

## Association between Vitamin D Deficiency and Psoriasis: A Case-Control Study

Ahmed Allayali<sup>1</sup>, Ghassan Niaz, Khalid Al Hawsawi, Mohammad Fatani, Irfanullah Siddiqui, Razan Baghdadi, Hatim Al Sulimani and Waseem Al Hawsawi

Department of Dermatology, Umm Alqura University Makkah, Saudi Arabia

**Corresponding author:** Ahmed Allayali, Department of Dermatology, Umm Alqura University Makkah, Saudi Arabia, Tel: + 966553278746; E-mail: ahmedz98@hotmail.com

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### Abstract

The immunomodulatory effect of vitamin D is well known, and some previous studies have found a potential association between vitamin D deficiency and psoriasis. If this is the case, correction of vitamin D levels could provide a simple, cost-effective treatment method for psoriasis patients. The aim of this case-control study was to confirm whether there was such an association. We also investigated several potential risk factors of psoriasis. We recruited 68 consecutive psoriasis outpatients at three hospitals in Saudi Arabia, as well as 68 control patients with dermatological conditions, and compared serum 25-hydroxycalciferol levels. However, we found no significant differences in vitamin D levels between the two groups. This finding supports similar negative findings of some previous studies, but further studies are needed to resolve this matter.

**Keywords:** Psoriasis; Vitamin D; Adalimumab; Infliximab; Etanercept

### Introduction

The immunomodulatory effect of vitamin D is well known [1]; for example, it has been shown to impact some circulating chemokines and cytokines and to inhibit T-cell differentiation and activation [2,3]. In addition, associations have been shown between vitamin D deficiency and autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, and diabetes mellitus [4-6].

Psoriasis is a chronic, noncontagious, multisystem disease that appears to be influenced by genetic and immune-mediated components. Its pathogenesis is not completely understood, but excessive T-cell activity has been shown to be associated with the condition [7], and proinflammatory mediators such as interleukin (IL)-17 and IL-23 have a considerable impact on the pathogenesis [8].

Many treatments for autoimmune diseases can be expensive and associated with adverse effects. In contrast, a simple intervention such as correction of vitamin D levels could have a great effect on patients affected by psoriasis. However, the controversy in the literature about whether or not serum vitamin D deficiency is associated with psoriasis [9,10] requires further study with an appropriately large sample size to establish and confirm the relationship.

The primary objective of this study, therefore, was to demonstrate the association between psoriasis and serum levels of vitamin D (25-hydroxycalciferol [25(OH)D]). The secondary objective was to investigate factors that could potentially affect the severity of psoriasis, including age, sex, body mass index (BMI), comorbid conditions, family history of psoriasis, type of psoriasis, treatment used, and duration of the treatment.

### Methods

This multicenter, case-control study was conducted in three major hospitals in Makkah, Saudi Arabia: King Abdulaziz General Hospital, Hera General Hospital, and King Faisal General Hospital. The study was approved by the Committee of Bio-Medical Ethics in the Faculty of Medicine, Umm Al Qura University, Makkah. After receiving an explanation of the purpose, benefits, and risks of the study, as well as their right not to provide any information, all participants provided written consent. All data were kept confidential.

The required sample size was calculated using the statistical software Epi Info ver. 3.01, based on a confidence interval of 95%, an alpha value of 5%, and a worldwide prevalence of vitamin D deficiency of around 2%. This resulted in a required sample size of 68 cases with 68 controls. The participants were enrolled using a non-probabilistic, consecutive sampling technique.

The following inclusion criteria were applied for the cases: consecutive patients aged  $\geq 16$  years with active psoriasis who attended the outpatient clinics of the three study hospitals; no phototherapy of any kind received in the previous three months; and no oral or topical vitamin D or its derivatives taken in the previous three months. The criteria for the control group were as follows: patients without psoriasis; no previously diagnosed vitamin D deficiency, regardless of whether it was treated; and no vitiligo or telogen effluvium (shedding of hair) as a condition for visiting outpatient clinic. The following exclusion criteria were applied to both cases and controls: a diagnosis of vitamin D deficiency; not consenting to participate; participation in any morning activity or job that took place outdoors; or suffering from multiple sclerosis, systemic lupus erythematosus, sarcoidosis, diabetes mellitus, rheumatoid arthritis, renal failure, any type of liver disease, celiac disease, or inflammatory bowel disease.

The participants' serum vitamin D (25(OH) D) levels were obtained by collecting 5 ml of blood at the time of the interview; this was kept at  $-20^{\circ}\text{C}$  until the analysis. Serum vitamin D deficiency was defined as serum 25(OH)D  $< 20$  ng/ml (50 nmol/l), as per the recommendations

of the Endocrine Society [11]. Other data were obtained from questionnaires. These were designed specifically for this study and were pre-tested. The questionnaires were completed by each participant after receiving a personal explanation of the questions from a medical student (Years 4, 5, or 6, or an intern) from Umm Al Qura University to ensure full understanding.

**Ethical consideration**

The approval was obtained from Committee of Bio-Medical Ethics, Faculty of Medicine, Umm Al Qura University, Makkah.

All the collected data kept confidential. An informed consent obtained from all participants and the purpose of the study, benefits and risks all explained to all participants and their right not to provide any information obtained from the study.

**Data analysis**

The SPSS ver. 22 was used to enter, clean and analyze the data. Mean, standard deviation and standard error were calculated for continuous variables like age, serum 25 D level, duration of psoriasis, BMI, duration of treatment and direct Sun exposure, while proportion/ percentages were calculated for qualitative data like gender, nationality, and residency. Student t test of independence was applied for comparing the continuous variables for cases and controls and Chi square test of significance was used to compare the categorical variables

**Results**

Of the 136 participants in this study (68 psoriasis patients and 68 controls), 133 (98%) were from Makkah city and 114 (84%) were of Saudi nationality (Table 1). There were 75 (55%) male and 61 (45%) female participants.

Table 2 compares characteristics between the cases and controls. The mean ages ( ± standard deviation) of the cases and controls were

37 ± 14 and 36 ± 13 years, respectively (range 16-73 years). There was no significant difference in BMI between the groups (28.68 ± 6.43 vs. 27.12 ± 5.6 kg/m<sup>2</sup>, respectively; p=0.133).

		Total (N=136)	Cases (N=68)	Controls (N=68)	Chi square	P
<b>Residence</b>						
Makkah		133 (97.8%)	65 (95.6%)	68 (100%)	3.068	0.244
Outside Makkah		3 (2.2%)	3 (4.4%)	0 (00.0%)		
<b>Sex</b>						
Male		75 (55.1%)	38 (55.9%)	37 (54.4%)	0.03	1
Female		61 (44.9%)	30 (44.1%)	31 (45.6%)		
<b>Nationality</b>						
Saudi		114 (83.8%)	56 (82.4%)	58 (85.3%)	0.217	0.816
Non-Saudi		22 (16.2%)	12 (17.6%)	10 (14.7%)		

**Table 1:** Demographic and social characteristics of the participants.

The mean serum 25(OH) D level for psoriatic patients was 16.29 ng/ml ± 10.49) with lowest measured serum 25(OH) D level was 3 ng/ml and highest of 53.26. Control serum 25(OH) D level was 15.76 ng/ml ± 9.00 with lowest measured serum level was 4.47 ng/ml and highest was 58.05 ng/ml) with no statistical significance observed between cases and control (P Value=0.754) (Table 2).

Factor		N	Mean	Standard Deviation	Standard Error	t value	P value
Age (y)	Cases	68	37.3	13.7	1.7	0.418	0.677
	Controls	68	36.3	13.0	1.6		
Serum vitamin D level at time of Interview	Cases	68	16.3	10.5	1.3	0.314	0.754
	Controls	68	15.8	9.0	1.1		
Duration of psoriasis (y)	Cases	68	7.8	7.3	0.9	a	a
	Controls	0 <sup>a</sup>	-	-	-	-	-
Body mass index	Cases	68	28.7	6.4	0.8	1.512	0.133
	Controls	68	27.1	5.6	0.7		
Duration of psoriasis treatment (months)	Cases	68	28.3	50.1	6.3	a	a
	Controls	0 <sup>a</sup>					
Time spent in direct sunlight (min per week)	Cases	67	214	438	54	0.814	0.417

	Controls	67	160	326	40		
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**Table 2:** Comparison of possible psoriasis risk factors between the cases and controls, and the duration of the psoriasis and its treatment (a. The t value could not be calculated because these factors were not relevant to the controls group).

The average years for patients having psoriasis was 7.75 years. In the Psoriasis group the mean BMI was  $28.68 \text{ Kg/m}^2 \pm 6.43$  while in in control group was  $27.12 \text{ Kg/m}^2 \pm 5.6$  with no statistical significance between the two groups (p Value=0.133) (Table 2). Forty seven (67.5%) of Psoriasis patients had tried any kind of treatment for average of 28.7 months  $\pm 50.15$  (Table 3).

Type of psoriasis	Cases (N=68)	Condition	Controls (N=68)
Plaque	58 (85.3%)	Eczema	14 (20.6%)
Guttate	2 (2.9%)	Acne Vulgaris	23 (33.8%)
Inverse	3 (4.4%)	Lichen Planus	3 (4.4%)
Pustular	1 (1.5%)	Alopecia Areata	1 (1.5%)
Erythrodermic	1 (1.5%)	Warts	7 (10.3%)
Linear	2 (2.9%)	Seborrheic Dermatitis	2 (2.9%)
Palmoplantar	1 (1.5%)	Other	18 (26.5%)

**Table 3:** Types of psoriasis of the cases and dermatological conditions of the controls.

Weekly Direct Sun Exposure for Psoriasis Group was  $214.47 \pm 438.5$  minutes per week while in Control group it was  $160.17 \pm 325.76$  minutes per week, with no statistical significance between the two groups (p Value=0.417) (Table 4).

	Total (N=136)	Case (N=68)	Control (N=68)	Chi square	P
Family history of psoriasis					
Positive	19 (14%)	11 (16.2%)	8 (11.8%)	0.551	0.622
Negative	117 (86%)	57 (83.8%)	60 (88.2%)		
Comorbid condition?					
Yes	22 (16.2%)	11 (16.2%)	11 (16.2%)	0	1
No	114 (83.8%)	57 (83.8%)	57 (83.8%)		
Comorbid condition					
Diabetes mellitus				0.217	

Hypertension	11 (8.1%)	4 (36.4%)	7 (63.6%)		0.816
Asthma	1 (0.7%)	0 (00.0%)	1 (100.0%)		
Others	1 (0.7%)	1 (100%)	0 (0.00%)		
Total	9 (%)	6 (66.7%)	3 (33.3%)		
	22 (16.2%)	11 (50%)	11 (50%)		
Previous psoriasis treatment?					
Yes	48 (35.3%)	48 (70.6%)	0 (0%)	70.07	0
No	88 (64.7%)	20 (29.4%)	68 (100%)		
Multivitamin supplements					
Yes	5 (3.7%)	1 (1.5%)	4 (5.9%)	1.869	0.366
No	131 (96.3%)	67 (98.5%)	64 (94.1%)		
Osteoporosis treatment					
Yes	0 (0%)	0 (0%)	0 (0%)	0	1
No	136 (100%)	68 (100%)	68 (100%)		

**Table 4:** Disease and treatment characteristics of the cases and controls.

As shown in Table 3, fifty eight cases of psoriasis patients had plaque Psoriasis (85.3%). Of the 68 control group 23 (33.8%) had Acne Vulgaris as most common complaint and Eczema, being the second most common complaint (20.6%).

Table 4 shows that only 19 of all participants of the study (14%) had positive family history of Psoriasis. While only 11 psoriasis patients (16.2%) had positive family history of psoriasis with no significant difference between cases and control (p value=0.622).

Similarly, there was no significant difference between cases and control regarding comorbid condition, type of comorbid condition and use of multivitamin supplement (Table 4). Adalimumab was the most tried treatment 13 (9.6%) followed by Calcipitriol/Betamethasone with 4 (2.9%) (Table 5).

Type of medication	Frequency	Cases	Control
None	63 (46.3%)	18 (28.6%)	45 (71.4%)
Adalimumab	13 (9.6%)	13 (100%)	0 (0.00%)
Infliximab	2 (1.5%)	2 (100%)	0 (0.00%)

Etanercept	2 (1.5%)	2 (100%)	0 (0.00%)
Calcipotriene/betamethazone	4 (2.9%)	4 (100%)	0 (0.00%)
Hypertension medication	5 (3.7%)	0 (0.00%)	5 (100%)
Hypertension and Diabetes	2 (1.4%)	1 (50.0%)	1 (50.0%)
Diabetes medication	3 (2.2%)	0 (0.00%)	3 (100%)
Diabetes & other	1 (0.7%)	1 (100.0 %)	0 (0.00%)
Others	23 (16.9%)	9 (39.1%)	14 (60.9%)
Non specified	18 (13.2%)	18 (100%)	0 (0.00%)
Total	136 (100%)	68 (50%)	68 (50%)

**Table 5:** Distribution of Other Medications taken.

## Discussion

The issue of whether vitamin D deficiency contributes to the pathogenesis of psoriasis remains unsettled, with scant data available in the literature. An early cross-sectional study of vitamin D serum levels in patients with psoriasis by Gisondi et al. [10] compared 145 patients with psoriasis to 112 patients with rheumatoid arthritis (RA) and 141 healthy controls and found significantly lower serum levels of 25(OH) D in both the RA and psoriatic patients than in the controls, especially during winter months, but no significant difference between the RA and psoriasis groups. The psoriasis patients presented with a 2.5 times greater risk of 25(OH)D deficiency than the controls [10]. In contrast, a recent cross-sectional analysis of NHANES data by Wilson et al. [12], with 5,841 participants of whom 148 had psoriasis, found no statistically significant difference in the prevalence of 25(OH)D deficiency between those with and without psoriasis, although the psoriasis patients were more likely to be obese and of non-Hispanic white ethnicity. A case-control study by Orgaz-Molina et al. [9] included 43 patients with psoriasis and 43 control subjects from a single outpatient clinic in Granada, Spain, and found significantly lower 25(OH)D levels in the cases than in the controls. This study also concluded that psoriasis patients with BMI  $\geq 27$  kg/m<sup>2</sup> were more likely to have vitamin D insufficiency [9]. Several studies using narrow band ultraviolet B (NB-UVB) have demonstrated an effect of systemic vitamin D on psoriasis [13-23]. Notably, Ryan et al. [21] showed that, in patients with psoriasis, mean serum levels of 25(OH) D increased from 23 to 42 ng/ml after 12 sessions of NB-UVB, increasing further to 51 ng/ml by the end of treatment; these changes were accompanied by decreases in PASI and Dermatologic Life Quality Index scores. The results of the present study showed a mean vitamin D level for the psoriasis patients of  $16 \pm 10$  ng/ml (range 3-53 ng/ml), which was not significantly different from the level of the control group of  $16 \pm 9$  ng/ml (range 4-58 ng/ml); this provided further support for the findings of Wilson et al. [12], Zuchi et al. [24], and Maleki et al. [25]. However, Ricceri et al. [26] found a prevalence of 68% of vitamin D deficiency and 97% of insufficiency in patients with psoriasis, compared with 10% deficiency and 53% insufficiency in their control group.

It is possible that a difference in vitamin D levels could account for the higher prevalence of psoriasis at higher latitudes compared with that in the tropics [27]. Genetic differences may also play a role, as some studies have shown that the polymorphism of vitamin D

receptors in psoriasis patients differs from that of the normal population [28-30], potentially contributing to a high prevalence of vitamin D deficiency in psoriasis patients in some populations.

Further research is required to explain the discrepancy in the results of these studies.

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