Serum 25-hydroxyvitamin D concentration in patients with psoriasis and rheumatoid arthritis and its association with disease activity and serum tumor necrosis factor-alpha

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ABSTRACT

الأهداف: دراسة فيتامين د في مرضى الصدفية والرثيان المفصلي و دراسة علاقته بنشاط المرض ودلائل الالتهاب ومستوى TNF-α بالمصل.

الطريقة: أجريت دراسة مقطعية في المستشفى الوطني بالرياض، المملكة العربية السعودية خلال الفترة من شهر مارس حتى شهر سبتمبر 2012م واشتملت الدراسة على 43 مريض صدفية و55 مريض رثيان مفصلي و40 من الأشخاص الأصحاء المتوافقين في العمر مع المرضى. تم أخذ عينات دم من جميع المشاركين بالدراسة وتم فحص فيتامين د25، TNF-α، CRP وسرعة الترسيب ،هرمون الغدة الجار درقية ونسبة الكالسيوم المعدلة ومن ثم تم حساب نسبة نشاط المرض لمرضى الصدفية و الرثيان المفصلي باستخدام كلا من PASI و DAS28.

النتائج: وجد اختلاف ذو دلالة إحصائية بين مرضى الصدفية و الرثيان المفصلي والعينة الضابطة في متوسط فيتامين د25 (11.74±3.60, 15.45±6.42, 24.55±11.21 ng/ml). أظهرت النتائج أن جميع مرضى الصدفية، و85.45% من مرضى الرثيان المفصلي، و40% من الأشخاص الاصحاء نسبة فيتامين د لديهم كانت أقل من 20 نانو جرام في المليليتر. كما وجد أنه لا يوجد ارتباط بين مستوى فيتامين د ونشاط المرض وكذلك مع مستوى TNF-α في مرضى الصدفية والرثيان المفصلي.

خاتمة: أثبتت الدراسة نقص معدل فيتامين د في المصل في مرضى الصدفية و الرثيان المفصلي مما يؤكد دوره و تأثيره في أمراض المناعة الذاتية.

Objectives: To assess vitamin D status in psoriasis and rheumatoid arthritis (RA) patients and to study whether it was associated with disease activity, inflammatory markers, and serum tumor necrosis factor-alpha (TNF-α).

Methods: This cross-sectional study was conducted at Riyadh National Hospital, Riyadh, Saudi Arabia between March and September 2012. It included 43 patients with plaque psoriasis, 55 RA patients and 40 healthy controls matched for age. Blood samples were drawn from all participants for assessment of 25-hydroxyvitamin D [25(OH)D], TNF-α, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), parathyroid hormone (PTH), and serum corrected calcium. Disease activity of psoriasis and RA were assessed using Psoriasis Area and Severity Index (PASI) and Disease Activity Score Index of a 28 joint count (DAS28).

Results: We found a significant difference between psoriatic patients, RA patients, and healthy controls in the mean 25(OH)D (11.74±3.60, 15.45±6.42, and 24.55±11.21 ng/ml; p=0.000). We found that 25(OH) D was not correlated with PASI, DAS28, TNF-α, CRP, or ESR in psoriatic and RA patients.

Conclusion: Serum 25-(OH)D levels are significantly lower in psoriatic and RA patients than in healthy control subjects. Low 25-OHD levels also may provide the rationale for vitamin D supplementation in the treatment of psoriasis and RA. More definitive evidence is also required to demonstrate the clinical benefit of vitamin D supplementation in the treatment of psoriasis and RA.

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Vitamin D deficiency is associated with the incidence or unfavorable prognosis of a broad variety of diseases; including autoimmune diseases, cardiovascular diseases, various types of cancer, and infectious diseases.[1-3] Autoimmune conditions associated with reduced vitamin D levels include rheumatoid arthritis (RA),[4] insulin-dependent diabetes mellitus (IDDM),[5] multiple sclerosis (MS),[6] and systemic lupus erythematosus (SLE).[7] 25-hydroxyvitamin D [25(OH) D] level ranging from 50-80 nmol/L (20-32 ng/ml) is considered to be optimal for the skeleton.[8,9] Vitamin D insufficiency has recently become an important medical concern, and is characterized as serum level of 25(OH)D ranging from 25-75 nmol/L (10-30 ng/ml) and without overt clinical symptoms.[10] Vitamin D insufficiency is now a common problem in Saudi Arabia and around the world.[11,12] There is a growing body of evidence indicating that vitamin D is important in the initiation and propagation of range of autoimmune diseases. The immune-regulatory role of vitamin D affects both the innate and adaptive immune system which are contributing to the immune tolerance of self-structures.[13] Psoriasis is a chronic inflammatory disease that involves the innate and acquired immune system.[14] Until recently, psoriasis has been considered mainly to be a Th1-driven autoimmune inflammatory disease defined by a cytokine pattern consisting of IFN-ß, tumor necrosis factor-alpha (TNF-α), IL-1, IL-2, IL-3, IL-6, IL-8, epidermal growth factor and transforming growth factor-alpha (TGF-α),[15,16] but recent findings have revealed a potential role for IL-23 and Th17 responses in the pathogenesis of psoriasis.[17,18] The psoriasis lesions usually deteriorate during the winter period and many patients are therefore given repeated ultraviolet (UV) B treatment during this season. The therapeutic effect of UVB radiation may be attributed at least in part to UVB-triggered cutaneous synthesis of vitamin D.[19-21] Furthermore, dermatologists and other physicians have observed the effectiveness of vitamin D analogs to treat psoriasis plaques in daily clinical practice.[22] An association between vitamin D deficiency and psoriasis has been recently described.[23] Rheumatoid arthritis is one of the most common human systemic autoimmune diseases. It is characterized by inflammation of synovial tissues and the formation of rheumatoid pannus, which is capable of eroding adjacent cartilage and bone and causing subsequent joint destruction. Rheumatoid arthritis shares some immunologic features with psoriasis, such as Th1/Th2 dysregulation and the role of Th17 in their pathogenesis.[17,18,23]

An association between vitamin D deficiency and psoriasis and RA has been described.[4,24,25] Tumor necrosis factor-beta is a proinflammatory cytokine that plays a major role in the pathogenesis of psoriasis and RA,[15,16,23] but no previous studies explored its relation with 25(OH)D. There is also controversies regarding the association between 25(OH)D level and disease activity and inflammatory markers in patients with psoriasis and RA. In this study, we aimed to assess vitamin D status in 2 autoimmune inflammatory diseases; psoriasis and RA, and to study whether 25(OH)D level is associated with disease activity, TNF-α, and other inflammatory markers.

Methods. This is a cross-sectional study conducted in the Dermatology and Rheumatology Clinics, Riyadh National Hospital, Riyadh, Kingdom of Saudi Arabia, between March and September 2012. It had been approved by the local Institutional Review Board at Riyadh National Hospital and is in accordance with the principles of Helsinki Declaration.

Adult patients with plaque psoriasis and who consented to participate after having received full information on the setup and the purpose of the study were enrolled in this study. All patients were 18 years or older, had a clinical diagnosis of chronic plaque psoriasis lasting at least 6 months and had not received any specific anti-psoriatic treatment including phototherapy and/or topical vitamin D derivatives within the last 2 months before blood sampling. Psoriasis Area and Severity Index (PASI) was used for assessment of disease severity. The presence of psoriatic arthritis (PsA) was diagnosed according to the CASPAR criteria.[26]

Rheumatoid arthritis was diagnosed according to the 1987 American College of Rheumatology (ACR) revised criteria,[27] and used 2010 ACR/European League Against Rheumatism (EULAR) criteria[28,29] when the first criteria was not applicable. Disease activity score index of a 28 joint count (DAS28) using the erythrocyte sedimentation rate (ESR) was used for assessment of disease activity.[30] Healthy controls matched for age were recruited from the partners or relatives of patients if not affected by psoriasis or RA, to minimize the difference due to dietary intake of vitamin D. Controls and patients who were pregnant, lactating, had other types of psoriasis (guttate, pustular and erythrodermic psoriasis), had inflammatory bowel diseases, other systemic autoimmune diseases or malignancy and

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those receiving treatment that might influence 25(OH)D level (bisphosphonates, systemic corticosteroids, vitamin D and calcium supplements) were excluded from the study. Exposure to sunlight was determined in all participants and quantified as <10, 10-20, 20-30, or >30 min daily.[31]

Laboratory assessment. Morning venous blood samples (5-10 mL) were taken from patients and controls. Serum was obtained from freshly drawn, rapidly centrifuged samples, and were quickly frozen at -70°C and stored until measurement of 25(OH)D and TNF-α. The serum level of 25(OH)D was measured using a commercial kit (LIAISON 25OH Vitamin D TOTAL Assay from DiaSorin Inc, 1951 Northwestern Ave-Stillwater, MN 55082- USA). This is a chemiluminescent immunoassay (CLIA) for the quantitative determination of 25(OH)D in human serum. Serum 25(OH)D is the best indicator of overall vitamin D status because it reflects total vitamin D from dietary intake, sun exposure, and the conversion of vitamin D from adipose stores in the liver.[12] Two cutoff points were used for vitamin D deficiency in this study. We used the first cutoff point if the serum level of 25(OH)D was <20 ng/ml (50 nmol/L),[10] the second if the serum level of 25(OH)D was <10 ng/ml (25 nmol/L).[32]

The TNF-α was measured by a commercial kit (DIAsource TNF-α EASIA). This is an immunoenzymometric assay for the quantitative measurement of human TNF-α in serum (DIA source S. A. Rue de IIndstrie, 8, B-1400 Nivelles, Belgium). The minimum detectable concentration (MDC) was 0.7 pg/mL. The fully automated micro-plate analyzer (Personal LAB ADALTIS machine) was used for TNF-α assay. An ELISA-AIDTM software used for data processing and generating the standard curves. The software read automatically the concentration of the assay in unknown samples and control.

Parathyroid hormone (PTH), serum corrected calcium, and C-reactive protein (CRP) were measured using LIAISON N-TACT PTH II Assay (DiaSorin Inc, 1951 Northwestern Ave-Stillwater, MN, USA), Calcium kit, and C-Reactive Extended Range (RCRP from Dimension, Siemens Healthcare Diagnostics Inc. Newark, DE, USA), respectively. Erythrocyte sedimentation rate (ESR) was measured by Westergren method.

Statistical analysis. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 17.0 software (SPSS Inc., Chicago, Illinois, USA). Kolmogorov-Smirnov test was carried out for collected data and for each variable to determine whether the data were parametric or non-parametric. For parametric data, Students t test was used for test of difference for quantitative variables between 2 groups and one-way analysis of variance (F-test) was used to compare between more than 2 groups. For non-parametric data, Mann-Whitney test was used to compare the 2 independent group means and Kruskal-Wallis test was used for comparing more than 2 groups. Chi square test was used as a test of significance for non-parametric variables. Fisher exact test was used for gender comparison in patients with different 25(OH)D levels due to the small expected numbers. Pearson's correlation coefficient (r) was used to test correlation of continuous variables. In all statistical assessments performed, the level of significance was recognized at 95% level of confidence (p<0.05) to indicate the statistical significance between the studied variables.

Results. This study included 43 psoriatic patients, 55 RA patients, and 40 healthy controls. The mean age for psoriatic patients was 48.81±8.53 years, RA 45.60±12.41 years, and controls 45.00±7.99 years (p=0.174). Thirty eight (88.4%) psoriatic patients, 12 (21.8%) RA patients, and 20 (50%) controls were males. The mean duration of psoriasis and RA was 8.47±3.83 and 4.93±3.11 years, respectively. The PASI was used for assessment of psoriasis severity, and we found that mean PASI in psoriatic patients was 6.47±2.85. Eight (18.6%) psoriatic patients had PsA. The mean DAS28 in RA patients was 4.54±1.31. The psoriatic patients were significantly more exposed to sunlight as compared with RA patients and healthy controls (mean: 16.98±7.80, 5.44±4.14, 11.80±6.34 min respectively; p=0.000). None of our patients or healthy controls was exposed to the sun for >30 min daily. Nine (20.9%) psoriatic patients were exposed to the sun for 20-30 min daily, 21 (48.8%) were exposed to the sun for 10-20 min daily, and 13 (30.2%) were exposed to the sun for <10 min daily. Fifty one (92.7%) RA patients and 24 (60.0%) healthy controls were exposed to the sun for <10 min daily. This difference between study groups in exposure to sunlight was found to be statistically significant (p=0.000).

Laboratory findings in psoriasis patients, RA patients and controls are presented in **Table 1**. There was significant difference in 25(OH)D level among the 3 groups (p=0.000) and psoriatic patients had lower 25(OH)D level compared with RA patients (mean: 11.74±3.60 and 15.45±6.42 ng/ml). Mean serum level of 25(OH)D was 12.88±4.00 ng/ml in psoriatic patients with PsA and 11.49±3.52 ng/ml in psoriatic patients without PsA (p=0.281). There were differences

in serum corrected calcium, CRP, and ESR among the 3 groups (p=0.007, p=0.000, and p=0.000) whereas there was no difference in PTH (p=0.072). Psoriatic patients had significantly lower serum corrected calcium, CRP, and ESR, and higher PTH compared with RA patients. Serum TNF-α level was significantly higher in RA patients compared with psoriatic patients and healthy controls (mean: 53.73±14.49, 42.32±10.80, and 16.50±4.84 pg/mL; p=0.000). In this study, 2 cutoff points were used for vitamin D deficiency; the first if the serum level of 25(OH)D was <20 ng/ml, the second if it was <10 ng/ml. All patients with psoriasis had 25(OH)D <20ng/ml, while 85.45% of RA patients and 40% of controls had 25(OH)D <20 ng/ml.

Table 2 shows comparison between RA patients with 25(OH)D less than and more than 20 ng/ml. Rheumatoid arthritis patients with 25(OH)D <20 ng/ml had significantly higher DAS28 and TNF-α, whereas they had significantly lower serum corrected calcium, hemoglobin and less exposure to sunlight. Thirteen (30.23%) psoriatic patients and 8 (14.55%) RA patients had 25(OH)D <10 ng/ml.

Table 3 shows the clinical and laboratory findings in patients with 25(OH)D less than and more than 10ng/ml. Psoriatic patients with 25(OH)D <10 ng/ml

Table 1 - Clinical and laboratory findings in psoriasis patients, rheumatoid arthritis (RA) patients, and controls.

Clinical and laboratory findings	Psoriasis (n=43)	95% CI	RA (n=55)	95% CI	Control (n=40)	95% CI	*P*-value between 3 groups	*P*-value between psoriasis and RA
Age (years)	48.81±8.53	5.2	45.60±12.41	6.7	45.00±7.99	5.1	0.174	0.150
Gender (%)							0.000	0.000
Male	38 (88.4)	-	12 (21.8)	-	20 (50)	-		
Female	5 (11.6)	-	43 (78.2)	-	20 (50)	-		
Duration (years)	8.47 ± 3.83	2.4	4.93 ± 3.11	1.7	-	-	-	0.000
25(OH)D (ng/ml)	11.74 ± 3.60	2.2	15.45 ± 6.42	3.5	24.55 ± 11.21	7.2	0.000	0.000
PTH (pg/mL)	68.24 ± 19.47	12.0	58.89 ± 24.92	13.5	60.61 ± 14.08	9.0	0.072	0.046
Corrected calcium (mmol/L)	2.27 ± 0.10	0.1	2.34 ± 0.15	0.1	2.30 ± 0.10	0.1	0.007	0.004
TNF-α (pg/mL)	42.32 ± 10.80	6.6	53.73 ± 14.49	7.8	16.50 ± 4.84	3.1	0.000	0.000
CRP (mg/L)	7.44 ± 7.37	4.5	9.92 ± 7.02	3.8	2.95 ± 1.25	0.8	0.000	0.005
ESR	25.42 ± 19.28	11.9	51.40 ± 27.48	14.9	10.20 ± 2.51	1.6	0.000	0.000
Hemoglobin (g/dl)	13.61 ± 1.78	1.1	12.10 ± 1.05	0.6	14.16 ± 1.44	0.9	0.000	0.000
Sun exposure (min)	16.98 ± 7.80	4.8	5.44 ± 4.14	2.2	11.80 ± 6.34	4.1	0.000	

95% CI - 95% confidence intervals, 25(OH)D - 25-hydroxyvitamin D, TNF-alpha - tumor necrosis factor-α, PTH - parathyroid hormone, CRP - C-reactive protein, ESR - erythrocyte sedimentation rate

Table 2 - Clinical and laboratory findings in rheumatoid arthritis (RA) patients with 25-hydroxyvitamin D [25(OH)D] less than and more than 20 ng/ml.

Clinical and laboratory findings	25(OH)D ≤20 ng/ml	25(OH)D >20 ng/ml	*P*-value
Age (years)	44.79±13.02	50.38±6.52	0.242
Gender (%)			0.059
Male	8 (17)	4 (50)	
Female	39 (83)	4 (50)	
Duration (years)	5.06 ± 3.33	4.13 ± 0.99	0.435
DAS28	4.76 ± 1.29	3.30 ± 0.59	0.003
PTH (pg/Ml)	60.02 ± 26.12	52.29 ± 15.75	0.422
Corrected calcium (mmol/L)	2.30 ± 0.10	2.57 ± 0.18	0.000
TNF-α (pg/Ml)	55.83 ± 13.91	41.38 ± 12.00	0.008
CRP (mg/L)	10.37 ± 7.27	7.29 ± 4.84	0.262
ESR	53.38 ± 27.17	39.75 ± 28.20	0.096
Hemoglobin (g/dl)	11.96 ± 1.01	12.95 ± 0.87	0.012
Sun Exposure (min)	4.55 ± 3.47	10.63 ± 4.17	0.000

DAS28 - disease activity score index of a 28 joint count, PTH - parathyroid hormone, TNF-α - tumor necrosis factor- alpha, CRP - C-reactive protein, ESR - erythrocyte sedimentation rate

Table 3 - Clinical and laboratory findings in psoriasis patients and rheumatoid arthritis patients with 25-hydroxyvitamin D [25(OH)D] less than and more than 10 ng/ml.

Clinical and laboratory findings	Psoriasis		*P*-value	Rheumatoid arthritis		*P*-value
	25(OH)D ≤10 ng/ml	25(OH)D >10 ng/ml		25(OH)D ≤10 ng/ml	25(OH)D >10 ng/ml	
Age (years)	43.23 ± 7.43	51.23 ± 7.90	0.003	35.75 ± 8.19	47.28 ± 12.28	0.014
Gender (%)			0.630			0.059
Male	11 (84.6)	27 (90)		4 (50)	8 (17)	
Female	2 (15.4)	3 (10)		4 (50)	39 (83)	
Duration (years)	4.23 ± 2.01	10.30 ± 2.84	0.000	6.63 ± 3.38	4.64 ± 3.00	0.095
PASI	7.10 ± 2.79	6.19 ± 2.88	0.343	-	-	-
DAS28	-	-	-	5.26 ± 1.10	4.42 ± 1.32	0.094
PTH (pg/Ml)	81.82 ± 25.68	62.36 ± 12.55	0.002	80.08 ± 41.67	55.29 ± 19.32	0.008
Corrected calcium (mmol/L)	2.21 ± 0.12	2.29 ± 0.08	0.013	2.28 ± 0.07	2.35 ± 0.15	0.204
TNF-α (pg/Ml)	49.02 ± 11.67	39.42 ± 9.15	0.006	62.25 ± 13.10	52.28 ± 14.34	0.072
CRP (mg/L)	8.71 ± 7.76	6.89 ± 7.26	0.009	9.03 ± 7.32	10.07 ± 7.04	0.489
ESR	33.31 ± 22.08	22.00 ± 17.22	0.002	53.63 ± 29.41	51.02 ± 27.46	0.783
Hemoglobin (g/dl)	12.52 ± 1.70	14.08 ± 1.63	0.007	11.99 ± 1.45	12.12 ± 0.98	0.738
Sun exposure (min)	12.31 ± 2.59	19.00 ± 8.45	0.008	4.25 ± 4.03	5.64 ± 4.17	0.386

PASI - psoriasis area and severity index, DAS28 - disease activity score index of a 28 joint count, PTH - parathyroid hormone, TNF-α - tumor necrosis factor- alpha, CRP - C-reactive protein, ESR - erythrocyte sedimentation rate

Table 4 - Correlation between 25-hydroxyvitamin D [25(OH)D] level and disease activity and inflammatory markers in psoriasis and rheumatoid arthritis (RA) patients.

Markers	Disease activity		TNF-α		CRP		ESR	
	r	*P*-value	r	*P*-value	r	*P*-value	r	*P*-value
25(OH)D in psoriasis	0.034	0.827	- 0.204	0.189	0.119	0.447	0.022	0.887
25(OH)D in RA	-0.104	0.466	-0.120	0.403	0.051	0.722	-0.033	0.818

TNF-α - tumor necrosis factor- alpha, CRP - C-reactive protein, ESR - erythrocyte sedimentation rate, r - Pearson's correlation coefficient

were significantly younger and had less disease duration. They also had significantly higher serum TNF-α and PTH (p=0.006, p=0.002). There was difference between RA patients with 25(OH)D <10 ng/ml and those with 25(OH)D >10ng/ml in age, gender, and PTH (p=0.01, p=0.03, and p=0.008).

The results of the present study showed that PASI was correlated with TNF-α, CRP and ESR (r=0.751, p=0.000; r=0.674, p=0.000; and r=0.670, p=0.000). DAS28 was also correlated with TNF-α, CRP and ESR (r=0.867, p=0.000; r=0.449, p=0.001; and r=0.620, p=0.000). We also found that 25(OH)D level was not correlated with PASI, DAS28, TNF-α, CRP or ESR in psoriatic and RA patients (**Table 4**).

Discussion. The major function of vitamin D is that it increases the absorption of calcium and phosphate from the intestinal tract, inhibits the secretion of PTH and the proliferation of the parathyroid glands, and therefore positively regulates bone formation.[33-35] Beside this function, it has a role in the maintenance of immune-homeostasis. Since the 1990s increasing number of findings support the idea that impaired vitamin D homeostasis contributes to autoimmune processes.[36,37] Autoimmune diseases as IDDM, MS, and SLE were associated with reduced vitamin D level.[5-7,38] In this study, we found significantly lower serum 25(OH) D levels in psoriatic and RA patients than in healthy matched controls. In agreement with our results, Orgaz-Molina et al[24] and Gisondi et al[39] recently found lower levels of 25(OH)D in psoriasis patients compared with healthy controls. Some studies revealed lower levels of 25(OH)D in RA patients than in healthy matched controls,[40,41] but other studies did not find such a difference.[42,43] The finding of low levels of vitamin D in psoriatic and RA patients may highlight the possible role of vitamin D deficiency in the pathogenesis of psoriasis and RA. Vitamin D receptors (VDRs) are found at high levels on dendritic cells, T and B lymphocytes and macrophages. The function of these cells is profoundly affected by binding of activated 1,25(OH)2D.[44,45] Moreover, the 1α-hydroxylase that converts 25(OH)D

to its active form is expressed in activated macrophages, dendritic cells and other tissues.[46] The expression of VDRs on resting CD4+T cells increases 5 fold with T cell activation.[47] These findings suggest that vitamin D plays a role in immune function. There is increasing evidence that compromised vitamin D status has been associated with an increased risk for Th1 cytokine mediated autoimmune diseases, including IDDM, MS, inflammatory bowel disease, and RA.[48] Polymorphisms in the VDR gene have been associated with increased risk of psoriasis and RA.[49,50] Deficient 25-OHD levels in patients with psoriasis and RA may also be associated with the isoenzyme polymorphisms that influence serum 25-OHD levels, such as 7-dehydrocholesterol reductase, liver 25-hydroxylase, CYP2R1, and CYP24A1.[51]

Low levels of vitamin D in psoriatic and RA patients may also have important implications in the management of psoriasis and RA. Systemic vitamin D administration has shown clinical benefits in psoriatic and RA patients.[52,53] However, more definitive evidence is required to demonstrate the clinical benefit of vitamin D supplementation in the treatment of psoriasis and RA. Narrowband phototherapy (NBUVB) has become an important treatment for psoriasis. The therapeutic effect of NBUVB may be mediated at least in part by UVB-triggered cutaneous synthesis of vitamin D.[19-21] Moreover, topical vitamin D derivatives are used as monotherapy or in combination with steroids for the topical treatment of psoriasis.[22]

In the present study, 25(OH)D level was not associated with disease severity assessed by PASI, serum TNF-α, ESR, or CRP in psoriatic patients. In agreement with our findings, Orgaz-Molina et al,[24] and Gisondi et al[39] did not find association between low level of vitamin D and PASI in psoriasis patients, but Orgaz-Molina et al[24] found inverse correlation between vitamin D and CRP. We also found that 25(OH)D level was not associated with disease activity or serum TNF-α in RA patients. Several studies have evaluated the association between vitamin D levels and RA activity. Some studies found an inverse association between vitamin D levels and disease activity in RA,[54-58] but other studies did not find such relation.[59-61] We also did not find association between vitamin D and ESR or CRP in RA patients. However, Kostoglou-Athanassiou et al[41] found that vitamin D was negatively correlated with ESR and CRP. Inverse associations between serum vitamin D levels and serum CRP concentrations have been found in patients with diabetes mellitus, atherosclerotic vascular disease, inflammatory polyarthritis, and prolonged chronic illness.[62,63] Up to our knowledge, no previous studies evaluated the association between vitamin D level and TNF-α in RA or psoriasis patients. Experimental data show that 25(OH)D can inhibit pro-inflammatory cytokines such as IL-6 and TNF-α, decrease serum levels of CRP, and upregulate production of the anti-inflammatory cytokine IL-10.[64] More studies are required to investigate the association of vitamin D deficiency with disease activity, TNF-αand inflammatory markers in psoriasis and RA.

The limitation of this study was the small number of patients and that most of psoriasis patients had mild or moderate psoriasis. Further studies on larger number of patients including large number of patients with severe psoriasis are required to study the relation between vitamin D deficiency and disease severity.

All subjects participating in this study were asked to estimate the average duration that they spent outdoors on weekdays and at weekends. All subjects were recruited from the same area between March and September which are sunny months in Riyadh. We found significant difference between psoriasis patients, RA patients, and healthy matched controls in exposure to sunlight. Psoriatic patients were exposed to the sun more than RA patients and healthy controls. This may be because the majority of psoriatic patients know the beneficial effect of sun exposure. Thus, we exclude that vitamin D deficiency in psoriatic patients was due to less sun exposure. The lower vitamin D level in psoriatic patients may be explained by low capacity of vitamin D synthesis of the skin. New studies are required to explore the underlying mechanisms of vitamin D deficiency in psoriasis and RA.

In conclusion, serum 25-(OH)D levels are significantly lower in psoriatic and RA patients than in healthy control subjects. However, new studies with larger numbers of patients are required to analyze the pathogenic mechanisms underlying the relationship between 25-OHD deficiency, and psoriasis and RA. Low 25-OHD levels also may provide the rationale for vitamin D supplementation in the treatment of psoriasis and RA. More definitive evidence is also required to demonstrate the clinical benefit of vitamin D supplementation in the treatment of psoriasis and RA. Further studies are required to explore the relation between vitamin D deficiency and TNF-α and the inflammatory markers in psoriasis and RA.

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