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The Relationship between Psoriasis and Serum Levels of Vitamin D

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Authors' contributions

This work was carried out in collaboration between all authors. Author RT designed the study, wrote the protocol , performed the statisticl analysis, wrote the first draft of the manuscript , managed the analyses of the study and managed the literature searches. Author RB was supervisor professor. Author FR was assistant supervisor professor. Author FH is head of dermatology department. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Introduction: Psoriasis is a common chronic inflammatory skin disease with complex pathophysiology. The role of vitamin D has recently arisen in many skin and systemic diseases including psoriasis through its modified effect of inflammatory and immunological mechanisms. Several studies have demonstrated its effects on keratinocytes' proliferation and differentiation, cutaneous immune system, regulating the microbial flora and the response to infective diseases.
Aim: this study aimed to compare serum levels of vitamin D in patients with psoriasis with its levels in control subjects without this disease, and to analyze the presence of a relationship between vitamin D status and the clinical features of psoriasis.
Methodology: This analytic observational case-control study included 174 patients (88 with psoriasis and 86 control subjects without psoriasis) all of them were resident in Latakia during a period of one year. Levels of 25-OH vitamin D were determined using ELISA test.
Results: Serum levels of vitamin D were significantly lower in the psoriatic patients than control individuals (12.51±9.57 vs. 16.53±7.22, P-v=0.002). There was no statistically significant

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correlation between serum vitamin D levels and the duration of disease, its clinical type, or the presence of nails, joints or palms and soles involvement. On the other hand, there was a significant negative correlation with severity of disease.

Conclusion: It is necessary to bear in mind that vitamin D deficiency is more common in psoriasis patients than controls and that infers the role of vitamin D in the pathogenesis of the disease.

Keywords: Psoriasis; serum levels of vitamin D; vitamin D deficiency.

ABBREVIATIONS

25(OH)D, OHD : 25 hydroxy vitamin D;
VDR : vitamin D receptor;
UV : ultraviolet;
Th cells : T helper cells;
IL : interleukin;
BMI : body mass index;
WHO : World Health Organization;
PASI : psoriasis area severity index;
ELISA : enzyme-linked immunoabsorbent assay;
CBC : complete blood count;
AST : aspartate aminotransferase;
ALT : alanine aminotransaminase;
CRP : C-reactive protein;
SD : standard deviation.

1. INTRODUCTION

Psoriasis is a common disease with a worldwide prevalence rates between 0.51% and 11.43% [1]. Although psoriasis can begin at any age, there seem to be two peaks for incidence: one between ages 20 and 30 and the other between 50 and 60 [2]. Until the late 1970s, psoriasis was originally thought to be a disease primarily of dysfunctional epidermal keratinocytes [3]. However, substantial clinical and basic research observations indicate that dysregulation or alteration of components of the innate and adaptive immune systems, keratinocyte function, and vascular structure play a role in the pathogenesis of psoriasis [4-6].

Vitamin D, the ‘‘sunshine’’ vitamin, is a hot topic that attracted ample attention over the past decades. It was primarily acknowledged for its importance in bone formation. However, increasing evidence point to its interference with the proper function of nearly every tissue in our body including brain, heart, muscles, immune system and skin. The major source of vitamin D is synthesized nonenzymatically in skin from 7-dehydrocholesterol, which is located in the membrane of keratinocytes of the basal and spinous layer of epidermis, during exposure to the ultraviolet rays (spectrum 280–320 UVB) in sunlight [7]. The other major source of vitamin D is intestinal absorption from food and dietary supplements. There are a few naturally occurring food sources of vitamin D. These include fatty fish, fish liver oil, and egg yolk [8]. It appears to function through a single vitamin D receptor (VDR), which is nearly universally expressed in nucleated cells [9].

Although the precise mechanism in which vitamin D contributes to psoriasis is still not completely clear, there is a lot of research studying this relationship and so far there are many confirmed aspects in this relationship. The skin is unique in being not only the main source of vitamin D for the body but also has the necessary enzymatic mechanism to metabolize it into its active form 1,25 (OH) 2D. The skin also has its receptor (VDR), therefor it is capable of responding to the active metabolite of vitamin D 1,25(OH)2D [10] [11]. Both calcium and 1,25(OH)2D perform important and interacting functions in regulating the skin differentiation process. Numerous in vitro and in vivo studies have demonstrated effects of vitamin D on proliferation, differentiation and apoptosis of keratinocytes, as well as on the skin barrier formation which is crucial in defending the skin [10-14]. It also has many effects on the cutaneous innate immune system as it affects the function of monocytes, macrophages, dendritic cells, and antigen presenting process [11]. Vitamin D also affects the cutaneous adaptive immune system where T helper (Th) cells appear to be the principal target for 1,25(OH)2D.

It has become well known that psoriasis is a systemic inflammatory process in which T lymphocytes play a key role in the subsequent production and activation of inflammatory cytokines, particularly tumor necrosis factor-α, interferon-γ, interleukin (IL)-2, and IL-8 [15-17]. tudies examining the role of vitamin D on the cutaneous immune system have demonstrated its ability to inhibit the production of cytokines needed for Th1 and Th17 differentiation, stimulate T cells to produce anti-inflammatory Th2 cytokines such as IL-10, and thus reduce the

production of inflammatory cytokines such as IL-2, IL-8, interferon-γ, and tumor necrosis factor-α, as well as reduce the density of major histocompatibility complex class II molecules on dendritic cells [12-14]. Moreover, vitamin D analogs have been shown to suppress the Th17 cytokine-mediated production of psoriasin and koebnerisin, two antimicrobial chemoattractant peptides that amplify inflammation in psoriasis [18]. Vitamin D has also been shown to induce the antimicrobial peptide cathelicidin (LL-37) in keratinocytes, which has anti-inflammatory effects that blunt activation of macrophages [19, 20].

Several studies identified an association between polymorphisms of vitamin D receptor (VDR) and psoriasis susceptibility [21,22]. In addition, in psoriatic skin a decreased expression of VDR and reduced tight-junction proteins is associated [23]. It is now accepted that vitamin D analogs are effective and safe for the topical treatment of skin. Many studies have proven the excellent efficacy and safety of vitamin D and its analogues in the treatment of psoriasis [24]. Although topical vitamin D supplementation has become known and available for psoriasis, the oral use of vitamin D is limited due to the fear of adverse effects such as hypercalcemia, hypercalciuria, nephrocalcinosis, nephrolithiasis and reduction in bone mineral density secondary to its calcemic effect [24]. However, there are many studies that prove its efficacy in improving psoriasis or psoriatic arthritis alone or in combination with other treatments and that it is well tolerated treatment and hypercalcemia can be easily monitored and avoided by administering the appropriate dose observation and limited intake of calcium [25-29]. UV phototherapy is a well-established and safe treatment option for psoriasis. Though it is well recognized that UV therapy works in part by inhibiting cutaneous immune function, its therapeutic efficacy in psoriasis, particularly of the UVB class, may be at least in part due to increased vitamin D synthesis as well. Several recent studies have put this concept to the test, demonstrating that increases in vitamin D post-UVB treatment correlated with clinical improvement of psoriasis [30-32]. Vitamin D analogues with phototherapy have been used in many clinical trials. It has been found that this combination was more effective than single therapy without increased side effects [30-35].

In view of the evolution in understanding the role of vitamin D in skin diseases including psoriasis, in addition to the expansion of the database regarding the pathogenesis of psoriasis and the role of vitamin D in the treatment of psoriasis, It was logical to study the role of vitamin D in occurrence and severity of the disease. Emerging literature supports this hypothesis and the majority of studies in this context, but not all, have demonstrated lower levels of vitamin d in psoriatic patients, yet none of them have been able to demonstrate a clear causal relationship [36-39]. In contrast to the continuous increase in global studies on the potential role of vitamin D, its receptors and its serum levels disturbances in the pathogenesis of psoriasis, we find few similar studies in the Middle East with no local studies of vitamin D and its role in the psoriasis. Hence the importance of this study in highlighting vitamin D and its relationship with a common disease in our society such as psoriasis in order to increase understanding of the exact pathophysiology and thus develop new treatments on the one hand, and the possibility of improving control over the clinical course of the disease by modifying serum levels in patients who are deficient in vitamin D on the other. The objective of this study is to compare serum levels of vitamin D in patients with psoriasis with a range of healthy controls and to test a relationship between disease characteristics and vitamin D levels.

2. METHODOLOGY

This analytic case-control study was conducted in a period of one year from January to December 2016. It included 88 psoriasis patients who attended the outpatient clinic of the Department of Dermatology and Venereology at Tishreen University Hospital during the study period. We enrolled all psoriasis patients aged above 18 years old who are resident in the city of Latakia,in order to reduce the geographical differences in sunlight exposure, regardless of the disease period, and except for the following:

1. Patients who received treatment for psoriasis within 3 months prior to participating in the study, whether it was topical treatment, including steroids or vitamin D analogs, systemic treatment or phototherapy, regardless of treatments used prior to this period.
2. Patients taking other drugs that affect vitamin D metabolism or its levels such as Phenytoin, steroids, bisphosphonates or vitamin D supplements.
3. Patients with renal or hepatic failure.

4. Patients with diseases that may be associated with vitamin D deficiency such as inflammatory bowel disease, multiple sclerosis, insulin-dependent diabetes, systemic lupus erythematosus, skin lymphoma, non-melanoma skin cancers, other body tumors, vitiligo, coronary artery disease.
5. Pregnant and lactating women

The control group included 86 individuals who don't have psoriasis of the same conditions and during the same period of time. All participants were interviewed and clinically examined after getting their signed consent. The information were saved into specific data forms.

The participants' personal data were gathered on age, sex, occupation, social status, Fitzpatrick phototype, smoking habits, body mass index (BMI) and family history of psoriasis. Current smokers were defined as participants who smoke cigarettes daily or who had stopped smoking < 5 years before enrolment in the study. Non-smokers were participants who had smoked < 5–10 packs of cigarettes during their lifetime or who had stopped smoking > 5 years before the enrolment. Overweight and obesity were defined according to WHO definitions as BMI≥25 and BMI 30, respectively. Data were also gathered on daily activities that may affect vitamin D levels, focusing on the disease period: the daily sunlight exposure estimated by minute per day (classified as: 15, 15-30, >30 min/day), the weekly number of outside activities (classified as: <2, 2-4, >4 times/week), and using sun screens; as well as data about diet (vegetarian, not vegetarian), weekly fish intake (distributed as: <1, 1, 1> times per week) and milk consumption (quantified as: nothing, <5, 5-10, >10 cups per week).

Psoriasis-related variables included disease duration, onset type: early (before 40 years old) and late (after 40 years old), clinical pattern (plaque, inverse, guttate, erythrodermic, generalized pustular and the presence of nails, joints or palmoplantar involvement) and severity according to the PASI. Regarding PASI, the psoriasis was categorized as mild (index ≤5), moderate (5 to 15) and severe (15 to 72), respectively. Detailed medical, pharmacological and familial history was collected for all participants.

Serum levels of 25 (OH) D were measured for all participants using commercial enzyme-linked immunosorbent assay (ELISA) kits available in the laboratory of the hospital (Euroimmun,Germany). Serum levels of vitamin D were distributed according to laboratory recommendation Table 1. Other laboratory tests performed were: CBC, Calcium, Alkaline Phosphatase, Iron, Albumin, AST, ALT, CRP and fasting glucose.

Table 1. Distribution of serum vitamin D levels according to laboratory recommendation

Very severe vitamin D deficiency	< 5 ng/ml
Severe vitamin D deficiency	5-10 ng/ml
Vitamin D deficiency	10-20 ng/ml
Suboptimal vitamin D provision	20-30 ng/ml
Optimal vitamin D level	30-50 ng/ml
Upper normal	50-70 ng/ml
Overdose but not toxic	70-150 ng/ml
Vitamin D intoxication	>150 ng/ml

Quantitative data were expressed using central tendency and dispersion scales (mean, standard deviation, minimum value, maximum value) and qualitative or descriptive data using percentages and diagrams. Chi-square test was used to study the relationship between two qualitative variables. Simple linear regression test was used to study the relationship between two quantitative variables. Means, One-Sample Test and One-Way Anova were used to study the relationship between quantitative and qualitative variables. *P-value* less than or equal to .05 was considered significant. IBM SPSS Statistics 20 software was used for the data analyses.

3. RESULTS AND DISCUSSION

The study included 88 psoriasis patients (mean age 44.19±15.26), 51 patients (58.0%) were males and 37 patients (42.0%) were females. Characteristics of psoriasis in the study population are shown in Table 2.

The control group comprised 86 outpatients without psoriasis, 46 males (53.5%) and 40 females (46.5%), with mean age 46.16±12.02. The two groups had no significant difference in age, sex, Fitzpatrick phototype distribution (most had phototypes III, or IV), BMI, the daily exposure to the sunlight, the weekly number of outside activities, type of diet (all participants were not vegetarian), weekly fish intake, milk consumption or time of year, when they were collected. While the proportion of smokers was significantly higher in patients, the users of sun screens were higher in control group. The characteristics of the study population are reported in Table 3.

Table 2. Characteristics of the disease in the study patients group

duration of disease	Mean	11.96 years
	SD	11.93
age of onset	Early onset (< 40 years old)	57 patients (64.8%)
	Late onset (>40 years old)	31 patients (35.2%)
Clinical pattern	Plaque psoriasis	71 patients (80.7%)
	Inverse psoriasis	2 patients (2.3%)
	Erythrodermic psoriasis	5 patients (5.7%)
	Guttate psoriasis	7 patients (8%)
	Generalized pustular psoriasis	3 patients (3.4%)
	Nail psoriasis	26 patients (29.5%)
	Psoriatic arthritis	16 patients (18.2%)
	palmoplantar involvement	19 patients (21.6%)
PASI*	Mean	21.80
	SD	20.97

**There is no PASI score in patients with pustular and guttate psoriasis.*
Abbreviations used in table 2: SD (standard deviation), PASI (psoriasis area severity index).

Table 3. Characteristics of study population

		Patients	**Controls**	***P***
Age	Mean	44.19318	46.16279	.34
	SD	15.25858	12.06537	
Gender	male	58.00%	53.50%	.32
	female	42.00%	46.50%	
Fitzpatrick phototype	2	2.30%	1.20%	.86
	3	22.70%	20.90%	
	4	73.90%	75.60%	
	5	1.10%	2.30%	
Smoking	yes	65.90%	44.20%	.003
	no	34.10%	55.80%	
BMI	normal (24.9>=)	38.60%	26.70%	.14
	Over weight (29.9-25)	44.30%	46.50%	
	Obese (30<=)	17.00%	26.70%	
Daily sun exposure	< 15 min	14.80%	14.00%	.07
	15- 30 min	11.40%	24.40%	
	> 30 min	73.90%	61.60%	
Weekly outdoor activities	2>	9.10%	5.80%	.26
	2 - 4	12.50%	20.90%	
	4<	78.40%	73.30%	
Using sunscreen	yes	28.40%	50.00%	.002
	no	71.60%	50.00%	
Weekly fish intake	1>	84.10%	81.40%	.31
	1	9.10%	15.10%	
	1<	6.80%	3.50%	
Weekly milk consumption	nothing	62.50%	54.70%	.12
	5>	33.00%	30.20%	
	5 _ 10	3.40%	12.80%	
	10<	1.10%	2.30%	
Time of participating in the study	winter	35.20%	34.90%	.34
	Spring	31.80%	31.40%	
	Summer	14.80%	18.60%	
	Autumn	18.20%	15.10%	
Familial history of psoriasis	yes	30.70%	11.60%	.002
	no	69.30%	88.40%	

Abbreviations used in table 3: SD (standard deviation), BMI (body mass index).

The mean serum 25(OH)D concentration was significantly lower in patients than in control subjects (12.51±9.57 in patients vs. 16.53±7.22, *P-v*=.002) Table 4 Fig. 1.

Vitamin D status according to our laboratory settings are shown in Table 5. We notice that the majority of patients (76 patients, 86.4%) had vitamin D levels ranging from 0 to 20 ng/mL, namely having varying degrees of deficiency, but no one of controls had very severe vitamin D deficiency. We notice that there were clear differences in the distribution of vitamin D levels among patients and controls. Analysis of these differences by Chi-square test showed that these differences were statistically significant (*P* = .000) Table 5 Fig. 2.

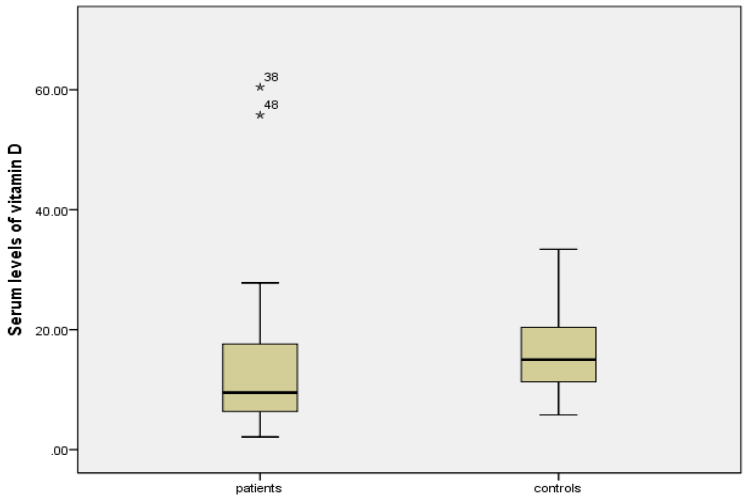

Fig. 1. Comparison of mean serum 25-hydroxyvitamin D (OHD) concentration between psoriasis and control groups. Serum 25-OHD concentration was significantly lower in patients with psoriasis versus control subjects (12.51±9.57 in patients vs. 16.53±7.22, P=.002

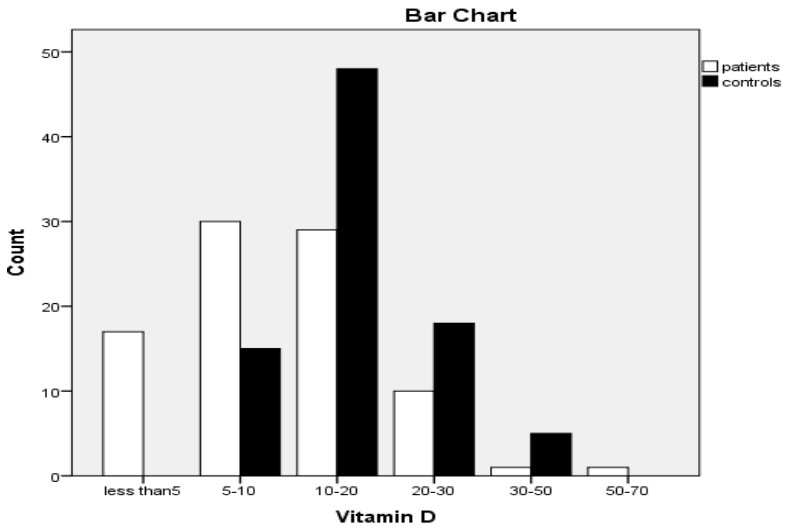

Fig. 2. Vitamin D status in both study groups. We notice that very severe vitamin D deficiency was observed in 19.3% of patients, while it was not found in any individual of controls. The majority of patients (76 patients, 86.4%) had vitamin D levels ranging from 0 to 20 ng/ml, namely having varying degrees of deficiency, whereas the majority of controls had vitamin D levels ranging from 10 to 30 ng/ml.

Table 4. Serum levels of vitamin D in the study population

	N	Mean	Std. deviation	Std. error	95% Confidence Interval for mean		Minimum	Maximum	*P*
					Lower bound	Upper bound			
Patients	88	12.5069	9.57575	1.02078	10.478	14.5358	2.13	60.45	.002
Controls	86	16.5345	7.2186	0.7784	14.9869	18.0822	5.8	33.4	
Total	174	14.4976	8.70592	0.65999	13.1949	15.8003	2.13	60.45	

Table 5. Vitamin D status in both patients and controls

			Study group		Total	*P*
			patients	controls		
Vitamin D	Very severe vitamin D deficiency (< 5 ng/ml)	Count	17	0	17	.000
		% within group	19.30%	0.00%	9.80%	
	Severe vitamin D deficiency (5-10 ng/ml)	Count	30	15	45	
		% within group	34.10%	17.40%	25.90%	
	Vitamin D deficiency (10-20 ng/ml)	Count	29	48	77	
		% within group	33.00%	55.80%	44.30%	
	Suboptimal vitamin D provision (20-30 ng/ml)	Count	10	18	28	
		% within group	11.40%	20.90%	16.10%	
	Optimal vitamin D level (30-50 ng/ml)	Count	1	5	6	
		% within group	1.10%	5.80%	3.40%	
	Upper normal (50-70 ng/ml)	Count	1	0	1	
		% within group	1.10%	0.00%	0.60%	
Total		Count	88	86	174	
		% within group	100.00%	100.00%	100.00%	

Table 6. Vitamin D levels in both study groups according to the sun exposure

Daily sun exposure (min/day)		Patients	Controls	*P-v*
<15	mean	10.67	15.13	.128
	SD	6.07	8.01	
15_30	mean	10.34	17.10	.026
	SD	6.63	7.89	
>30	mean	13.21	16.63	.043
	SD	10.47	6.86	

We observed a weak, but statistically significant, correlation between age and vitamin D in patients group (r = 21.4%, *P* = .04), but we did not notice a statistically significant correlation between vitamin D levels and sex, skin phototype, smoking, body mass index, family history of psoriasis, daily sun exposure, weekly outside activities, use of sun blockers, or fish and milk consumption per week (*P* > .05).

We did not notice a statistically significant difference between the patients and the controls who were not exposed to the sun very much (less than 15 minutes per day). But with increased exposure to sunlight, vitamin D levels increased in controls more than in patients and this difference between two groups became statistically important in those exposed to the sun more than 15 minutes / day (Table 6).

When studying the relationship between serum levels of vitamin D and clinical variables of psoriasis, we found a very low and not statistically important correlation between disease duration and vitamin D levels (r = 8.3%, *P* = .44). There were also no significant differences in vitamin D levels among patients with early-onset of the disease and those with late onset (*P* = .32). When the vitamin D levels were analyzed according to the clinical pattern of the disease, the highest mean level of vitamin D was in patients with plaque psoriasis (13.08±10.26), followed by patients with guttate psoriasis (12.18±6.86) and those with inverse psoriasis (11.47±11.38) then those with erythrodermic psoriasis (9.22±1.53); and the lowest mean level of vitamin D was observed in patients with pustular psoriasis (8.24 ± 4.29). These difference in vitamin D levels between clinical patterns were not statistically significant (*P*>.05). There was also no significant correlation between vitamin D levels and the presence of nails, joints or palmoplantar involvement (*P*>.05). There was significant negative association between vitamin D levels and psoriasis severity measured by PASI (*P* = .001). We did not notice significant correlation between serum levels of vitamin D and laboratory variables measured in this study (*P*> .05).

The relationship between vitamin D and psoriasis has been studied since the 1980s, when it was reported that psoriatic fibroblasts were partially sensitive to the antiproliferative effects of 1,25(OH)2D [40]. It was also observed by chance that a patient being treated orally with 1-hydroxyvitamin D3 for osteoporosis had remission of their psoriatic skin lesions [41]. Then studies regarding the role of vitamin D and its benefits in the treatment of psoriasis have increased [24,42]. In recent decades, there has been increasing knowledge about the importance of vitamin D and the effect of its low levels on various body organs and extra-skeletal health, especially inflammatory immune-mediated diseases [43]. In order to better understand the role of vitamin D in psoriasis, we conducted this study to show differences in vitamin D levels among psoriasis patients and non-psoriasis control individuals. We found out that the levels were significantly lower in patients than in controls. Looking at early phases of studying vitamin D in psoriasis, Gisondi et al. at the University Hospital of Verona and University Hospital of L'Aquila in Italy in 2009-2010 found that psoriasis patients had significantly lower serum levels of vitamin D compared to controls and they presented a 2.5 times greater risk of having 25-hydroxyvitamin D deficiency than those without the disease, while there was no difference between psoriasis patients and rheumatoid arthritis patients [38]. In another study, Orgaz-Molina et al. At the University Hospital of San Cecilio in Spain in 2011 observed that serum levels of vitamin D were significantly lower in psoriasis patients than in controls [36]. A follow-up study by the same investigators looked specifically at the relationship between vitamin D levels, psoriasis, and the metabolic syndrome. The study's findings corroborated their earlier results, demonstrating that patients with psoriasis had significantly lower levels of 25(OH)D than controls, patients with metabolic syndrome had

significantly lower serum levels of 25(OH)D than those without [37]. In the study by Abdalla et al. at Khartoum Dermatology Hospital in 2014, there was also significant difference in vitamin D levels among psoriasis patients and healthy individuals [44]. The studies conducted by Rameshwar et al. at the Hiranandani hospital in India in 2014 [45] and by Bergler-Czop et al. at Silesia University in Poland in 2014-2015 [46] also found similar results. Also, Ricceri et al. in their studies at the Department of Dermatology at Florence University in Italy found that vitamin D deficiency or insufficiency in psoriasis patients was significantly higher than controls [39]. It is clear that the result of our study is consistent with the results of above studies that serum levels of vitamin D in the patient group are significantly lower than in the control group. While the results of the population-based study conducted by Wilson in the United States in 2013 using the National Health and Nutrition Examination Survey (NHANES) data failed to establish a difference in serum vitamin D levels among psoriasis patients and people who do not have psoriasis [47], do not agree with the outcome of our study or any of the studies mentioned earlier.

In this study, there was no significant association between vitamin D levels and mean duration of the disease. This is consistent with the study conducted by Bergler-Czop [46], Abdalla [44] and Orgaz-Molina [36]. In a retrospective study conducted by Pavlov et al. at the Dermatology and Venerology Clinic at the University of Varna in Bulgaria during 2013-2014, they observed a lack of vitamin D levels in psoriasis patients, but they did not find significant difference in vitamin D levels among early and late-onset types of psoriasis [48], and this is consistent with what we found in our study.

None of the previous studies have studied the relationship between vitamin D levels and the clinical pattern of psoriasis. In this study, however, the lowest levels of vitamin D were found in patients with generalized pustular psoriasis and erythrodermic psoriasis, but these differences were not statistically significant, possibly because of the low number of patients in these two clinical forms.

The levels of vitamin D in psoriasis patients were similar in the presence or absence of psoriatic arthritis. This was consistent with the results of Gisondi et al. [38] and Orgaz-Molina et al. [36]. Orgaz-Molina et al. [36] also found no differences in vitamin D levels in the presence or absence of nail psoriasis.

In this study, there was negative association between vitamin D levels and psoriasis severity according to PASI. This is consistent with the findings of Pavlov et al. [48] Bergler-Czop et al. [46] and Ricceri et al. [39], who found an inverse relationship between the severity of vitamin D deficiency and PASI score. On the contrary to the results of Orgaz-Molina et al. [36] and Gisondi et al. [38], as well as the findings of Wilson [47], who showed in his study no link between vitamin D deficiency and body surface area (BSA).

The studies that examine the relationship between polymorphisms of vitamin D receptor (VDR) and psoriasis susceptibility are conflicting. Many of these studies identified that some of polymorphisms of vitamin D receptor (VDR) correlate with psoriasis [22,49,50]. In this context, Richetta et al. have found that the A-1012G promoter polymorphism of the VDR gene is associated with psoriasis risk through a lower expression of VDR mRNA, favoring conditions that may alter cutaneous barrier and the development of psoriatic lesions [21]. But other studies had shown that no genetic variant in the VDR gene has a robust and reproducible association with risk for psoriasis, and any association that may exist is likely to be weak and potentially restricted to specific populations [51].

As 1,25(OH)2D exerts its effects through binding to VDR, it has been postulated that the responsiveness to vitamin D therapy depends on the level of expression of VDR in keratinocytes [14,12,13,52]. Recent studies have demonstrated that mice, deficient in epidermal VDR, are unable to respond to vitamin D, suggesting that the improvement of psoriasis with vitamin D treatment correlates directly with the level of VDR present in lesioned skin [14,52]. Moreover, it has been shown that VDR expression is related to the cell cycle: VDR levels decrease during the arresting phase and increase once the cell re-enters the cell cycle [52]. Thus, it can be inferred that vitamin D would preferentially act on proliferating cells [12,13,14,52]. In addition to their intrinsic antiproliferative effects, vitamin D analogs have been shown to upregulate the expression of VDR on epidermal keratinocytes, thus temporally amplifying their own potency and enhancing their regulatory role on cell differentiation and proliferation [14,12,13,52,53].

The limitation of this study were the difficult financial situation which limited the sample size, as well as repeating analysis for the same patient in order to study changes in vitamin D and its relationship with changes in the clinical state or seasons and the sample size was relatively low, especially for clinical forms other than plaque psoriasis (inverse, guttate, erythrodermic, and pustular). So that broader studies need to be undertaken to confirm the results for these forms.

4. CONCLUSION

The serum levels of vitamin D in psoriasis patients in our community are significantly lower than in healthy individuals who do not have psoriasis so that psoriasis patients can be considered high risk groups for vitamin D deficiency. But we could not establish a clear causal relationship between psoriasis and vitamin D serum levels. We found negative correlation between vitamin D levels and disease severity according to PASI score. Whereas the relationship between the presence of psoriasis and the decrease of vitamin D levels was independent of the duration of the disease, its onset pattern (early onset or late), its clinical form.

5. RECOMMENDATION

We recommend conducting expanded studies to assess the state of vitamin D in our community in order to identify the appropriate cut points (levels of deficiency and inadequacy) and to adopt them as reference values and to study the prevalence of vitamin D deficiency in our community according to these cut points. We conclude that psoriatic patients are high risk group for vitamin D deficiency, therefore, it is reasonable to screen vitamin D level routinely in all patients with psoriasis and replenish its deficiency, which might benefit in the treatment of psoriasis. So, we also recommend performing interventional studies with vitamin-D supplementation to monitor their impact on psoriasis and its possible future use as part of treatment plans for psoriasis.

More studies to analyze vitamin D changes in patients during the seasons and their relationship to clinical changes in the disease, as well as broader studies of vitamin D levels according to the clinical forms of psoriasis (especially pustular and erythrodermic) with a larger sample number are warranted. Future studies looking at the exact mechanism that explains the association between low levels of vitamin D and psoriasis are necessary to reveal the exact correlations.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical permission has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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