ORIGINAL ARTICLE

Vitamin D status in a monocentric cohort of systemic lupus erythematosus (SLE) patients and correlations with clinical and immunological profile

Ong Swee Gaik, MRCP, Ding Hui Jen, MRCP

Rheumatology Unit, Department of Medicine, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia

ABSTRACT

Introduction: Numerous studies have found that a majority of systemic lupus erythematosus (SLE) patients have sub-optimal vitamin D levels. The major contributory factor is most likely attributed to sun protection measures in order to avoid SLE flares. The objectives of this research included the assessment of vitamin D status and its association with clinical manifestations of SLE, cardiovascular risk factors, autoantibodies, SLE disease activity and damage accrual.

Method: This retrospective study involved SLE patients who attended the Rheumatology Clinic at the Hospital Kuala Lumpur from January 2014 to December 2016. Vitamin D was categorised as normal, insufficient or deficient, and the clinical variables were compared across vitamin D categories with chi-squared tests and Pearson correlation coefficient.

Results: We included 216 patients. The mean 25(OH)D concentration was 51.3(Standard Deviation; SD 14.8) nmol/L. Fifty (23.1%) patients had vitamin D deficiency, 120 (55.6%) had vitamin D insufficiency, while 46 (21.3%) had adequate vitamin D levels. There were statistically significant associations between vitamin D status and ethnic group, lupus nephritis and hypertension. No correlations were observed between vitamin D status with SLEDAI score (Pearson correlation coefficient -0.015, p=0.829) as well as SDI score (Pearson correlation coefficient -0.017, p=0.801).

Conclusion: SLE patients should be screened for vitamin D concentrations and their levels optimised.

KEY WORDS:
Systemic lupus erythematosus; Vitamin D; disease activity

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that involves multiple organs with a heterogeneous presentation. Vitamin D is a fat-soluble vitamin which plays a major role in bone growth and remodelling. It promotes calcium absorption and regulates calcium and phosphate concentrations to ensure adequate bone mineralization. Therefore, adequate vitamin D and calcium intake is paramount in the prevention of osteoporotic fractures. Apart from bone health, vitamin D insufficiency has been linked to the development of several autoimmune diseases.[1] Indeed, more research is necessary to address the role of vitamin D relating to this issue.

Sub-optimal vitamin D levels have been reported in numerous SLE cohorts in different geographic locations and at various periods of the year.[2-6] This situation is probably enhanced by the common advice of sunlight avoidance. In addition, low vitamin D concentrations demonstrated an inverse relationship with disease activity.[2,7-10] This study was conducted given the paucity of data on vitamin D status among Malaysian SLE patients.

METHODOLOGY

This retrospective study involved SLE patients attending the Rheumatology Clinic, Hospital Kuala Lumpur from January 2014 to December 2016. Patients that fulfilled at least four of the 1997 American College of Rheumatology (ACR) revised classification criteria for SLE and had at least one serum 25-hydroxyvitamin D [25(OH)D] concentration measured were included. Patients who had received vitamin D replacement therapy were excluded. Approval from the Malaysian Research and Ethics Committee, Ministry of Health Malaysia was obtained; and registration was done in accordance with the National Medical Research Register Malaysia (NMRR-16-2108-33162(IIR).

Data was obtained from patients' medical records. The following variables were recorded: demographic data; duration of SLE when vitamin D was analysed; age of patients when vitamin D levels were taken; selected clinical manifestations of SLE including cutaneous lesions (malar rash, photosensitivity, discoid rash), arthritis, neuropsychiatric manifestations (NPSLE), lupus nephritis; Schirmer's test; cardiovascular risk factors which included hypertension, dyslipidaemia and diabetes mellitus; and T-score from bone mineral densitometry using dual energy X-ray absorptiometry. Laboratory parameters documented were vitamin D concentrations, and autoantibody profile which included anti-dsDNA (anti-double-stranded deoxyribonucleic acid) antibodies, anti-Ro/SSA antibodies, anticardiolipin antibodies and rheumatoid factor. Disease activity evaluated by the SLE Disease Activity Index 2000 (SLEDAI-2K)[11] and damage accrual evaluated according to the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI),[12] were included at the time vitamin D concentrations were taken.

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Corresponding Author: Ong Swee Gaik
Email: ongsweeg@gmail.com

Table I: Demographic, clinical and immunological characteristics of SLE patients

VARIABLE	NUMBER (%)	Mean (SD)	RANGE
Gender			
Male	11 (5.1)		
Female	205 (94.9)		
Ethnic group			
Malay	141 (65.3)		
Chinese	53 (24.5)		
Indian	19 (8.8)		
Others	3 (1.4)		
Age		35.9 (7.1)	14-75
Duration of SLE when Vit D was analysed (years)		6.9	0-39
Age when Vit D was analysed (years)		35.1 (6.4)	14-75
Vitamin D concentration (nmol/L)		51.3 (14.8)	7.5-156.1
Vitamin D status (nmol/L)			
Deficiency (<25)	50 (23.1)		
Insufficiency (25 to <75)	120 (55.6)		
Adequate (≥75)	46 (21.3)		
Vitamin D concentration (nmol/L)			
Deficiency (<25)		16.9 (6.6)	
Insufficiency (25 to <75)		46.5 (14.9)	
Adequate (≥75)		100.5 (20.9)	
Cutaneous lesions (malar rash, photosensitivity, discoid rash)	158 (73.1)		
Arthritis	100 (46.3)		
Neuropsychiatric manifestations (NPSLE)	46 (21.3)		
Lupus nephritis	72 (46.3)		
Schirmer's test positivity (n=213)	62 (29.1)		
Hypertension	44 (20.4)		
Dyslipidaemia	46 (21.3)		
Diabetes mellitus	9 (4.2)		
Osteoporosis (n=155)	18 (11.6)		
Anti-dsDNA (n=202)	114 (56.4)		
Anti-Ro Ab (n=209)	97 (46.4)		
Anticardiolipin Ab (n=204)	21 (10.3)		
Rheumatoid factor (n=198)	27 (13.6)		

*where n is not stated, it indicates 216 subjects, SD Standard Deviation

Serum 25(OH)D concentration was measured by chemiluminescence immunoassay on an automated analyser (Beckman Coulter UniCel Dxl 800). Serum 25(OH)D concentration of <25nmol/L was defined as vitamin D deficiency and level between 25 and <75nmol/L was defined as vitamin D insufficiency. Serum 25(OH)D of ≥75nmol/L was considered adequate.

Anti-dsDNA and anti-Ro antibody tests were performed using fluoroenzyme immunoassay technique (EliA, Phadia, Sweden) and levels were recorded in IU/ml and U/ml, respectively. Anticardiolipin antibody was measured using ELISA (Immuno Concepts) while rheumatoid factor was analysed by latex agglutination method (Omega Diagnostics).

Schirmer's test was considered positive when moisture on the filter paper placed in the lower eyelid pouch is less than 5mm in 5 minutes.

Hypertension was defined as a systolic blood pressure (SBP) of 140mmHg or greater, or a diastolic blood pressure (DBP) of 90mmHg or greater, or patient was on antihypertensive medication. Diabetes mellitus was defined as a fasting blood glucose of >6.1mmol/L or patient was on antidiabetic medications.

Dyslipidaemia was defined as elevation of total cholesterol, low-density lipoprotein (LDL) cholesterol or triglyceride, or patient was on current lipid-lowering medications. The cut-off levels are: >6.2mmol/L for total cholesterol, >4.9mmol/L for LDL cholesterol and >2.3mmol/L for triglyceride.

Statistical Analysis

Categorical variables were described as number and percentage and continuous variables as mean and standard deviation (SD). Vitamin D was categorised as normal, insufficient or deficient and the clinical variables were compared across vitamin D categories with chi-squared tests and Pearson correlation coefficient. A p-value of <0.05 was considered of significant statistical value. All statistical analyses were performed using SPSS version 20.0 (IBM SPSS Inc., Chicago, IL, USA).

RESULTS

A total of 216 SLE patients were included in this study. Eleven (5.1%) were males and 205 (94.9%) were females. There were 141 (65.3%) Malays, 53 (24.5%) Chinese, 19 (8.8%) Indians and three (1.4%) of other ethnicities. This corresponded with the pattern of ethnic distribution in the Malaysian population. Their ages ranged from 14 to 75 years, with a mean age of 35.9 (SD 7.1) years.

Table II: Demographic characteristics, clinical manifestations and autoantibodies in SLE patients by serum 25(OH)D concentrations

Variables	25(OH)D (nmol/L) N=216			
	Deficiency (<25) n (%)	Insufficiency (25 to <75) n (%)	Adequate (≥75) n (%)	p-value
Ethnic group				
Malay	36 (25.5)	86 (61.0)	19 (13.5)	<0.001
Chinese	7 (13.2)	25 (47.2)	21 (39.6)	
Indian	5 (26.3)	9 (47.4)	5 (26.3)	
Gender				
Male	1 (9.1)	6 (54.5)	4 (36.4)	0.328
Female	49 (23.9)	114 (55.6)	42 (20.5)	
Cutaneous				
Yes	40 (25.3)	87 (55.1)	31 (19.6)	0.368
No	10 (17.2)	33 (56.9)	15 (25.9)	
Arthritis				
Yes	21 (21.0)	57 (57.0)	22 (22.0)	0.785
No	29 (25.0)	63 (54.3)	24 (20.7)	
NPSLE				
Yes	10 (21.7)	22 (47.8)	14 (30.5)	0.226
No	40 (23.5)	98 (57.7)	32 (18.8)	
Lupus nephritis				
Yes	29 (40.3)	32 (44.4)	11 (15.3)	<0.001
No	20 (13.9)	89 (61.8)	35 (24.3)	
Schirmer's test				
Positive	13 (21.0)	34 (54.8)	15 (24.2)	0.710
Negative	35 (23.2)	87 (57.6)	29 (19.2)	
Hypertension				
Yes	16 (36.3)	18 (41.0)	10 (22.7)	0.032
No	33 (19.2)	103 (59.9)	36 (20.9)	
Dyslipidaemia				
Yes	16 (34.8)	21 (45.6)	9 (19.6)	0.104
No	34 (20.0)	99 (58.2)	37 (21.8)	
Diabetes mellitus				
Yes	4 (44.4)	4 (44.4)	1 (11.2)	0.267
No	45 (21.7)	117 (56.6)	45 (21.7)	
Osteoporosis				
Yes	5 (27.8)	7 (38.9)	6 (33.3)	0.448
No	28 (20.4)	75 (54.8)	34 (24.8)	
Anti-dsDNA Ab				
Yes	28 (24.6)	60 (52.6)	26 (22.8)	0.910
No	20 (22.7)	49 (55.7)	19 (21.6)	
Rheumatoid factor				
Yes	5 (18.5)	16 (59.3)	6 (22.2)	0.850
No	40 (23.4)	94 (55.0)	37 (21.6)	
Anticardiolipin Ab				
Yes	6 (28.6)	11 (52.4)	4 (19.0)	0.774
No	40 (21.9)	102 (55.7)	41 (22.4)	
Anti-Ro Ab				
Yes	22 (22.7)	49 (50.5)	26 (26.8)	0.163
No	28 (25.0)	66 (58.9)	18 (16.1)	
SLEDAI	50 (23.1)	120 (55.6)	46 (21.3)	0.829
SDI	50 (23.1)	120 (55.6)	46 (21.3)	0.801

Mean duration of SLE at the time of 25(OH)D analysis was 6.9 years (range from 0 to 39 years), and mean age was 35.1 (SD 6.4 years, range from 14 to 75 years). Mean 25(OH)D concentration was 51.3 (SD 14.8nmol/L, range from 7.5 to 156.1nmol/L). Fifty (23.1%) patients had vitamin D deficiency, 120 (55.6%) had vitamin D insufficiency, while 46 (21.3%) had adequate vitamin D levels. Table I shows selected demographic, clinical and immunological characteristics of the study group.

Our study showed statistically significant association between vitamin D status and ethnic group (p<0.001). Chinese had the lowest proportion of patients with vitamin D deficiency and insufficiency (60.4%), while Malay (86.5%) had the highest proportion. The mean levels of serum 25(OH)D in Chinese, Indian and Malay SLE patients were 66.3 (SD 36.7) nmol/L, 54.9 (SD 36.4) nmol/L, and 45.0 (SD 27.5) nmol/L, respectively.

Among the various clinical manifestations of SLE, only lupus nephritis showed a statistically significant association with vitamin D status (p<0.001). However, further analysis failed to reveal any correlation between vitamin D status and the classes of lupus nephritis. In terms of cardiovascular risk factors, hypertension demonstrated significant correlation with vitamin D status (p=0.032).

Table III: Prevalence of vitamin D insufficiency and deficiency in SLE patients in studies from various geographic locations

Author	Year	Country	Type of Participant	Number of SLE patients	Mean 25(OH)D level (nmol/L) SD	Vitamin D status: 25(OH)D levels (nmol/L)	Prevalence (%)
Garcia-Carrasco M et al.[16]	2017	Mexico	Mexican Mestizo	137	49.3 (15.8)	Deficiency (<75) Insufficiency (<25)	89.0 2.9 (91.9)
Zheng ZH et al.[14]	2016	China	Han Chinese	121	33.7 (19.4)	Deficiency (<50) Insufficiency (<75)	84.3 13.2 (97.5)
Abaza NM et al.[8]	2016	Egypt	Han Chinese	60	44.0 (17.3)	Deficiency (not stated Insufficiency (not stated)	23.3 73.3 (96.6)
Gao CC et al.[7]	2016	China	Chinese	121	33.8 (19.5)	Deficiency (<25) Insufficiency (<75)	34.7 62.8 (97.5)
Yap KS et al.[10]	2015	Australia	Asian, Caucasian, other	119	56.3 (26.0)	Deficiency (<40)	27.7
Lertratanakul A et al.[19]	2014	Canada, USA, UK, Korea, Sweden, Spain, Switzerland	Caucasian, African American, Hispanic, Asian, other	875	59.5 (33.5)	Deficiency (<75)	72.3
Mok CC et al.[15]	2012	Hong Kong	Not stated	290	47.8 (15.5)	Deficiency (<37.5) Insufficiency (<75)	27.0 96.0 (96)
Attar SM et al.[31]	2012	Saudi Arabia	Not stated	95	23.9 (14.0)	Deficiency (<25) Insufficiency (<50)	48.0 39.0 (87)
Yeap SS et al.[13]	2012	Malaysia	Malay, Chinese, Indian	38	54.0 (11.5)	Deficiency (<50) Insufficiency (<75)	32.0 65.8 (97.8)
Souto M et al.[20]	2011	Brazil	Caucasian, Non-Caucasian	159	87.5	Deficiency (<50) Insufficiency (<75)	8.2 37.7 (45.9)
Toloza S et al.[17]	2010	Canada	Caucasian, Black, Asian, other	124	68.5 (31.0)	Deficiency (<40) Insufficiency (<80)	17.9 66.7 (84.6)
Wu PW et al.[18]	2009	USA	Asian, other African-American, Hispanic, Asian	181	67.8 (29.8)	Deficiency (≤37.5) Insufficiency (<75)	20.0 62.2 (82.2)
Ruiz-Irastorza G et al.[5]	2008	Spain	Caucasian, Non-Caucasian	92	55.0 (30.0)	Deficiency (<25) Insufficiency (<75)	15.0 75.0 (90)

*SD – standard deviation

We did not find any association between vitamin D status and duration of SLE. Neither was there a relationship with gender. Nonetheless, male SLE patients had higher mean 25(OH)D concentrations at 69.4 (SD 36.9) nmol/L, compared to female at 50.2 (SD 31.6) nmol/L. There were no significant correlations between vitamin D status and clinical features of lupus which included cutaneous lesions, arthritis, NPSLE and positive Schirmer's test; cardiovascular risk factors, which comprised dyslipidaemia and diabetes mellitus; osteoporosis; and autoantibodies which included anti-dsDNA, anti-Ro antibody, anticardiolipin antibody and rheumatoid factor.

With regards to disease activity and disease damage, no correlations were observed between vitamin D status with SLEDAI score (Pearson correlation coefficient -0.015, p=0.829) as well as SDI score (Pearson correlation coefficient -0.017, p=0.801).

Table II shows the demographic characteristics, clinical manifestations of SLE and autoantibodies by serum 25(OH)D levels.

DISCUSSION

Suboptimal vitamin D levels among SLE patients is a well-known fact that have been demonstrated in numerous studies across different geographical settings, including countries around the equator.[2-10]

Our study revealed that the prevalence of vitamin D deficiency and insufficiency among Malaysian SLE patients was high, at 78.7%. Nevertheless, this proportion is much lower than that reported by a previous Malaysian study conducted by Yeap et al.,[13] who reported a prevalence of 97.8%. Prevalence of suboptimal vitamin D levels that exceeded 90% or greater was reported in studies conducted in China,[7,14] Egypt,[8] Hong Kong,[15] Mexico[16] and Spain.[5] Two studies conducted in Canada[17] and the USA[18], respectively, reported levels of 84.6% and 82.2%. On the other hand, there were several studies that reported levels lower than ours. This included the multi-centre study by Letratanakul et al.[19] which described the prevalence at 72.3%, and involved patients from Europe, North America and Asia. Studies conducted by Souto et al.[20] in Brazil and Yap et al.[10] in Australia reported prevalence of 45.9% and 27.7%, respectively.

A summary of the studies describing the prevalence of vitamin D deficiency and insufficiency in SLE patients is illustrated in Table III. Of note, the definition of the various categories of vitamin D differed from one to the other.

Mean vitamin D levels in our patient cohort was 51.3 (SD 14.8) nmol/L, which is comparable with the study by Yeap et al.,[13] who reported a mean of 54 (SD 11.5) nmol/L (equivalent to 21.6 (SD 4.6) ng/ml). The other studies described in Table III observed mean vitamin D levels that ranged from 23.9nmol/L to 87.5nmol/L, with more than half of them reporting values that were greater than 50nmol/L. Vitamin D deficiency was noted in 23.1% of our patient cohort. Garcia-Carrasco et al.[16] and Zheng et al.,[14] however, reported values that are significantly higher, at 89% and 84.3%, respectively. Interestingly, our study showed statistically significant association between vitamin D status and ethnic group (p<0.001), wherein Chinese had the lowest proportion of patients with vitamin D deficiency and insufficiency (60.4%), while Malays (86.5%) had the highest proportion. The reason why Malay ethnic group comprised the highest percentage of suboptimal vitamin D concentrations may be attributed to their more conservative manner of dressing, since it is a well-known fact that dermal synthesis is the main natural source of vitamin D. A study by Rahman et al.,[21] which assessed the nutrient intake among postmenopausal Malay and Chinese women in Malaysia found that there was no significant difference in the vitamin D intake between the two ethnic groups. According to Nesby-O'Dell et al.[22] and Clemens et al.,[23] increased skin pigmentation diminishes the capacity of skin to synthesize vitamin D. This point is reflected in our study which demonstrated lower vitamin D levels among Malay and Indian ethnic groups. In general, both these races tend to have higher melanin concentration in their skin as compared to Chinese.

Even though our findings showed that vitamin D deficiency was more prevalent in female (23.9%) SLE patients compared to male (9.1%), there was no statistically significant association between vitamin D status and gender. Zheng et al.[14] reported similar findings, wherein 64.9% of female and 42.0% of male SLE patients had vitamin D deficiency. However, no correlation was demonstrated between vitamin D deficiency and gender. The explanation for this outcome is unclear and remains to be determined. Interestingly, Ruiz-Irastorza et al.[5] identified female sex to be a predictor of higher vitamin D levels (p=0.001).

Numerous studies have indicated a link between vitamin D deficiency and certain clinical features of SLE. Among the selected clinical manifestations of lupus, our analysis identified lupus nephritis to have a statistically significant association with vitamin D status (p<0.001). Our result was, however, not in agreement with the findings by Miskovic et al.[24] Interestingly, most of our patients with lupus nephritis had normal serum creatinine levels. Only 8.3% (6 of 72) had estimated glomerular filtration rate (eGFR) of less than 60ml/min/1.73m^2. Hence the explanation for this positive association in our study requires further investigation. It is a well-recognised fact that low vitamin D levels occur in patients with chronic kidney disease, and this is supported by studies conducted by several researchers,[3,6,17] which demonstrated a significant correlation between renal disease and suboptimal vitamin D levels in their patient cohorts. Souto et al.[20] who excluded patients with creatinine clearance of <60ml/min; and McGhie et al.[4] whose subjects had normal mean creatinine clearance values of 105.9ml/min/1.73m^2, did not find any association between low vitamin D concentrations and normal creatinine levels.

Apart from lupus nephritis, we did not find any significant relationship between vitamin D and cutaneous LE, arthritis, NPSLE and positive Schirmer's test. Similarly, Miskovic et al.[24] failed to identify significant associations between vitamin D status and photosensitivity, skin lesions and arthritis among Serbian SLE patients. The predominant source of vitamin D is from synthesis in the skin through the action of sunlight. Because SLE may be exacerbated with sun exposure, we

would expect patients with cutaneous LE to avoid sunlight resulting in lower levels of vitamin D. Interestingly, this was not demonstrated in our study. This result was further substantiated by studies from Gao et al.,[7] Garcia-Carrasco et al.[16] and Souto et al.,[20] who also failed to demonstrate significant correlation between suboptimal vitamin D levels and photosensitivity among Chinese, Brazilian and Mexican SLE patients, respectively. Considering the climate in Malaysia, Brazil and Mexico being tropical with massive amounts of sunshine, a possible explanation is that SLE patients did not practise adequate photo-protective measures. On the other hand, Ruiz-Irastorza et al.[5] and Kamen et al.[6] reported a correlation between suboptimal vitamin D level and photosensitivity.

Patients with systemic lupus erythematosus have a much higher risk of coronary heart disease at an earlier age, due to accelerated atherosclerosis. There is increasing evidence to suggest suboptimal vitamin D levels may be linked to cardiovascular events among the general population, namely, myocardial infarction, heart failure, stroke, diabetes mellitus, hypertension, dyslipidaemia and obesity.[25-27] Among the cardiovascular risk factors, we found hypertension to be significantly associated with low vitamin D level. Our findings concurred with that reported by Lertratanakul et al.[19] and Wang et al.[28] Similar findings have been repeatedly reported in the general population[29,30] and are believed to be attributed to effects of vitamin D on the renin-angiotensin system though the exact mechanism remains unclear. On the contrary, Wu et al.[18] failed to demonstrate a relationship between cardiovascular risk factors and low vitamin D level in 181 SLE patients in a multivariate model.

SLE patients are largely at risk for osteoporosis given that they avoid sunlight exposure, have low vitamin D levels and receive long-term corticosteroids. Nonetheless, our study failed to demonstrate an association between low vitamin D levels and osteoporosis, the reasons of which are not explored.

With regards to immunological response, we did not find a correlation between low vitamin D levels and specific autoantibodies, namely, anti-dsDNA, rheumatoid factor, anti-Ro antibody and anticardiolipin antibody. In terms of association between anti-dsDNA antibodies and vitamin D status, our results are in line with those reported by several other researchers which showed a negative correlation between low vitamin D levels and anti-dsDNA.[3,9,17,31,32] This may be explained by the presence of antivitamin D antibodies as observed by Carvalho et al.[33] in his patient cohort. On the other hand, studies by Abaza et al.[8] and Mok et al.[15] confirmed significant correlation between vitamin D levels and anti-dsDNA antibodies. Given the inconsistent findings, we were unable to establish a causal relationship between vitamin D status and anti-dsDNA antibodies. Miskovic et al.,[24] who tested for anti-SSA antibodies and anticardiolipin antibodies, found that none of these autoantibodies showed statistically significant correlation with vitamin D status. This finding is in total agreement with ours. To date, there has been no study examining the association between rheumatoid factor and vitamin D status in SLE patients.

Evidence on the relationship between low vitamin D levels and higher disease activity is still debatable. Even though numerous studies had reported relationships between low vitamin D levels and higher disease activity,[2,7-10,13] there are also many that failed to show any associations.[5,16,20,24,31,32] This controversial finding is similarly observed in studies that examined vitamin D concentrations and damage accrual in SLE.[5,8] Given these conflicting results, it is possible vitamin D levels do not have any bearing on SLE disease activity or disease damage, contrary to what researchers may wish to consider.

We recognise our study has several limitations. This is a cross-sectional study which only included one measurement of serum 25(OH)D concentration. We did not control for certain confounders, in particular, corticosteroid use and duration. Nevertheless, the strength of our study is the relatively large sample size and its heterogeneous population. Various aspects of SLE which encompassed clinical features, cardiovascular risk factors as well as autoantibodies, were examined with regards to the vitamin D status.

In conclusion, our findings supported associations between low vitamin D levels and ethnic groups, lupus nephritis, in addition to certain cardiovascular risk factor, which was, hypertension. Therefore, these results strongly recommend routine sampling of serum 25(OH)D concentrations in all SLE patients, and management should emphasize on the maintenance of SLE patients at optimal 25(OH)D levels.

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CONFLICT OF INTEREST STATEMENT

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