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ORIGINAL ARTICLE

Serum Concentration of 25-Hydroxy Vitamin D in Patients with Chronic Plaque Psoriasis: A Case Control Study

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ABSTRACT

Objective: To determine 25-hydroxy vitamin D levels in patients of chronic plaque psoriasis and to assess any relationship between vitamin D deficiency and other disease parameters.

Methods: This case-control study included 140 subjects (70 with chronic plaque psoriasis and 70 controls), and conducted in out-patient department of Dermatology Unit of The Indus Hospital, Karachi, Pakistan from 12th September 2018 to 18th November 2019. Body mass index (BMI) calculated and 25-hydroxy vitamin D (25-HVD) levels were checked in all subjects. Psoriasis Area and Severity Index (PASI) was calculated in psoriasis patients.

Results: Serum concentration of 25-HVD in psoriasis patients is lower as compared to controls (17.1 ± 9.1 vs 18.3 ± 10.7) but it is not statistically significant (P=0.66). Similarly, gender and BMI were not statistically different between cases and controls. On comparative analysis, type I plaque psoriasis patients had more lower levels of 25-HVD (P=0.03), especially those who had disease for ≤ 5 years (P=0.01). Stratified analysis revealed males of type I plaque psoriasis had significantly lower levels of 25-HVD as compared to males from type II group (P=0.003).

Conclusion: 25-HVD levels were almost similar in both cases and controls. There was no significant 25-HVD deficiency found in chronic plaque psoriasis patients, neither any relation with age, gender, BMI or PASI. However, 25-HVD levels were much lower in males, type I cases and with shorter duration of disease.

Keywords: Psoriasis, body mass index, case control study

INTRODUCTION

Psoriasis is a chronic, life-long, multisystem, inflammatory and proliferative condition which predominantly involves skin.[1] It has a typical relapsing and remitting course. The estimated world population which is known to be affected with psoriasis is around 3.2%.[2] Psoriasis affects adult women and men equally. In 75% of cases, the disease first manifests before 46 years of age.[3]

Several environmental factors along with paramount genetic influencing components played their all-important crucial role in the development of psoriasis. Among the various notified genes and HLA associations, PSORS-1 gene is the prime determinant for psoriasis which is alone accountable for almost half of the inherited cases.[4]

Psoriasis is an immune-mediated disorder and involves both innate and acquired immune systems. Cutaneous T-lymphocytes, keratinocytes, histiocytes, mastocytes, dendritic cells and vascular endothelial cells play their complex roles in development of inflammation, leading to an imbalance between Th1/Th2 immune responses with a diversion towards Th1 response.[5]

Vitamin D is an oil-soluble vitamin which was discovered in cod liver oil during the first quarter of the 20th century. Later on, vitamin D deficiency responsible for rickets in children and osteomalacia in adults were confirmed and subsequently Adolf Windaus, a German chemist, received the Nobel Prize in 1928 for his breakthrough discovery.[6] Vitamin D, also known as calciferol, can be produced in the body by the help of ultraviolet B (UVB) radiation and also obtain from diet. Two major and natural precursors of vitamin D are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Both are biologically inert and need activation before functioning.[7]

It is reported that psoriasis patients having low levels of vitamin D are more prone to arthritis, joint deformities, increase severity of psoriasis and a higher Psoriasis Area and Severity Index (PASI) score.[8] During last two decades all major CVD risk factors have been associated with vitamin D deficiency (VDD) like diabetes, hypertension and hyperlipidemia.[9-12] Furthermore, psoriatic patients with VDD are more prone to develop CVD complications, MetS and other comorbidities with

subsequent increased mortality and reduced life span.[13] The purpose to conduct this study was to determine 25-hydroxy vitamin D levels in patients of chronic plaque psoriasis; and to assess any relationship between vitamin D deficiency and other disease parameters. Early identification and prompt treatment of VDD might help in reducing or controlling CVD comorbidities in psoriatic subjects.

METHODS

This case-control study was conducted in out-patient department of Dermatology Unit of The Indus Hospital, Karachi, Pakistan from 12th September 2018 to 18th November 2019. All patients aged ≥ 18 years of either gender were consecutively enrolled. Whereas patients with other types of psoriasis (like pustular, erythrodermic, guttate), with concomitant inflammatory bowel diseases (i.e. Crohn's disease and ulcerative colitis) and malabsorption, with chronic liver and chronic kidney diseases, taking any medication which is known to affect serum vitamin D levels (like corticosteroids, bisphosphonates, multivitamin supplements, fish oil), pregnant and lactating mothers, infections (like T.B, active hepatitis) and debilitating illnesses (like HIV & AIDS and cancers), and patients and controls who were on vitamin D supplements were excluded.

The sample size was calculated using open epi web-based sample size calculator with the following assumptions: confidence interval: 95%, power: 80%, Mean ± SD of 25-HVD level in psoriasis patients (cases): 18.24±4.55, Mean ± SD of 25-HVD level in non-psoriasis patients (controls): 22.13±10.64 and required sample size was estimated to be 70 per group.

Cases was defined as clinically diagnosed patients who were having plaque psoriasis for more than 6 months. These patients were either never treated with oral and/or topical vitamin D analogues or stopped their treatment at least 3 months before the investigation. While controls were defined as patients without psoriasis coming to dermatology OPD for other skin diseases like acne, melasma, and fungal infections.

A total of 70 cases and 70 controls meeting the selection criteria for this study were selected after obtaining informed consent. Approval from the institutional review board (IRB) was taken prior to conduct the study. Study IRB# IRD_IRB_2018_08_001.

After enrolment; age, gender, weight, height and body mass index (BMI) in kg/m^2 were noted in all subjects. In psoriasis cases; duration of disease, type of plaque psoriasis and PASI were calculated. 25-hydroxy vitamin D levels were performed in all subjects.

Chronic was defined as the disease with a minimum of 6 months. A plaque is a circumscribed, superficial, elevated area of more than 1.0 cm in diameter. Its surface is usually flat. Plaque psoriasis consists of erythematous, scaly, sharply demarcated, indurated plaques present particularly over the extensor surfaces and scalp.

Obesity was defined by WHO Western Pacific Regional Office for Asians was used.[14] Patients having BMI of < 18.5 kg/m^2 were labeled as underweight, 18.5 – 22.9 kg/m^2 as healthy, 23.0 – 24.9 kg/m^2 as overweight, and obesity was labeled when BMI ≥ 25.0 kg/m^2.

Henseler and Christophers' division[3] was used to define type of plaque psoriasis i.e. those who developed plaque psoriasis before 40 years were labelled as type 1 while those who developed plaque psoriasis at or after 40 years were labelled as type 2.

Serum levels of 25-hydroxy vitamin D (25-HVD) were categorized as: 25-hydroxy vitamin D level ≥ 30 ng/mL as sufficient, < 30 but ≥ 20 ng/mL as insufficient, while < 20 ng/mL as deficient.[15]

Categorization of severity of psoriasis on the basis of PASI was done as: PASI score of less than 7 was labeled as mild psoriasis, PASI score from 7 to 12 was labeled as moderate psoriasis, and PASI score of more than 12 was labeled as severe psoriasis.[16]

Data were entered and analyzed by using version 26.0 of statistical package of social sciences (SPSS) software. Median (IQR) and Mean ± SD were computed for quantitative variables while frequency and percentages were computed for categorical variables. Independent sample T-test, Mann-Whitney U test, Chi Square and Fisher's exact tests were applied as appropriate to assess significant difference in 25-HVD level between both the groups. p-value ≤0.05 was considered as statistically significant.

RESULTS

Out of 70 psoriatic patients; male to female ratio of 1:1. Mean age of cases was 41.3 ± 13.2 years. 2 (2.8%), 19 (27.1%), 14 (20%) and 35 (50%) patients were underweight, normal (healthy), overweight and obese respectively. Mean 25-hydroxy vitamin D level of cases was 17.1 ± 9.1 ng/mL. Median (IQR) 25-HVD level of cases was 15.1 (10.1-23.2) ng/mL. On categorization; 25-HVD was deficient in 47 (67.1%), insufficient in 19 (27.1%) and sufficient in 4 (5.7%) psoriatic patients (Table 1).

Out of 70 selected controls; 40 (57%) were male and 30 (43%) were female. Mean age of controls was 29.4 ± 10.3 years. 4 (5.7%), 22 (31.4%), 24 (34.2%) and 20 (28.5%)

patients were underweight, normal (healthy), overweight and obese respectively. Mean 25-hydroxy vitamin D level of controls was 18.3 ± 10.7 ng/mL. Median (IQR) 25-HVD level of controls was 15.1 (11.7-21.9) ng/mL. On categorization; 25-HVD was deficient in 50 (71.4%), insufficient in 8 (11.4%) and sufficient in 12 (17.1%) controls (Table 1).

On comparative analysis; more psoriatic patients were found to have obesity as compared to controls (P-value 0.05). The median value of 25-HVD level was 15.1 ng/mL in both cases and controls (P-value 0.66). No statistically significant association was found with respect to gender, BMI and 25-HVD levels between cases and controls upon analysis (Table 1).

Median (IQR) value of 25-hydroxy vitamin D level of type I plaque psoriasis group was notably lower than type II plaque psoriasis group (13.2 ng/mL vs 18.1 ng/mL). Statistically significant difference was detected between the 25-HVD levels (P-value 0.03), age (P-value <0.001), and duration of psoriasis (P-value 0.01) of the two study groups, while no association was detected between the gender, BMI and PASI score of the two study groups (Table 3).

Stratified analysis was performed to assess the relationship between the outcome i.e. 25-hydroxy

Table 1: Patient demographics among study groups

Variable	Cases (Psoriasis +ve)	Controls (Psoriasis -ve)	P-value
Age (years)			
Mean ± SD	41.3 ± 13.2	29.4 ± 10.3	<0.001
Gender; n (%)			
Male	35 (50%)	40 (57%)	0.13
Female	35 (50%)	30 (43%)	
Body Mass Index (BMI); n (%)			
Underweight	02 (2.8%)	04 (5.7%)	0.05
Normal	19 (27.1%)	22 (31.4%)	
Overweight	14 (20%)	24 (34.2%)	
Obese	35 (50%)	20 (28.5%)	
25-hydroxy vitamin D categories; n (%)			
Deficient	47 (67.1%)	50 (71.4%)	0.01[$]
Insufficient	19 (27.1%)	08 (11.4%)	
Sufficient	04 (5.7%)	12 (17.1%)	
25-hydroxy vitamin D (ng/mL)			
Median (IQR)	15.1 (10.1 - 23.2)	15.1 (11.7 - 21.9)	0.66

T-test, Mann-Whitney U test,[$] Chi-Square, Fisher Exact, PASI: Psoriasis Area and Severity Index

Table 2: Disease parameters in psoriatic patients

Disease Parameter	Values
PASI Score	
Median (IQR)	4.45
Min-Max	0.8-43.8
Division of PASI Score	
Mild	46 (32.9%)
Moderate	09 (6.4%)
Severe	15 (10.7%)
Duration of Psoriasis	
≤ 5 Years	40 (57.1%)
> 5 Years	30 (42.9%)
Types of Plaque Psoriasis	
Type I	42 (60%)
Type II	28 (40%)

vitamin D levels and the exposure variable i.e. type of plaque psoriasis after controlling for confounders. Statistically significant associations were detected between the 25-HVD levels and the type of plaque psoriasis after controlling for confounders i.e. gender and duration of psoriasis. When controlled for gender we found that males having type I plaque psoriasis had lesser median (IQR) 25-HVD levels as compared to the males of type II plaque psoriasis group (P-value 0.003). Similarly, the patients who had a ≤ 5 years duration of psoriasis in type I plaque psoriasis group had a lower median (IQR) 25-HVD level as compared to those who were in the type II plaque psoriasis group (P-value 0.01). No statistical association was detected with other confounders i.e. age, BMI and PASI score (Table 4).

DISCUSSION

The traditional causative element of rickets, stunted growth, osteoporosis, fractures and osteomalacia, the "vitamin D deficiency", has already taken the shape of a pandemic.[8] VDD is now known to affect all ages, genders, races, religions, ethnicities, social classes and geographical zones. Besides above-mentioned ailments, VDD has also been coupled with several systemic, autoimmune and metabolic diseases, supported byinnumerable accumulating and growing literature evidences.[8,16,17]Among the several clinical types, plaque psoriasis is the most frequently encountered one. All types have many localized and generalized morphological variants which are known to affect all races across the globe. The systemic inflammatory condition produces erythematous, scaly plaques of psoriasis over skin and scalp, while on the other side it is also responsible for development of PsA, CVD and metabolic syndrome.[1]

The mean age of psoriatic cases in this study was 41.3 ± 13.2 years. Similar ages of psoriatic patients were also reported by Maleki et al. from Iran (42.8 ± 13.68 years), Srirama from India (47.8 ± 12.8 years), Hassab-El-Naby et al. from Egypt (31.3 ± 7 years), and Zuchi et al. from Brazil (46.4 ± 14.9 years) and in their respective case-control studies.[18-21]

In this study; no association of vitamin D deficiency was found in relation to age, gender, BMI and PASI score in psoriatic subjects. Studies carried out by Srirama,[19]Gisondi et al,[17]Orgaz-Molina et al,[5]Hassab-El-Naby et al,[20]Zuchi et al,[21] and Ricceri et al,[22] which also evaluated these variables, but did not discover any notable correlation between vitamin D levels and age, gender, BMI and PASI scores. However, Pavlov et al. reported positive correlation with high PASI score and

Table 3: Comparative analysis between type I and type II plaque psoriasis patients

Variable	Plaque Psoriasis Type I Group	Plaque Psoriasis Type II Group	P-value
Vitamin D (ng/mL) Median (IQR)	13.2 (8.6 - 22.3)	18.1 (13.3 - 24.6)	0.03*
Age (years) (Mean± SD)	32.8 ± 8.4	53.9 ± 7.6	<0.001T*
Gender; n (%)			
Male	18 (42.9%)	17 (60.7%)	0.14S
Female	24 (57.1%)	11 (39.3%)	
Body Mass Index; n (%)			
≤ Normal	14 (33.3%)	07 (25%)	0.80T
Overweight	08 (19.1%)	06 (21.4%)	
Obese	20 (47.6%)	15 (53.6%)	
Duration of Psoriasis; n (%)			
≤ 5 Years	17 (40.5%)	23 (82.1%)	0.01S*
> 5 Years	25 (59.5%)	05 (17.9%)	
PASI Score			
Mild	29 (69.0%)	17 (60.7%)	0.76S
Moderate	05 (11.9%)	04 (14.3%)	
Severe	08 (19.1%)	07 (25%)	

Independent T-test, Mann-Whitney U test, SChi-Square, ł Fisher Exact, * p-value <0.05

Table 4: Difference in vitamin D levels between characteristics of patients with psoriasis

Variables	Study Groups		P-value
	Psoriasis Type I Group	Psoriasis Type II Group	
	Median (IQR)	Median (IQR)	
Gender			
Male	13.2 (9.6 – 16.2)	18.2 (15.2 – 24.6)	0.003Ŧ*
Female	13.4 (7.9 – 25.3)	14.4 (8.9 – 23.1)	0.66Ŧ
Age			
≤ 40	12.9 (8.4 – 18.6)	17.8 (16 – 19.8)	0.31Ŧ
> 40	24.3 (11 – 27.7)	18.1 (13.3 – 24.6)	0.56Ŧ
Body Mass Index (BMI)			
≤ Normal	13 (10.1 – 15)	15.5 (13.3 – 22.4)	0.1Ŧ
Overweight	12.7 (10.1 – 21.9)	21.6 (18.2 – 24.6)	0.15Ŧ
Obese	15.8 (6.7 – 23.6)	18 (9.6 – 24.8)	0.2Ŧ
Duration of Psoriasis			
≤ 5 Years	11.6 (8.2 – 17.4)	18.2 (13.4 – 24.6)	0.01Ŧ*
>5 Years	14.2 (10.1 – 24.3)	14.4 (13 – 24.8)	0.71Ŧ
PASI			
Mild	13.9 (7.7 – 24.2)	16 (13.4 – 24.8)	0.16Ŧ
Moderate	13.3 (13.1 – 15)	18.1 (13.4 – 27.5)	0.14Ŧ
Severe	11.3 (9.8 – 18.5)	19.78 (13.3 – 24.6)	0.22Ŧ

Ŧ Mann-Whitney U Test, * p-value <0.05, PASI: Psoriasis Area and Severity Index

lower 25-HVD levels but not with other variables.[23]

This study showed no difference ofstatistical significance between 25-HVD levels of cases and controls. Maleki et al. compared serum 25-HVD levels in 50 psoriasis patients & 50 healthy controls, and failed to detect any statistically significant difference in serum 25-HVD levels between the two groups.[18]Authors suggested dressing habits and skin phenotype as possible causative factors for VDD in cases and control.Zuchi and colleagues reported no difference between serum 25-HVD levels of psoriasis cases and healthy controls in their case-control study which involved 20 subjects in each group.[21]Solak et al. delineated in their study of 43 psoriasis patients without arthritis and 41 healthy controls that there was no statistically significant difference between 25-HVD levels of the two studied groups.[24]Romani and colleagues described lower levels of 25-HVDboth among psoriasis cases and controls in their age and gender matched case-control study involving 50 subjects in each group.[25]This deficiency was independent of duration of sun exposure, Fitzpatrick's skin phototype, age of subjects and month of blood testing.

Srirama et al highlighted difference between 25-HVD levels of psoriatic cases and controls in her case-control study, although both groups showed low levels. The study had 30 subjects in each arm, and mean 25-HVD of cases and controls were 18.24±4.55 and 22.13±10.64 respectively.[19] Presumed reasons were poor diet, sun-avoidance and inadequate exposure. Wilson

performed a cross-sectional analysis of 5841 participants and found no difference in serum levels of 25-HVD between subjects with and without psoriasis.[26] Moreover, Morimoto et al. documented no significant differences in the mean basal values of 25-HVD and 1,25-dihydroxyvitamin D between psoriasis cases and controls.[27] Furthermore, Merola et al. notified that there is no preventive role of dietary or supplemental vitamin D intake against development of psoriasis.[28]All above mentioned studies are in accordance with this study.

This study reported that 25-HVD level of type I plaque psoriasis group is lower than type II plaque psoriasis group and it was also statistically associated with age and duration of psoriasis, while it was not correlated with gender, BMI and PASI score. Pavlov et al. in their cross-sectional analysis, described no differences in 25-HVD levels between two types of plaque psoriasis.In addition, no correlation was found with gender, waist circumference and BMI but 25-HVD levels wereinversely correlated with PASI scores.[23]

CONCLUSION

This study concluded that vitamin D level of psoriatic cases is similar to that of controls. Both of them were detected with VDD. Psoriatic cases might have 25-HVD deficiency as a part of community problem and overall altered or affected nutritional status. But whenever vitamin D deficiency is detected in psoriasis, it should be immediately replaced. The group among psoriasis patients which was more affectedwith 25-HVD deficiency were males, type 1 cases and those with shorter duration of disease.

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