systemic Lupus Erythematosus Disease Activity Index.
PSQI: Sleep quality assessment by Pittsburgh Sleep Quality Index
FACIT-F: Fatigue assessment by Functional Assessment of Chronic Illness Therapy-Fatigue.
HAQ: Assessment of functional capacity by Health Assessment Questionnaire.
HRQOL: Health Related Quality of Life.
SLICC: Systemic lupus International Collaborating Clinics.

SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000.
ELISA: enzyme immunosorbent assay.
LN: Lupus Nephritis.
SD: standard deviation.

Declarations:

Ethics approval and consent to participate

The study was approved by the local Ethics Committee of Faculty of Medicine, Tanta University. Approval Code 36171/12/22. The written informed consent from all the patients was obtained and the trial was conducted according to the Declaration of Helsinki principles.

Competing interests

The authors declare that they have no competing interests" in this section.

Author contributions

A.E performed the conception, S.G made the design, H.E analyzed and interpreted of the data and W.S performed the draft of paper and revised it for intellectual content. All authors gave the final approval of the version to be published; and agree to be accountable for all aspects of the work.

Declaration of interest

This original work has not been previously published or simultaneously submitted for publication elsewhere. The manuscript has been read and approved by all the authors, and all the conditions as previously stated by the ICMJE have been met.

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