


Original Research Article

Serum concentration of 25-hydroxy vitamin D in psoriatic patients in a tertiary care hospital - A case control study

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Abstract

Background: Vitamin D is a fat soluble vitamin and synthesized by skin from 7-dehydroxy cholesterol during exposure to UV-B. Vitamin D is essential for calcium homeostasis, bone growth and immune regulation. Vitamin D deficiency causes Rickets, Osteomalacia, Osteoporosis and Muscle weakness. Vitamin D deficiency associated with Cancers, Cardiovascular diseases, Schizophrenia, Wheezing illness and autoimmune diseases like systemic lupus erythromatosus, Rheumatoid Arthritis, Type 1 Diabetes Mellitus, Multiple sclerosis, Crohn's Disease, Psoriasis, Vitiligo and Chronic Urticaria.

Objective: The main objective of this study was to analyze the 25-hydroxy vitamin D status of patients with psoriasis in comparison with control subjects without psoriasis.

Material and methods: This study included 30 patients (age and sex matched control subjects) from the outpatient department of Narayana Hospital dermatology department in Nellore, Andhra Pradesh. All patients and control subjects were studied during 4 months period from July to October, 2015.

Results: Serum 25-hydroxy vitamin D levels were significantly lower in psoriatic patients than in control subjects even after adjusting for confounding factors in a multivariate analysis. Low 25-hydroxy vitamin D levels were positively associated with psoriasis and body mass index in multiple linear regression analysis. Psoriatic patients with body mass index greater than or equal to 27 kg/m² had a higher risk of 25-hydroxy vitamin D insufficiency.

Conclusion: The 25-hydroxy vitamin D values are significantly lower in psoriatic patients than in control subjects. Low 25-hydroxy vitamin D levels are positively associated with psoriasis and with obesity.

Key words

25-hydroxyvitamin D, Psoriasis, Body mass index.

Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease, associated with metabolic and cardiovascular disease [1]. Psoriasis is considered to be a T-cell mediated inflammatory skin disease, which is characterized by hyper proliferation and poor differentiation of epidermal keratinocytes. Psoriasis is estimated to affect about 2–4% of the population in Western countries [2]. From the available studies, the prevalence of psoriasis in India ranges from 0.44 to 2.8% [3]. A number of risk factors have been recognized in the etiology and pathogenesis of psoriasis, including family history and environmental risk factors, such as diet, obesity, smoking, stress, and alcohol consumption [4]. Moreover, dietary factors can also affect both drug pharmacokinetics and pharmacodynamics. A number of single food components have been suggested to play a role in psoriasis. The ability of dietary antioxidants, such as omega-3 polyunsaturated fatty acids from fish oil, some vitamins (A, E and C), and oligoelements (iron, copper, manganese, zinc and selenium), which decrease oxidative stress and the production of reactive oxygen species, might be of particular relevance mainly in a chronic systemic inflammatory diseases, like psoriasis [5]. In addition, due to its role in proliferation and maturation of keratinocytes, vitamin D has become an important therapeutic option in the treatment of psoriasis [5].

Vitamin D (25-hydroxyvitamin D) is a hormone whose synthesis is stimulated by cutaneous exposure to ultraviolet B radiation. It acts on calcium homeostasis, on bone metabolism and has immune regulating functions that have been recently recognized. Some studies have demonstrated a relationship between vitamin D deficiency and psoriasis [6, 7]. The immune-regulatory role of vitamin D affects both the innate and adaptive immune system contributing to the immune-tolerance of self-structures.

1,25(OH)₂D₃ is one of the most important gene regulators; as a ligand binds to vitamin D receptors (VDR), enters the nucleus and by binding to different genes regulates mRNA synthesis. The major function of 1,25(OH)₂D₃ vitamin D is that it increases the absorption of calcium and phosphate from the intestinal tract, inhibits the secretion of parathormone (PTH) and the proliferation of the parathyroid glands, therefore positively regulates bone formation [8-10]. Active vitamin D has a regulatory function in the calcium homeostasis, endocrine system, proliferation of skin keratinocytes and importantly plays a significant role in the regulation of the immune system [11].

Defining a level of serum 25(OH)D as low or insufficient depends on the level that is defined as normal. Health authorities used different cut-offs for their definitions of sufficient and optimal status. The Institute of Medicine Committee found 20 ng mL⁻¹ to be the level that is needed for good bone health for all individuals [12]. Substantial evidence suggests that vitamin D plays a pivotal role in modulating dendritic cell function and regulating keratinocytes and T-cell proliferation [13, 14]. Epidemiological data have also confirmed that vitamin D deficiency may be a risk for development of autoimmune diseases including rheumatoid arthritis (RA), multiple sclerosis, systemic lupus erythematosus and Crohn disease [15-18].

Previous studies of the relationship of diet and nutrition with psoriasis have focused on either individual nutrients (e.g. fish oil, omega 3, vitamin B12, vitamin D, vitamin A, selenium, inositol and zinc and antioxidants) or individual food groups (e.g. fruit, vegetables, and fish) [7, 19].

However, while many studies have evaluated the role of vitamin D in psoriatic disease, there are less/no studies have been investigated at coastal

Andhra region Vitamin D levels in psoriatic patients. Hence current study undertaken to analyze Vitamin D levels in psoriasis at this region in comparison to age sex matched control subjects.

Material and methods

Sample size: Thirty cases and thirty control.

Setting: department of DVL, Narayana Medical College and Hospital, Nellore, Andhra Pradesh.

Cases: Thirty outpatients; 20 males and 10 females, diagnosed clinically with psoriasis were enrolled in this study.

Control: Thirty; 20 males and 10 females, age and sex matched controls were taken from patients coming for routine health checkup from department of DVL in our hospital.

Inclusion criteria

Clinically diagnosed cases of psoriasis. Age >18 years.

Exclusion criteria

Pregnancy or lactation, Topical or UVB therapy within previous 2 weeks, Systemic corticosteroids, PUVA, or laser phototherapy within previous 4 weeks; Other systemic therapies or biologicals within previous 12 weeks. Patients on vitamin D supplement/Receiving steroid preparations or those having any other autoimmune disease were excluded from both cases and control groups. Age <18 years.

Investigation

After an informed consent, blood samples were taken from all the subjects for estimation of levels of vitamin D. Electrochemiluminescence method used to analyze 25-hydroxy (OH) vitamin D. Mean vitamin D levels were calculated for both groups.

Statistical analysis

Data recorded on a pre-designed proforma were entered on an excel spreadsheet and entries double checked for any errors. The Pearson test was used to explore the linear correlation

between PASI and 25(OH)D serum levels. Independence of the association of vitamin D deficiency and presence of psoriasis was assessed by multivariate regression analysis. In the fully adjusted regression model, age, sex, smoking habit, BMI, psoriasis, psoriasis duration and PASI score were also included as independent covariates. A P-value < 0.05 was considered statistically significant.

Results

Anthropometric and demographic characteristics

Thirty subjects were participated in this study. In cases, the mean BMI was $24.56 \pm 3.8 \text{ kg/m}^2$ and the mean weight and height were $63.4 \pm 10.6 \text{ kg}$ and $159.0 \pm 8.2 \text{ cm}$, respectively whereas, in control, the mean BMI was $25.47 \pm 3.4 \text{ kg/m}^2$ and the mean weight and height were $63.4 \pm 10.6 \text{ kg}$ and $159.0 \pm 8.2 \text{ cm}$, respectively.

The mean age in the psoriasis group was 47.8 ± 12.8 years, while it was 49.8 ± 10.5 years in the control group. There were 3 subjects in cases and 2 subjects in control belongs to ≤ 20 years age group. 8 subjects in cases and 7 subjects in control belonged to 21-40 years age group. There were 10 subjects in cases and 11 subjects in control belonged to 41-60 years age group. There were 9 subjects in cases and 10 subjects in control belonged to 61-80 years age group.

There were 1 male and 2 females belongs to ≤ 20 years age group. There were 3 male and 5 female belongs to 21-40 years age group. There were 7 male and 3 female belonged to 41-60 years age group. There were 9 male and 0 female belonged to 61-80 years age group. There was no significance difference observed among the age groups.

There were 8 subjects in cases and 10 subjects in control had smoking habit whereas, 10 subjects in cases and 5 subjects in control were of alcoholics. There was no significant difference observed among the smoking/ alcoholics.

Vitamin D levels

The mean vitamin D level in patients was 18.24±4.55 ng/ml (Minimum 4.2 ng/ml and maximum 30.53ng/ml) while in controls it was 24.23±10.64ng/ml (minimum 7.9 ng/ml and maximum 34.3 ng/ml). There was statistical

difference was observed between case and control subjects with P value <0.0001. Vitamin D deficiency was observed in 76% psoriasis patients as compared 27% in controls. (P value <0.001). Vitamin D deficiency was seen in 13 non-obese and 10 obese subjects (**Table – 1**).

Table - 1: Vitamin D levels in cases and controls.

Vitamin D level	Psoriasis	Control	P-value
Mean±SD	18.24±4.55	22.13±10.64	0.001
Minimum	4.2	6.4	-
Maximum	30.53	34.3	-

1 male and 0 female recorded in Palmoplantar psoriasis. 1 male and 1 female recorded in Psoriatic erythroderma. 17 males and 9 females recorded in psoriasis vulgaris. 1 male and 0 female recorded in scalp psoriasis. There was no significant difference observed between types of psoriasis.

Psoriasis Area and Severity Index(PASI): There were 16 cases showed PASI ≤10; 12 cases showed PASI 11-20; 0 case showed PASI 21-30; 0 case showed PASI 31-40; 1 case showed PASI 41-50; 0 case showed PASI 51-60 and 1 case showed PASI >60.

Fitz patricks skin phototype (FPSP): There were 8 subjects in cases belongs to IV FPSP. There were 19 subjects in cases belongs to V FPSP. There were 3 subjects in cases VI FPSP. There was no significant difference observed in these types.

Daily direct sun exposure (DDSE): There were 4 cases with 30 DDSE/Min; 3 cases with 40 DDSE/Min; 12 cases with 60 DDSE/Min; 5 cases with 120 DDSE/Min; 1 case with 240 DDSE/Min; 4 cases with 480 DDSE/Min and 1 case with 600 DDSE/min were recorded (**Table – 2**).

Discussion

The major finding of this study is that vitamin D deficiency is very frequent in patients with

psoriasis vulgaris. P. Gisondi, et al., found this finding was more common in winter, but it was found also in summer in approximately 50% of patients. The present study was conducted in summer months and this coincides with above study. The association between vitamin D insufficiency and psoriasis was confirmed independently of age, sex, BMI, and PASI score. Vitamin levels are more in those who have more BMI and this finding also coincides with Orgaz-Molina et al.study [20, 21]. Few studies explored low levels of 25-OHD associated with Vitiligo. In the present study, two patients of psoriasis also had Vitiligo, supports above study and the study conducted by Claudia Diniz LM, et al., which explored Vitamin D deficiency related to autoimmunity [22].

The relation between 25(OH)D and psoriasis has been studied since the 1930s. In 1985, Morimoto et al. made a chance discovery; vitamin D3 administration improved psoriasis in isolated cases [23]. It has been clearly established that vitamin D deficiency is a risk factor for osteoporosis and increases the risk of falling in the elderly [24].

The finding of vitamin D deficiency in patients with psoriasis could be relevant for several reasons. Deficient 25-OHD levels in patients with psoriasis may be associated with alterations in isoenzymes that affect the synthesis of vitamin D. Some studies have shown differences in VDR

polymorphisms between patients with psoriasis and the general population [25]. However, few data are available on the isoenzyme polymorphisms that influence serum 25-OHD levels, such as 7-dehydrocholesterol reductase (responsible for the availability of 7-dehydrocholesterol in the skin), liver 25-hydroxylase, CYP2R1 (involved in the conversion of vitamin D into 25-OHD), and CYP24A1 (a key degradation enzyme). In addition, polymorphisms in GC gene, which

encodes vitamin D-binding protein, have a major effect on serum 25-OHD concentration [26]. Deficient 25-OHD levels in psoriatic patients may also be secondary to an inflammatory environment, and CRP was negatively correlated with 25-OHD in the current study. A recent study showed low 25-OHD levels to be associated with endothelial dysfunction and inflammatory activation markers (CRP and asymmetric dimethylarginine concentrations) [27].

Table – 2: Comparison of variables studied between the psoriasis group and the control group.

Variable		Psoriasis	Controls	Odds ratio	p
		(n=30)	(n=30)		
Sex ¹	Females	20	20	-	-
	Males	10	10	2.14 (0.49 to 5.17)	0.85 ²
Smoking habit (%)		26.7	25		0.34
BMI (kg/m ²), mean ± SD		24.56 ± 3.8	25.47 ± 3.4	reference	0.25
Alcohol consumption (%)		33.3	26		0.26
Type 2 Diabetes Mellitus		4	2	-	-
Other auto immune condition		2 (vitiligo)	-	-	-
Current age ³		47.8± 12.8	49.8± 10.5	-	0.952 ⁴
Daily direct sun exposure (min.) ⁵		55.0±10.0	35.0±100.0	-	0.256 ⁶
Deficiency VD ^{1,7}		22	9		0.001 [*]
Insufficiency VD ^{1,7}		4	10		0.865 ²
Sufficiency VD ^{1,7}		4	11		0.789 ²

¹Represented by absolute numbers

²Fisher's Exact test

³Means and standard deviations

⁴Unpaired Student's t-test

⁵Medians and inter quartile deviation

⁶Nonparametric Mann-Whitney test

⁷VD: Vitamin D; Strata defined according to reference values of the laboratory performing serum dosage of 25-hydroxyvitamin D: deficiency (<20 ng/ml), insufficiency (≥20 and <30 ng/ml) and sufficiency (≥30 ng/ml).

Several conditions may contribute to low serum levels of vitamin D in the general population, including poor dietary intake of vitamin D; sun avoidance and/or negligible sun exposure, possibly related also to impaired quality of life; malabsorption due to inflammatory bowel disease, gluten enteropathy, gastric surgery, biliary disease, or intestinal bacteria overgrowth;

use of antiseizure medications (e.g. phenobarbital or phenytoin) and long-term use of glucocorticoids. The reason for the higher prevalence of vitamin D deficiency in patients with psoriasis is not clear. However, we can exclude the possibility that this difference was related to different sun exposure between groups. Vitamin D deficiency has been already reported

in other chronic immune-mediated inflammatory skin diseases including atopic dermatitis, vitiligo and chronic urticaria. A possible role of vitamin D deficiency in the development of these conditions has been also proposed.

Once detected, vitamin D deficiency could be corrected, although no evidence of the possible benefits of vitamin D supplementation in reducing inflammation and/or the risk of other incident autoimmune diseases has yet been proven. Moreover, optimal dosage regimens for vitamin D remain uncertain. In general, for every 100 IU of vitamin D taken in, there is an increase of roughly 1 ng mL^{-1} (3 nmol L^{-1}) in the serum level of 25(OH)D. Most trials assessing the effectiveness of the supplementation of 25(OH)D levels and the risk of fractures and falling have used daily doses of vitamin D between 400 and 1000 IU. Toxicity from vitamin D supplementation is very rare and consists principally of acute hypercalcaemia, which usually results from doses that exceed 10 000 IU per day. The tolerable upper level of daily vitamin D intake recently set by the Institute of Medicine is 4000 IU.

Morimoto, et al. [28] detected less circulating vitamin D₃ in subjects with severe psoriasis, this relationship can be partially explained by the liposolubility of vitamin D and its reduced bioavailability in bodies with a high fat content [29]. Obesity is associated with basic systemic inflammation, characterised by an increase in pro-inflammatory markers such as TNF- α and IL-6 [30]. Adipokines are also dysregulated, which might be the basis of vascular diseases [30], and of insulin resistance and subsequent DM. The quantity of 25(OH)D is very important for general population and psoriasis population, because this group display an altered metabolism [31]. Metabolic syndrome [32, 33] (diabetes, hypertension, dyslipidemia, being overweight and obesity) is related with 25(OH)D. Thus evaluating its optimum levels in blood could prevent less comorbidities from appearing.

Conclusion

In conclusion, vitamin D deficiency may be common in patients with psoriasis, and vitamin D has role in immune regulation. Therefore, patients could be routinely screened for serum vitamin D levels for a more comprehensive management.

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