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Vitamin D Pattern in Patients with Systemic Lupus Erythematosus with and without Nephritis

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease where chronic inflammation and organ damage is observed due to various suspected causes e.g. inadequate levels of vitamin D (a steroid hormone with immunomodulatory effects).

Objective: To assess vitamin D (VD) levels in serum of patients with lupus nephritis (LN) in comparison with patients with extra-renal lupus and healthy controls, and to assess the relation between VD levels and the various clinical and laboratory disease parameters.

Patients and Methods: This was a case-control study that was held in Zagazig University Hospitals between June 2019 and July 2020. The study included 40 patients admitted with systemic lupus erythematosus (SLE) with and without lupus nephritis (LN), and 20 age-matched healthy subjects. Laboratory investigations such as complete blood count, electrolytes, PTH, acute phase reactant, complements, Ads DNA and 25(OH) D levels of the subjects were measured.

Results: Patients with SLE with lupus nephritis were significantly lower regarding vitamin D with no significant difference between patients with SLE without LN and control group.

Conclusions: Our study revealed a high frequency of Vit D deficiency and insufficiency among patients with SLE with LN compared to SLE without LN and healthy controls.

Keywords: Systemic lupus erythematosus, Lupus nephritis, Vitamin D.

INTRODUCTION

VD is a lipo-soluble vitamin that plays a key role in calcium and phosphorus metabolism and bone mineralization. The main source of VD in our body comes from the conversion of 7-dehydro-cholesterol into preVD3 in the skin, while smaller amounts of VD come from dietary sources [(1)].

However, it had been reported that several immune cells express VD receptors (VDRs) on their surfaces [(2)] and many immune cells synthesize the 1α-hydroxylase enzyme responsible for synthesis of the active form of VD in the microenvironment of lymph tissues. These findings indicate that VD is involved in the immune modulation [(3)].

SLE is an autoimmune disorder that affects multiple organ systems including the skin, kidneys, and brain [(4)]. Clinical features are highly variable, ranging from skin and joint involvement to organ involvement and life-threatening complications [(5)]. LN is one of the most serious consequences of SLE and is one of the major factors predicting poor outcome, or End-Stage Renal Disease (ESRD) 10 years after onset of LN [(6)]. Renal involvement can interfere with 1-hydroxylation that is essential to make active form of VD [(7)].

Low serum VD is prevalent in SLE patients, ranging from 16% [(8)] to 95% [(9)] and can be attributed to several factors such as photosensitivity, sunscreen application, renal damage, chronic glucocorticoids or anti-malarial therapy [(10)].

PATIENTS AND METHODS

A case-control study that was conducted in Nephrology Outpatients Clinic of Internal Medicine Department from June 2019 to July 2020.

60 individuals, 40 of them were patients admitted with SLE with and without LN.

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee Board (ZU-IRB#5839-29.12.2019). Every patient signed an informed written consent for acceptance of the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

Age > 18 years and of either sex. All patients were diagnosed according to revised American college of Rheumatology (ACR) classification criteria for SLE (The new 2019 EULAR/ACR classification criteria for SLE). The criteria for LN [(11)] include persistent proteinuria > 0.5 grams/day, renal biopsy class II, III, IV or V. The study included also healthy matched controls.

Exclusion criteria:

Patients with SLE without overlapping with other inflammatory arthritis or other connective tissue disease. Underlying chronic kidney disease other than LN. Malignancy or suspected malignancy and those on VD therapy. Patients with serious chronic illness including advanced difficult to be controlled chronic obstructive pulmonary disease, inflammatory bowel disease, inflammatory arthritis, connective tissue

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disorders with or without renal involvement and HIV/AIDS.

The subjects were divided into: **Group I** including 20 patients with SLE without LN. **Group II** included 20 patients with SLE with lupus nephritis. **Group (III)** included 20 healthy controls.

Diagnosis of SLE was done according to revised American college of Rheumatology (ACR) classification criteria for SLE that requires a positive ANA as obligatory entry criterion. Other criteria were chosen from 7 clinical (constitutional, hematologic, neuropsychiatric, mucocutaneous, serosal, musculoskeletal and renal) and 3 immunologic (antiphospholipid antibodies, complement protein and SLE-specific antibodies) categories and weighted from 2 to10 patients with >10 points are classified as having SLE.

All participants were subjected to the following:

1. **Full history talking** including age, sex, duration of SLE, photosensitivity, skin changes, active arthritis, and activity of LN and drug intake.
2. **Medication history** of hydroxychloroquine and glucocorticoids drugs taken.
3. **Complete physical and clinical examination** including vital signs with special concentration on SLE signs.
4. **Laboratory assessment** including concentration of parathyroid hormone, ESR, C-Reactive Protein (CRP), serum creatinine, albumin/creatinine ratio, anti-nuclear-antibodies (ANA), anti-ds-DNA and 25-OH vitamin D and urinalysis. Urine samples were obtained for evaluation of 24-hours protein in urine and presence of urine casts.
5. **Assessment of SLE disease activity:** The disease activity in the SLE patient was assessed by the systemic lupus erythematosus disease activity index (SLEDAI). The SLEDAI is a global index that was developed and introduced in 1985 as a clinical index for the assessment of lupus disease activity in the preceding 10 days. It consists of 24 weighted clinical and laboratory variables of nine organ systems. This instrument was derived by consensus among experts in rheumatology followed by application of regression models to assign relative weights to each parameter. SLEDAI was modeled on the basis of clinician global judgment. The scores of the descriptors range from 1 to 8, and the total possible score for all 24 descriptors is 105 **(12).**

Statistic analysis

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA). According to the type of data, qualitative were represented as number and percentage, quantitative continues were represented as mean ± SD. The following tests were used to test differences for significance: Difference and association of qualitative variable by Chi square test (X2).

Differences between quantitative independent groups by t test, multiple by ANOVA and correlation by Pearson's correlation. P value was set at ≤ 0.05 for significant results & < 0.001 for highly significant and p-value > 0.05 was considered statistically non-significant (NS).

RESULTS

Table (1): Demographic data distribution among studied groups

			Group I	Group II	Group III	F/ X^2	P
Age (Years)			**35.80 ± 5.6**	**34.30 ± 7.36**	**34.75 ± 6.07**	**0.290**	**0.749**
SLE duration (Years)			**5.40 ± 1.78**	**7.85 ± 2.68**	**--------**	**t= 3.080**	**0.007***
BMI (kg/m^2)			**25.53 ± 3.98**	**25.90 ± 4.23**	**25.21±4.53**	**0.130**	**0.878**
Sex	**Female**	**N**	**18**	**19**	**17**		
		%	**90.0%**	**95.0%**	**85.0%**		
	Male	**N**	**2**	**1**	**3**	**1.11**	**0.57**
		%	**10.0%**	**5.0%**	**15.0%**		
Total		**N**	**20**	**20**	**20**		
		%	**100.0%**	**100.0%**	**100.0%**		

Age was distributed as 35.80 ± 5.6, 34.30 ± 7.36 and 34.75 ± 6.07 years respectively among studied groups with no significant difference among them. Also there was non-significant difference regarding BMI and sex distribution. But regarding SLE duration (between SLE without LN and SLE with LN Groups) group II had significantly longer duration (Table 1).

Table (2): LAB distribution among studied groups

	Group I	Group II	Group III	F	P
ESR (mm)	50.30±10.95	96.10±14.55*	11.30±2.93#	317.627	0.00**
C3 (mg/dl)	68.05±2.64	54.60±8.96	-----	t=4.342	0.00**
C4 (mg/dl)	32.85±1.74	18.30±6.33	------	t=8.716	0.00**
HB (g/dl)	11.23±1.02	10.74±0.97	13.65±1.08*	58.244	0.00**
WBCs (x103/µL)	4.93±1.35	4.75±1.41	5.98±1.0*	5.438	0.007*
Platelets (x103/µL)	236.70±9.06	219.10±7.0	338.80±49.60*	19.721	0.00**
CRP (mg/dl)	28.95±5.87	32.94±1.47	4.39±1.18#	29.448	0.00**
Cholesterol (mg/dl)	155.45±6.98	185.50±6.99*	150.45±6.98	147.233	0.00**
Triglycerides (mg/dl)	144.35±7.93	147.45±10.24	131.35±7.93#	18.966	0.00**
HDL (mg/dl)	41.75±4.08	34.35±4.11#	43.35±3.98	26.810	0.00**
LDL (mg/dl)	108.05±6.40	111.05±6.40	86.30±6.49#	88.123	0.00**
Trig/HDL	3.53±0.47	4.34±0.57*	3.05±0.36#	36.510	0.00**
Calcium (mg/dl)	8.51±0.60	7.94±0.65#	9.21±0.71*	18.537	0.00**
Phosphorus (mg/dl)	4.31±0.63	4.32±0.61	4.61±0.74	1.362	0.264
PTH (ng/L)	68.45±9.22	67.20±16.86	48.35±8.62#	10.445	0.00**
S albumin (g/dl)	4.28±0.41	2.87±0.39#	4.29±0.53	77.802	0.00**
ALP (u/l)	103.55±3.96	110.20±4.06	78.95±14.84#	6.416	0.003*

PTH: parathormone hormone ALP: alkaline phosphatase HDL: high-density lipoprotein LDL: low-density lipoprotein C3 & 4: complement 3 & 4 WBCs: white blood cells * group significantly higher by LSD # group significantly lower by LSD.

ESR was significantly higher among group II and significantly lower among group III and C3 & C4 were significantly higher among group I. Regarding HB, WBCs and PLT, group III was significantly higher with non-significant difference between cases groups. Regarding CRP, group III was significantly lower with non-significant difference between cases groups. Cholesterol was significantly higher among group II. TG was significantly lower among group III with non-significant difference between cases groups. Regarding HDL, group II was significantly lower without significant difference between group I and III. LDL was significantly lower among group III with non-significant difference between cases groups. Trig/HDL was significantly higher among group II and significantly lower among group III. Regarding calcium, it was significantly higher among group III and significantly lower among group II. PTH was significantly lower among group III and albumin was significantly lower among group II with non-significant difference between group I and III. ALP was significantly lower among group III with non-significant difference between cases groups.

Table (3): Biomarker distribution between cases groups

			Group		X^2	P
			Group I	Group II		
ANA	Negative	N	1	2		
		%	5.0%	10.0%		
	Positive	N	19	18	0.28	0.84
		%	95.0%	90.0%		
Antids DNA titer	Negative	N	11	4		
		%	55.0%	20.0%		
	Positive	N	9	16	5.22	0.022*
		%	45.0%	80.0%		
Proteinuria	NA	N	20	0		
		%	100.0%	0.0%		
	Negative	N	0	7	40.0	0.00**
		%	0.0%	35.0%		
	Positive	N	0	13		
		%	0.0%	65.0%		
Total		N	20	20		
		%	100.0%	100.0%		

Anti ds DNA titer and proteinuria were significantly associated with group II (Table 3).

Table (4): Vitamin D distribution between cases groups

	Group I	Group II	Group III	F	P
Vit D (ng/ml)	**26.90 ± 8.25**	**18.05 ± 5.68#**	**30.35 ± 10.01**	**5.999**	**0.004***

Table (4) showed that group II was significantly lower regarding vitamin D with non-significant difference between groups I and III.

Table (5): Correlation between vitamin D and other parameters

		Vit D
BMI	**r**	**-.281-***
	P	**.029**
SLE duration	**r**	**-.288-***
	P	**.026**
ESR	**r**	**-.419-****
	P	**.001**
Lupus nephritis Class	**r**	**-.095-**
	P	**.691**
C3	**r**	**.041**
	P	**.755**
C4	**r**	**.137**
	P	**.297**
Hb level	**r**	**.382****
	P	**.003**
WBS	**r**	**.034**
	P	**.794**
Platelets	**r**	**.289***
	P	**.025**
CRP	**r**	**-.375-****
	P	**.003**
Cholesterol	**r**	**-.399-****
	P	**.002**
Triglycerides	**r**	**-.288-***
	P	**.026**
HDL	**r**	**.398****
	P	**.002**
LDL	**r**	**-.307-***
	P	**.017**
Trig/HDL	**r**	**-.423-****
	P	**.001**
Calcium	**r**	**.530****
	P	**.000**
Phosphorus	**r**	**.134**
	P	**.307**
PTH	**r**	**-.414-****
	P	**.001**
S albumin	**r**	**.309***
	P	**.016**
ALP	**r**	**-.352-****
	P	**.006**

Vitamin D was significantly positively correlated with HB, PLT, HDL, calcium and albumin but significantly negatively correlated with BMI, SLE duration, ESR, CRP, cholesterol, TG, LDL, TG/ HDL, PTH and ALP as showed in table (5).

DISCUSSION

Regarding SLE duration (between SLE without LN and SLE with LN Groups) we found that the 2nd group had significantly longer duration. Concerning age, BMI and sex distribution, there was no significant difference among groups. These results agree with **Khairallah *et al.*** [13] who showed that systemic lupus erythematosus group included 88 females (88%) and 12 males (12%), and their disease duration ranged from 0.5 to 12.0 years with a mean of 4.0 ± 3.2 years. The 66 healthy controls included 58 females (87.87%) and eight males (12.12%), with a mean age of 25.32 ± 6.98 years with a range of 18.0–51.0 years. There was no significant difference among the patients and the control group regarding age and sex.

The level of ESR in our study was significantly higher among SLE with LN group and significantly lower among control. This result is consistent with **Hassanalilou *et al.*** [14]. Alterations in the concentration of proinflammatory mediators have been described in SLE patients such as cytokines. In this study C3 & C4 were significantly higher among SLE without LN group compared to SLE with LN. These findings were matched with those of **Khairallah *et al.*** [13] and **Mok *et al.*** [15].

Regard Hb, WBCs and PLT in our study, control group showed significant higher level with no significant difference between cases groups. CRP in control group was significant lower with no significant difference between cases groups. Cholesterol was sig higher among 2nd group. TG was significantly lower among control with non-significant difference between cases groups. Regarding HDL, 2nd group was significantly lower without significant difference between 1st and 3rd groups. LDL was significantly lower among control group with non-significant difference between cases groups. Trig/HDL was sig higher among 2nd group and significantly lower among control. Regarding calcium, it was significant higher among control and significantly lower among 2nd group. These results concur with **Ezzat *et al.*** [16] who revealed that there is an association between lower 25(OH)D levels and increased CVD risk factors, increased SLE disease activity and damage indices as well as with the presence of proteinuria, low complement levels and steroid use.

In our study, PTH was significantly lower among control and albumin was significantly lower among 2nd group with no significant difference between 1st and 3rd groups. Our results are in harmony with **Robinson *et al.*** [17] who reported that serum 25(OH) D levels in patients with SLE were directly

connected with serum albumin and inversely connected with the UP/C ratio and urinary DBP/C.

In our study, ALP was significantly lower among control with no significant difference between cases groups. These results are in agreement with **Khairallah *et al.*** [13] who showed a significant increase in the levels of ALP (84.88 ± 63.78) (P = 0.03) in SLE patients with LN.

Our results showed that Anti ds DNA titer and proteinuria were significantly associated with 2nd group. These results agree with **Giles and Boackle** [18] who showed high titers of anti-dsDNA, and low complement levels that are useful tools to monitor SLE disease activity. **Ezzat *et al.*** [16] revealed that there is an association between lower 25(OH)D levels and the presence of proteinuria in SLE patients with LN.

The attainable results showed that SLE with LN group had significantly lower vitamin D with no significant difference between SLE without LN group and control group. These results are in agreement with **Korah *et al.*** [19] who found that Egyptian SLE patients had lower VD levels in comparison to healthy controls. Also, **Mok *et al.*** [15] showed a significant inverse relationship between the levels of 25(OH) D3 and SLE disease activity scores. **Fakhfakh *et al.*** [20] found that high prevalence of vit D deficiency was recorded in the newly diagnosed SLE patients and among their SLE patients, only 37% have sufficient vit D levels. Particularly, the reduced sun exposure due to photosensitivity, the use of photo-protection, the alteration of renal vit D metabolism, hormonal and immunological factors as well as dark skin are all further explanations for vit D insufficiency [21]. In the study by **Yap *et al.*** [22] that was conducted on a large group of Australian patients with SLE, it had been shown that vitamin D insufficiency was associated with a higher disease activity and a rise in serum vitamin D level was associated with reduced disease activity over time.

In our study, vit D was significantly positively correlated with HB, PLT, HDL, calcium and albumin but significantly negatively correlated with BMI, SLE duration, ESR, CRP, cholesterol, TG, LDL, TG/ HDL, PTH and ALP. These results agree with **Ye *et al.*** [23] who revealed that higher 25(OH) D levels were found to be positively associated with higher levels of serum calcium and lower levels of phosphorus, which is related to the role of parathyroid hormone in regulating the levels of calcium under the circumstances of vitamin D deficiency and hypocalcemia [24]. Also, **Bonakdar *et al.*** [25] and **Nerviani *et al.*** [26] found a significant correlation between VD deficiencies, lower serum albumin, higher levels of liver enzymes, and higher hemoglobin concentrations. This controversy could be attributed to the immunosuppressive effect of the corticosteroids taken by 84% of our patients.

Our findings showed no significant association between VD levels with ESR and CRP. This is in agreement with several studies that also did not find this association [2, 8, 13].

Although, SLE is not usually correlated with hypovitaminosis D, other studies showed variations in vit D level among lupus patients [27, 28]. These variations may be derived from differences in duration of disease, latitude, season, and ethnicity [29]. A meta-analysis study demonstrated an inverse correlation between 25[OH] D levels and disease activity of SLE [30, 31]. Indeed, the direct relationship between them has not been established, which suggests the impact of the genetically determined features of several key cytochromes P450 (CYP) enzymes of vitamin D metabolism. That vit D levels in SLE patients have a direct association with the disease or with the genetically determined features remains unclear [20].

Vitamin D deficiency is widely predominant in patients with active SLE with LN in Egypt. This is in accordance with **Elsaid *et al.*** [32] who found that the prevalence of vitamin D deficiency and insufficiency in LN patients is as high as 93.4% in Egyptian patients.

CONCLUSION

We concluded that vitamin D plays an important role in the pathogenesis and progression of SLE. Our study revealed a high frequency of vit D deficiency and insufficiency among patients with SLE with LN compared to healthy controls. The correction of vit D status may be beneficial in controlling inflammation and disease activity.

REFERENCES

1. **Holick M (2007):** Vitamin D deficiency. N Engl J Med., 357: 266- 281.
2. **Miskovic R, Plavsic A, Raskovic S *et al.* (2015):** Vitamin D status in patients with systemic lupus erythematosus in Serbia: Correlation with disease activity and clinical manifestations. Open Access Maced J Med Sci, 3 (2): 256–261.
3. **White J (2012):** Review Vitamin D metabolism and signaling in the immune system. Rev Endocr Metab Disord., 13: 21–29.
4. **Bernknopf A, Rowley K, Bailey T (2011):** A review of systemic lupus erythematosus and current treatment options. Formulary, 46 (5): 178.
5. **Dall'Era M (2013):** Systemic lupus ErythromatosisIn: Current Diagnosis & Treatment (Rheumatology): edited by Imboden J, Hellmann D and Stone J., Pp: 187–197. https://accessmedicine.mhmedical.com/ content.aspx? bookid=506&sectionid=42584906
6. **Feldman C, Hiraki L, Liu J *et al.* (2013):** Epidemiology and socio-demographics of systemic lupus erythematosus and lupus nephritis among US adults with Medicaid coverage, 2000-2004. Arthritis. Rheum., 65 (3): 753–763.
7. **Nabih B, Elewa A, Shabana A (2018):** Serum vitamin D in Egyptian patients with systemic lupus erythematous and its association with lupus nephritis. International Journal of Clinical Rheumatology, 13 (5): 270-75.
8. **Kim H, Sung J, Jeon J *et al.* (2011):**Vitamin D may not be a good marker of disease activity in Korean patients

with systemic lupus erythematosus. Rheumatol Int., 31 (9): 1189-1894.

9. **Cutillas-Marco E, Morales-Suárez-Varela M, Marquina A *et al.* (2010):** Serum 25-hydroxyvitamin D levels in patients with cutaneous lupus erythematosus in a Mediterranean region. Lupus, 19 (7): 810-814.
10. **Barnes T, Bucknall R (2004):** Vitamin D deficiency in a patient with systemic lupus erythematosus. Rheumatol., 43: 393–394.
11. **Aringer M, Costenbader K, Daikh D *et al.* (2019)** 2019 European league against rheumatism/ American College of Rheumatology classification criteria for systemic lupus erythematosus. Arthritis Rheumatol., 71 (9): 1400–1412.
12. **Mikdashi J, Nived O (2015):** Measuring disease activity in adults with systemic lupus erythematosus: the challenges of administrative burden and responsiveness to patient concerns in clinical research. Arthritis Research & Therapy, 17 (1): 183-185.
13. **Khairallah M, Makarem Y, Dahpy M (2020):** Vitamin D in active systemic lupus erythematosus and lupus nephritis: a forgotten player. The Egyptian Journal of Internal Medicine, 32 (1): 1-9.
14. **Hassanalilou T, Khalili L, Ghavamzadeh S (2018):** Role of vitamin D deficiency in systemic lupus erythematosus incidence and aggravation. Autoimmunity Highlights, 9:1.
15. **Mok C, Birmingham D, Leung H *et al.* (2012):** Vitamin D levels in Chinese patients with systemic lupus erythematosus: relationship with disease activity, vascular risk factors and atherosclerosis. Rheumatology (Oxford), 51 (4): 644-652.
16. **Ezzat Y, Sayed S, Gaber W *et al.* (2011):** 25-Hydroxy vitamin D levels and its relation to disease activity and cardiovascular risk factors in women with systemic lupus erythematosus. The Egyptian Rheumatologist, 33 (4): 195-201.
17. **Robinson A, Thierry-Palmer M, Gibson K *et al.* (2012):** Disease activity, proteinuria, and vitamin D status in children with systemic lupus erythematosus and juvenile dermatomyositis. J Pediatr., 160: 297–302.
18. **Giles B, Boackle S (2013):** Linking complement and anti-dsDNA antibodies in the pathogenesis of systemic lupus erythematosus. Immunologic Research, 55 (1–3): 10– 21.
19. **Korah T, Soliman S, Al-Sharaki D *et al.* (2013)**: Vitamin D in systemic lupus erythematosus patients with and without nephropathy. Egypt Rheumatol Rehabil., 40 (3): 165–175.
20. **Fakhfakh R, Feki S, Elleuch A *et al.* (2021):** Vitamin D status and CYP27B 1-1260 promoter polymorphism in Tunisian patients with systemic lupus erythematosus. Molecular Genetics & Genomic Medicine, 9 (3): 1618-23.
21. **Azrielant S, Shoenfeld Y (2016):** Eppur Si Muove: Vitamin D is essential in preventing and modulating SLE. Lupus, 25 (6): 563– 572.
22. **Yap K, Northcott M, Hoi A *et al.* (2015):** Association of low vitamin D with high disease activity in an Australian systemic lupus erythematosus cohort. Lupus Sci Med., 2: 64-69.
23. **Ye Q, Wang G, Huang Y *et al.* (2021):** Mycophenolic Acid Exposure Optimization Based on Vitamin D Status in Children with Systemic Lupus Erythematosus: A Single-Center Retrospective Study. Rheumatology and Therapy, 21: 1-15.
24. **Goldsmith D, Massy Z, Brandenburg V (2014):** The uses and abuses of vitamin D compounds in chronic kidney disease- mineral bone disease (CKD-MBD). Semin Nephrol., 34 (6): 660–8.
25. **Bonakdar Z, Jahanshahifar L, Jahanshahifar F *et al.* (2011):** Vitamin D deficiency and its association with disease activity in new cases of systemic lupus erythematosus. Lupus, 20 (11): 1155-1160.
26. **Nerviani A, Mauro D, Gilio M *et al.* (2018):** To Supplement or not to Supplement? The Rationale of Vitamin D Supplementation in Systemic Lupus Erythematosus. The Open Rheumatology Journal, 12 (1): 226-247.
27. **Bogaczewicz J, Sysa-Jedrzejowska A, Arkuszewska C *et al.* (2012):** Vitamin D status in systemic lupus erythematosus patients and its association with selected clinical and laboratory parameters. Lupus, 21 (5): 477– 484.
28. **McGhie T, DeCeulaer K, Walters C *et al.* (2014):** Vitamin D levels in Jamaican patients with systemic lupus erythematosus. Lupus, 23 (10): 1092– 1096.
29. **Iruretagoyena M, Hirigoyen D, Naves R *et al.* (2015):** Immune response modulation by vitamin D: Role in systemic lupus erythematosus. Frontiers in Immunology, 6: 513-516.
30. **Petri M, Bello K, Fang H *et al.* (2013):** Vitamin D in systemic lupus erythematosus: modest association with disease activity and the urine protein-to-creatinine ratio. Arthritis Rheum., 65:1865–71.
31. **Sahebari M, Nabavi N, Salehi M (2014):** Correlation between serum 25(OH)D values and lupus disease activity: an original article and a systematic review with meta-analysis focusing on serum Vitamin D confounders. Lupus, 23 (11): 1164– 1177.
32. **Elsaid T, Basma A, Nabih A *et al.* (2018):** Serum vitamin D in Egyptian patients with systemic lupus erythematous and its association with lupus nephritis. Int J Clin Rheumatol., 13 (5): 270-277.