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Correction of hypovitaminosis D lead to reduction of anti-double-stranded DNA antibody levels in Bahraini patients with systemic lupus erythematosus

Abstract

Introduction: The relationship between serum vitamin D3 (25-OH-Cholecalciferol) and anti-double stranded-DNA (ds-DNA) antibodies in systemic lupus erythematosus (SLE) has been revealed separately; however, a possible link between these two factors and its effect on disease severity in patients with SLE has not been clarified yet. This is the first study investigating the conjoint association of vitamin D3 (VD_3) and anti-ds-DNA antibodies on disease activity in Bahraini patients with SLE.

Objectives: To evaluate serum VD3 and anti-ds-DNA antibodies as important factors in clinical status in adult Bahraini patients with SLE and to look into the possible correlation between these two factors and their relation to disease activity in this patient's group.

Material and methods: Fifty-one Bahraini SLE patients (mean age of 40.8 years, females were 84.3%) followed at Salmanyia Medical Complex in the period between 2016-2018 were included in this retrospective longitudinal (two-time points) study. Only patients who had blood samples that were taken before (baseline) and after oral VD_3 therapy and had anti-ds-DNA antibodies and serum uric acid tested at the same time-point with vitamin D_3 were included. The vitamin D therapy was VD3 tablet 50.000 IU once per week for 3months. Blood samples were obtained at any time between 2-3 months after starting the therapy for determination of serum levels of vitamin D, anti- ds-DNA antibodies, UA, complements (C_3&C_4), but also for calcium, phosphorus, alkaline phosphatase (ALP), parathyroid hormone (PTH), C-reactive protein (CRP) and antinuclear antibodies (ANA).

Results: The current study showed that VD therapy bring about two-fold increment in its mean serum level ($P<0.0001$) with increased serum calcium ($P<0.05$). Wonderfully, the mean serum levels of ds-DNA auto-antibodies and UA were significantly decreased after VD therapy ($p=0.015$ and $p=0.010$, respectively). Interestingly, when the group was segregated by gender and age; the female group and the age group<40 years, independently, showed statistically significant difference in all parameters exactly as the whole group.

Conclusion: We evaluated serum levels of anti-ds-DNA antibody and vitamin D as important factors in SLE disease. Our study showed strong inverse correlation between these two factors, thus, the correction of hypovitaminosis D resulted in reduced serum ds-DNA auto antibodies. The current study established the inverse correlation between vitamin D_3 and the disease activity as measured by anti-ds-DNA antibody levels in adult Bahraini patients with SLE. Consequently, we strongly recommend continuous vitamin D_3 supplementation for Bahraini patients with SLE.

Keywords: vitamin D, SLE, Uric Acid

Volume 8 Issue 4 - 2019

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Received: June 05, 2019 | **Published:** July 01, 2019

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease, in which monitoring of disease activity could be achieved by measuring anti-ds-DNA antibody titres, Anti-nuclear antibody titres and complements. Vitamin D_3 (25-OH Cholecalciferol) is a steroid hormone that has well-established roles in calcium regulation.[1] recently, vitamin D has been observed to modulate the immune response in autoimmune diseases, including systemic lupus erythematosus (SLE). In SLE vitamin D has been reported to ameliorate endothelial dysfunction. [2] On the other hand, VD role in restoring immune homeostasis in SLE patients through its inhibitory effects on dendritic cell maturation and activation has also been reported.[3] Vitamin D deficiency is more prevalent among South Asian, Middle Eastern and African healthy women exactly as in patients with SLE in these regions.[4–7] Inadequate VD status can compound the problem of low BMD or osteoporosis, commonly seen in patients with SLE induced by corticosteroids.[8] A longitudinal study in 2012 highlighted the importance of prevention and treatment of VD deficiency and osteoporosis in SLE patients, especially those using glucocorticoids or anti-malarial drugs.[9]

Although, VD deficiency was associated with SLE flare, but the cause and effect relationship has not been well established.[10] another

study by Schoindre et al.,[11] has found a low vitamin D status in the majority of patients with SLE, and a modest association with high disease activity, but not between baseline level and relapse-free survival rate.[11] A prospective study showed that vitamin D deficiency was more prevalent in patients with SLE and was associated with higher levels of IL-6 and hematuria, but no correlation with disease activity as assessed by SLEDAI index.[12] On the contrary, data from a single centre registry in Hungary showed negative correlation of SLEDAI score, as well as, anti-double-stranded (ds)DNA autoantibody titres with reduced vitamin D levels in patients with SLE, moreover, they showed that anti-ds-DNA increased from normal to insufficient and further increased from insufficient to deficient patient subsets.[13]A randomaized clinical trial demonstrated that vitamin D_3 supplementation up to 4,000 IU daily was safe and well-tolerated, but failed to diminish the IFN signature in vitamin D-deficient SLE.[14] More recent study in animal model showed that pre-treatment of lupus induced mice with vitamin D3 resulted in reduced anti-ds DNA antibody titer.[15] Coexistence of gout (high serum UA) and autoimmune rheumatic diseases such as SLE, progressive systemic sclerosis (PSS) and mixed connective tissue disease (MCTD) has rarely been reported. In MCTD a case report of intraarticular crystal deposition has been reported showing the importance of differentiating gout from the arthropathy in MCTD patients.[16, 17]Unlike in rheumatoid arthritis where negative association has been widely established, in SLE, gout has been reported to be rare as only a few sporadic cases have been reported from 1985 to 2001. Hence similar negative association could not be ruled out between SLE and gout. Lack of awareness of the possibility of the presence of gout and concurrent SLE may increase the prevalence of renal involvement in patients with SLE, thus, allopurinol therapy improved the renal function in SLE.[18] Gout should be considered in the differential diagnoses of patients with SLE who present with acute arthritis and stable renal disease.[19] After the year 2000 the concomitant gout and SLE have received increasing attention. High UA levels in SLE patients is independently associated with the occurrence of hypertension, hyperlipidemia, arterial thrombosis, stroke, myocardial infarction, peripheral neuropathy,[20] but also arterial stiffness and subclinical atherosclerosis[21] and preterm birth.[22] High UA levels are also associated with pulmonary arterial hypertension (PAH) in SLE patients [23] and may be useful as a surrogate marker for screening of PAH in patients with SLE.[24] A recent study 2017 revealed that higher UA levels contributed to the development of new renal damage in SLE patients independent of other well-known risk factors for such occurrence.[25] The relationship between UA and VD serum levels is still debatable. A possible cause- and effect relationship between renal hypouricemia and high VD levels has been suggested by a recent study that stated the serum UA might directly decrease serum VD in patients with hyperuricaemia by inhibiting 1-alpha-hydroxylase activity.[26] In SLE patients, it has been shown that in ambulatory elderly women with VD deficiency, supplementation with VD appeared to be well tolerated with no significant effects on creatinine clearance, but on high serum UA.[27] In addition, a recent Chinese study revealed that insufficient VD level was significantly associated with elevated UA in middle-aged and elderly women.[28] Other study demonstrated that allopurinol administration might be an effective drug to lower hyperuricemia, and to treat hypovitaminosis D.[29] The aim of the present study is to assess the effects of VD therapy on its levels and on the disease activity in patients with SLE as assessed by ds-DNA antibodies and serum C_3 and C_4 levels. Furthermore, we intended to test the association of elevated serum levels of VD and UA, but also we aimed to investigate a possible link between these two factors, particularly their interaction with disease severity in Bahraini patients with SLE.

Materials and methods

Fifty-one adult (more than 12 years) Bahraini SLE patients, who followed at Salmanyia Medical Complex in the period between 2016-2018, were included in this retrospective longitudinal (two-time points) study. The SLE patient was diagnosed according to The ACR criteria. Only patients who had blood samples that were taken before (baseline) and after oral VD_3 therapy and had anti-ds-DNA antibodies and serum uric acid tested at the same time-point with vitamin D_3 were included. All patients received oral VD^3 therapy in the form of tablets (50.000 IU) once per week for 3 months duration. Blood samples should be obtained after 3 months (12 tablets), however, in some patients for unknown reason blood samples collected after two months, but less than three months. Blood samples obtained for determination of VD serum levels and the factor that are involved in its regulation such as calcium, phosphorus, alkaline phosphatase (ALP) and parathyroid hormone (PTH). Determination of other factors such as serum UA, complement (C_3&C_4), C-reactive protein (CRP) and some auto antibodies including, antinuclear antibodies (ANA), anti-double-stranded DNA (ds-DNA) were also performed. Measurement of the serum VD levels was done using chemilumenescence immunoassay on Advia Centaur Analyzer (LoD 8.0 nmol/L). VD deficiency was considered as serum levels<30 nmol/L, levels between 30 nmol/L and 50 nmol/L (≥30 50) were considered as VD insufficiency and optimal levels were≥50 nmol/L. The complements, C_3&C_4, were done by automated nephlometry using seimens reagents and BN Prospect machine. ANA test was done by indirect immunofloresence (IIF) method using hep2 slides from BIORAD Company. Anti-dsDNA levels were tested by automated ELIA using uniCAP machine from Phadi (pharmacia diagnostics-Thermo scientific co). Serum alkaline phosphatase, uric acid, calcium and phosphorus levels were analyzed using spectrophotometric technique on Advia Chemistry XPT Analyzer. The Alkaline Phosphatase (ALPAMP IFCC modified method) with reference range 45–129 U/L was used for alkaline phosphatase estimation. The uric acid measured with the reference range of 2.4-6.0 mg/dL (female) and 3.4-7.0 mg/dL (male). Serum calcium measured using Arsenazo III assay principle with reference range 2.15–2.50 mmol/L, whereas Phosphomolybdate/UV assay method with reference range 0.78–1.65 mmol/L was used for serum phosphorus estimation. Intact PTH was determined in serum by two-site sandwich immunoassay, using direct chemiluminometric technology on Advia centaur analyzer (analytical sensitivity 0.265 pmol/L).

Statistics

Data was entered and analyzed using SPSS version 23.0. Quantitative variables were presented as mean±SD and qualitative variables were parented as counts and percentages. Paired t-test was used to test the significance difference in population means. P-value<0.05 was considered as statistically significant.

Results

Fifty-one Bahraini patients included in this study. The mean age of the patients was 40.8 years (range 13–61 years, SD=13.2). However, most of the patients are females 43 (84.3%). Table 1, our results depicted in this table, as well as in Figure 1, showed that VD serum level was significantly increased after VD therapy from

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35.17 to 67.04 with an increment in the mean serum levels of 31.78 nmol/l (P<0.0001). The serum calcium was also increased after VD therapy and that was statistically significant (P<0.05). On the other hand, the mean serum levels of ds-DNA auto-antibodies and UA were significantly decreased after VD therapy from 207.41 to 49.56 (P=0.015) and from 349.84 to 301.69 (P=0.010), respectively (Figure 1).

Table 1 Comparison of SLE patient's lab results; before and after vitamin D therapy

	Before		After		Mean diff.		95% C.I.	P-Value
Variable	**Mean**	**SD**	**Mean**	**SD**		**Lower**	**Upper**	
Vitamin D	35.17	12.72	67.04	21.26	-31.87	-38.11	-25.62	0
Calcium	2.17	0.18	2.24	0.1	-0.07	-0.13	-0.01	0.025
Phosphorus	1.36	0.62	1.21	0.21	0.15	-0.04	0.34	0.119
PTH	6.55	4.29	6.26	4.56	0.29	-1.2	1.78	0.699
ALP	72.3	25.38	66.86	21.02	5.43	-2.25	13.12	0.16
C3	94.87	26.49	96.82	31.74	-1.95	-13.13	9.23	0.724
C4	18.96	11.57	18.08	12.73	0.87	-1.92	3.67	0.529
ds-DNA	207.41	394.98	49.56	111.74	157.84	32.89	282.79	0.015
CRP	4.78	6.58	4.44	6.15	0.33	-1.28	1.95	0.674
Uric Acid	349.84	105.87	301.69	106.92	48.16	12.3	84.01	0.01

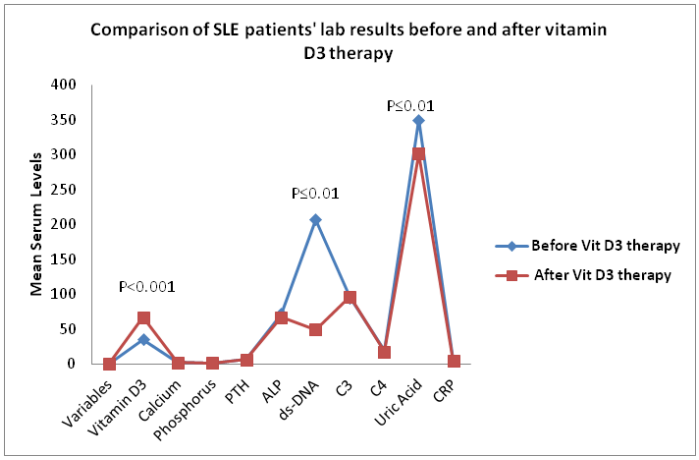
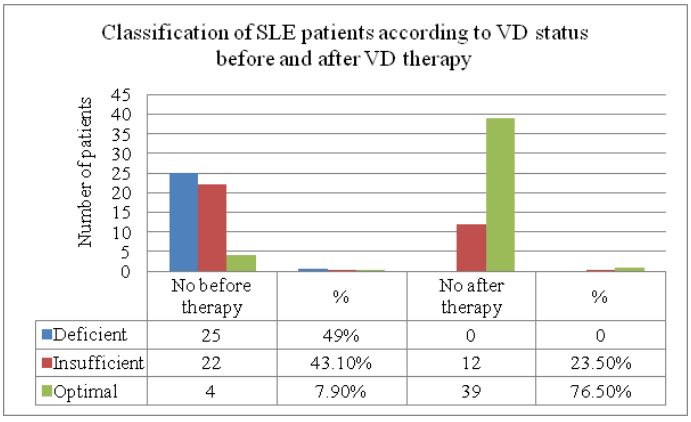


Figure 1 Comparison of lab results before and after vitamin D3 therapy in SLE patients.

Vit, Vitamin; SLE, Systemic lupus erythematosus; before, before vitamin D therapy; after, after vitamin D therapy; ALP, alkaline phosphatase; PTH, parathyroid hormone; C3 & C4, Complements; CRP, C-reactive protein; ds-DNA, anti-double-stranded DNA

Table 2, showed that when segregate the group by gender; the female group showed that there is statistically significant difference in serum VD (from 35.37 to 68.20, P = 0.000), ds-DNA reduced from 195.56 to 30.67 (P=0.037), ALP reduce from 75.03 to 65.17 (P=0.020) and mean serum UA reduced from 345.07 to 287.78 (P=0.008). Regarding, the males group the difference was for VD from 33.07 to 60.00 (P=0.002), calcium increased from 2.10 to 2.27(P=0.030), phosphorus reduced from 1.33 to 1.1 (P=0.018). UA did not change before and after therapy, mean serum levels were 375.60 and 376.80, respectively. Table 3, showed segregation of patients according to the age irrespective to the gender, the age group < 40 years showed increase mean serum levels of VD from 28.44 to 65.61 (P=0.000). UA reduced from 369.92 to 312.77 (P=0.005). For those>40 years old VD increased from 39.345 to 67.92 (P=0.000), while the mean serum UA reduced from 336.11 to 294.11, but that did not reach statistical difference. Figure 2, showed the classification of VD status before and after VD therapy. Before the therapy the number of the patients who were deficient was 25 (49%), insufficient patients were 22 (43.1%) and who had optimal levels were 4 (7.9%). After VD therapy the patients who were deficient were zero (0%), insufficient were 12 (23.5%) and optimal were 39 (76.5%). Figure 3, data depicted in this figure showed that the relation between VD and UA in SLE patients with Lupus Nephritis. There were only 13 patients among our cohort with lupus nephritis 12 were females and only one was male. In those patients mean serum level of VD was increased to two folds after therapy from 33.500 to72.077 and the difference was statistically significant (p=0.0001). However, the mean serum UA was reduced from 318.31 to 293.54, but that was statistically not significant. Only in the male patient the UA level was increased significantly.



	No before therapy	%	No after therapy	%
Deficient	25	49%	0	0
Insufficient	22	43.10%	12	23.50%
Optimal	4	7.90%	39	76.50%

Figure 2 Classification of SLE patients according to VD status before and after VD therapy

VD, vitamin D3; SLE, Systemic lupus erythematosus

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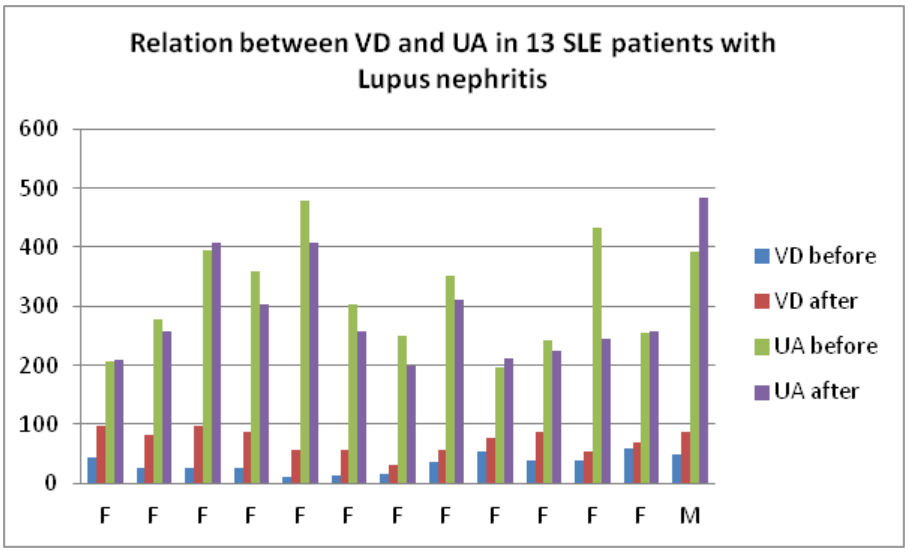

Figure 3 Relation between Vitamin D and Uric Acid in SLE patients with Lupus Nephritis.

VD, vitamin D3; UA, Uric Acid; SLE, Systemic lupus erythematosus; before, before vitamin D therapy; after, after vitamin D therapy; F, female; M, Male

Table 2 Comparison of SLE patients segregated by gender before and after vitamin D therapy

		Before		After		Mean diff.	95% C.I.		P-Value
	Variable	Mean	SD	Mean	SD		Lower	Upper	
Female	Vitamin D	35.37	12.89	68.2	22.03	-32.83	-40.06	-25.6	0
	Calcium	2.18	0.18	2.23	0.1	-0.05	-0.12	0.02	0.139
	Phosphorus	1.37	0.66	1.23	0.22	0.14	-0.08	0.36	0.197
	PTH	6.5	4.05	5.78	3.62	0.71	-1.01	2.43	0.403
	ALP	75.03	26.4	65.17	19.82	9.87	1.66	18.07	0.02
	C3	96.8	24.96	99.44	31.38	-2.64	-13.05	7.76	0.606
	C4	18.7	12.19	18	13.3	0.7	-2.28	3.69	0.632
	ds-DNA	195.56	373.61	30.67	43.8	164.88	11.11	318.66	0.037
	CRP	5.57	7.27	4.39	6.9	1.18	-0.72	3.08	0.211
	Uric Acid	345.07	106.93	287.78	99.56	57.3	16.1	98.49	0.008
Male	Vitamin D	33.07	13.47	60	17.37	-26.93	-38.93	-14.94	0.002
	Calcium	2.1	0.11	2.27	0.11	-0.17	-0.31	-0.02	0.03
	Phosphorus	1.33	0.24	1.1	0.14	0.23	0.07	0.38	0.018
	PTH	6.82	6.09	9	7.78	-2.18	-5.76	1.39	0.177
	ALP	63.17	17.39	78.67	25.29	-15.5	-35.68	4.68	0.105
	C3	86.1	40.21	87.5	37.12	-1.4	-97.77	94.97	0.966
	C4	21.5	9.2	18.78	11.91	2.72	-10.82	16.26	0.607
	ds-DNA	286.25	523.94	129.08	233.19	157.17	-153.83	468.16	0.251
	CRP	1.66	1.44	4.82	2.75	-3.16	-5.1	-1.22	0.011
	Uric Acid	375.6	107.47	376.8	125.75	-1.2	-63.97	61.57	0.96

Vit, Vitamin; SLE, Systemic lupus erythematosus; before, before vitamin D therapy; after, after vitamin D therapy; ALP, alkaline phosphatase; PTH, parathyroid hormone; C3 & C4, Complements; CRP, C-reactive protein; ds-DNA, anti-double-stranded DNA

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Table 3 Comparison of SLE patients segregated by age before and after vitamin D therapy

		Before		After		Mean diff.	95% C.I.		P-Value
	Variable	Mean	SD	Mean	SD		Lower	Upper	
< 40	Vitamin D	28.444	10.3766	65.61	20.1	-37.17	-47.25	-27.09	0
	Calcium	2.16	0.16	2.24	0.1	-0.09	-0.18	0	0.06
	Phosphorus	1.56	0.89	1.31	0.17	0.25	-0.2	0.7	0.249
	PTH	5.38	2.66	4.48	2.32	0.9	-1.28	3.08	0.387
	ALP	71.6	25.13	66.4	24.82	5.2	-8.47	18.87	0.428
	C3	93.25	24.19	87.45	28.24	5.8	-12.95	24.55	0.513
	C4	16.29	11.81	15.11	15.2	1.19	-4.02	6.39	0.63
	ds-DNA	302.78	471.65	101.48	165.73	201.31	-16.44	419.06	0.057
	CRP	2.2	2.65	3.25	3.56	-1.05	-4.02	1.91	0.447
	Uric Acid	369.92	107.87	312.77	106.42	57.15	20.38	93.92	0.005
≥ 40	Vitamin D	39.345	12.3762	67.92	22.26	-28.58	-36.78	-20.38	0
	Calcium	2.18	0.19	2.24	0.1	-0.06	-0.15	0.03	0.165
	Phosphorus	1.23	0.3	1.15	0.22	0.08	-0.06	0.22	0.261
	PTH	7.21	4.92	7.27	5.21	-0.06	-2.15	2.03	0.952
	ALP	72.77	26.13	67.18	18.61	5.59	-4.37	15.55	0.256
	C3	96.04	28.67	103.59	33.15	-7.54	-22.3	7.21	0.296
	C4	20.82	11.31	20.17	10.59	0.66	-2.83	4.14	0.699
	ds-DNA	143.82	333.9	14.96	18.84	128.87	-38.14	295.88	0.122
	CRP	6.55	7.89	5.26	7.44	1.29	-0.68	3.26	0.184
	Uric Acid	336.11	105.14	294.11	109.5	42	-15.98	99.98	0.145

Discussion

The relationship between serum 25(OH)D_3 and anti-ds-DNA antibody levels and UA in patients with SLE has been revealed separately; however, a possible link between these factors and their interaction with SLE disease severity has not been exposed yet. This is the first study investigating the conjoint association of VD and anti-ds-DNA antibody on disease activity in Bahraini patients with SLE. We have previously described the VD status in Bahraini patients with SLE,[30] but anti-ds-DNA and UA were not investigated before. We performed the present longitudinal study (at two time points) to expand the clinical data and to examine possible correlation between VD and ds-DNA by investigating the effect of correcting hypovitaminosis on serum anti-ds-DNA antibody, as well as, complements levels as markers for clinical disease activity in a well characterized group of SLE patients. VD supplementation in patients with SLE was recommended previously since increased VD levels seemed to show tendency toward subsequent clinical improvement.[31] we classified our patients according to their VD status. We found that before VD therapy more than 90% of the patients had abnormal low levels of vitamin D and only 7.9% had optimal levels. These results were consistent with our previous study in VD status that showed more than 95% of the SLE patients had abnormal low vitamin D levels, while only 3.8% had optimal levels.[30] Only 20% were excluded of our patients, since we could not find another time point or reading after VD therapy. Interestingly, although those were not the same patients, but our previous results are still reproducible. Thus, after VD therapy none of our patients had VD deficiency, only 23.5% had insufficiency and the rest achieved optimal levels. The insufficient levels found in some of our patients could either be due to a second blood sample was taken before three months i.e. before completing the therapeutic dose or incompliance with the drug.

In the current study, VD mean serum level was increased to two folds after VD therapy compared to the baseline and the difference was statistically significant. The most interesting finding in our study was that with correction of the hypovitaminosis D, both anti-ds-DNA antibodies and UA serum levels were reduced significantly in our patients with normalization of VD serum levels. The mean serum level of complement (C_3) were noted to be increased after therapy in all groups (Table 1-3), but that did not reach statistical difference, however, there was no change in C_4 following VD therapy. Our findings are consistent with another study which showed that

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serum VD levels are inversely correlated with SLE disease activity.[32] Our results were also consistent with three interesting studies from 2011-2013, respectively; the first study showed strong association between vitamin D deficiency and higher titers of antibodies to double-stranded DNA (ds-DNA) in patients with newly diagnosed SLE.[33] The second one proved that $25(OH)D_3$ correlated inversely with clinical SLE activity, anti-C1q and anti-dsDNA titers, but not with complement levels or damage scores.[34] The third study revealed negative correlation between $25(OH)D_3$ and anti-ds-DNA, but a positive correlation between 25(OH)D levels and C_4.[35]

The presentation of gout in SLE could be misinterpreted as SLE arthritis and might be modified or suppressed by VD therapy, since in our cohort both high serum levels of UA and high disease activity, as assessed by anti-ds-DNA antibodies levels, goes down with VD therapy. One study has suggested that UA per se may directly decrease serum VD since administration of anti-gout therapy to patients with gout was associated with a significant decrease in serum UA, but a significant increase in serum VD, admitting that serum concentrations of VD was not affected by those drugs.[29] Thus, our results with reduced serum UA after vitamin D therapy should be confirmed with another prospective study assessing the mechanism by which vitamin D reduce the UA. Interestingly, when we segregated the patients according to the age irrespective to the gender we found that in the patient's group less than 40 years, VD therapy accompanied by statistically significant reduction in serum UA. However, in age group 40 years or more, the mean serum UA reduced, but that did not reach statistical difference, this could be explained by the fact that with age (≥55 years) the UA increased, the known second peak, and with reduced renal function in this age group, whereas, the first peak of high UA is from 20-30 years due to lifestyle-related risk factors, but no normal renal function.[36] However, this could be true it needs to be proved by clinical trial. Thus, the knowledge of new modifiable risk factors for hyperuricaemia can be integrated into the management strategy to improve the patient outcomes.[37]

When we segregated the group by gender; the female group showed statistically significant difference, thus, with increased serum VD levels there was a statistically significant reduction in ds-DNA, ALP and serum UA. However, the notable reduction of Pho, PTH or CRP did not reach statistical significance. In males the increased VD levels after therapy was accompanied by statistically significant increase in serum calcium and reduction in phosphorus. Moreover, the notable reduction in ds-DNA, and UA along with the notable increase in C_3 that did not reach statistical significance. On the contrary, only in males the mean serum UA did not change; but the mean serum level of CRP was increased and that was statistically significant. CRP is an acute phase protein that is known as biomarker, its level traditionally used to detect or predict outcome of infection, inflammation or monitor efficacy of therapy. In the current study the rationale behind low CRP in our SLE patient's cohort before the therapy and the more reduction in mean serum levels after therapy in all studied groups except the male group was not fully understood. However, the possible role of CRP in the handling and clearance of immune complexes in patients with SLE has been suggested.[38] The association of VD deficiency and CRP was occasionally reported. One study reported an association between hypovitaminosis D and inflammatory markers (hsCRP) that contributed to CVD and that VD may be important in maintaining cardiovascular health.[39] The SLE patients, especially those with leucopenia or renal involvement, are at high risk of VD deficiency and require VD supplementation.[40] On the other hand, the UA level has been shown to be independently associated with the development of LN in SLE patients.[32] Recent study, in Bahraini SLE patients performed by our group, revealed that the presence of anti-Smith, anti-Ro/SSA and anti-RNP antibodies and the absence of anti-dsDNA antibodies are independent predictive markers for renal involvement. However, VD levels were not investigated at that time.[41] In our current study, there were only 13 patients with biopsy proven lupus nephritis (LN) among our current 51 SLE patients. All were females except one male patient. Our results showed that the two folds increment in VD serum level, which was statistically significant, accompanied by notable reduction in serum UA, but not statistically significant. On the contrary, significant increase in serum UA was noticed in males. Due to small number of patients with LN we could not be able to draw any conclusion as high UA or Low VD could be consider as risk factor for development of LN in Bahraini patient with SLE.

Conclusion

We evaluated serum VD status, ds-DNA and UA as important factors in SLE disease activity. Our study showed strong inverse correlation between these factors, thus, the correction of hypovitaminosis D in SLE patients may result in clinical improvement, since ds-DNA antibodies is the main indicator for disease activity in SLE patients who has positive anti-ds-DNA antibodies. The current study established that serum VD levels are inversely correlated with both serum ds-DNA and UA independently, in adult Bahraini patients with SLE. New knowledge of the modifiable risk factors for SLE such as low vitamin D or high UA could be integrated into the management strategy to optimize long-term patient outcomes in SLE cohort. Whether deficiency of $25(OH)D_3$ may become a novel therapeutic target in SLE, deserves further studies of randomized controlled trials to confirm the clinical beneficial role of vitamin D in SLE patients.

Limitation of our study

The present study has some potential limitations; being a retrospective study is one factor. In addition to, VD levels are variables and were measured at only two time points (longitudinal) during the study, but the second sample in some samples was not taken at the end of the therapeutic period, which should be minimum three months for the oral therapy. Also, our sample was small in this longitudinal retrospective study; hence our findings should be interpreted cautiously. Unavailability of data on dietary intake of VD containing foods, as well as, important factors such as; medications, body mass index (BMI) and genetics can be considered as another important limitation.

Acknowledgments

None.

Conflicts of interest

The author declares there are no conflicts of interest.

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Citation: Hassan AB, Farid E, Jaradat AA, et al. Correction of hypovitaminosis d lead to reduction of anti-double-stranded DNA antibody levels in Bahraini patients with systemic lupus erythematosus. *MOJ Womens Health.* 2019;8(4):239–245. DOI: 10.15406/mojwh.2019.08.00244