Section: Dermatology

Original Research Article

CORRELATION OF PSORIASIS AND SERUM VITAMIN D AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

Background: 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.

Materials and Methods: This is a prospective, observational and case-control study was conducted in the Department of Dermatology, American International Institute of Medical Sciences. Clinically diagnosed 186 patients of chronic plaque psoriasis and 63 healthy controls were studied. A detailed history was inquired and clinical examination was done with evaluation of serum vitamin D levels. Clinically diagnosed chronic plaque psoriasis patients and healthy controls of age > 15 years of any sex were included. All patients were subjected to full history taking, clinical examination, and laboratory investigations. Serum vitamin D levels were measured by using enzyme-linked immunosorbent assay technique.

Results: Among the cases with severe PASI, 26 (97%) had vitamin D deficiency and 1 normal vitamin D level. With moderate disease, 42 (71.9%), 13 (22.1%), and 5 (6%) had deficient, insufficient, and normal levels of vitamin D respectively. Ten (28%), 25 (65.9%), and 4 (8.2%) had a normal, insufficient, and deficient vitamin D in mild disease. A significant negative correlation was found between serum 25(OH) D level and PASI ($r = -0.6289$, $P = 0.01$). A receiver operating characteristic curve was performed and an optimal cutoff PASI value of 4.05 (AUC=0.889, $P<0.001$) was obtained. Above this value, patients had a high risk of vitamin D deficiency with the sensitivity of 84.1% and specificity of 82.4%.

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. Decreased 25 OH vitamin D serum level was found in psoriatic patients. The 25 OH vitamin D serum level may be used as a marker of psoriasis severity and response to treatment.

Keywords: Psoriasis, oral vitamin D, treatment.

INTRODUCTION

Psoriasis is a chronic, recurrent, immune mediated disease of the skin and joints that may affect negatively the physical, emotional, and psychosocial well being of affected patients.[1] Indeed, nowadays psoriasis is considered a systemic pathology, including also other conditions, from psoriatic arthritis to obesity and metabolic disease, which increased cardiovascular risk in psoriatic patients.[2] Psoriasis is a serious condition strongly affecting the way a person sees himself and the way he is seen by others. It has tremendous economic and financial ramifications. Psoriasis is linked with social

stigmatization, pain, discomfort, physical disability, and psychological distress.[3] Psoriasis is considered an autoimmune disorder mediated by T cells which, after priming by bacterial antigens, migrate to the skin where they are activated by self-antigens expressed by the epithelia and the key participation of dendritic cells that appear also increased in the skin [4]. Vitamin D is a fat soluble vitamin that is obtained from food supplements and sun exposure. Vitamin D3 is produced from 7 dehydrocholesterol and irradiation of 7 dehydrocholesterol that produces pre D3, lumisterol, and tachysterol.[5] Ultraviolet (UV) irradiation further converts pre D3 to lumisterol and tachysterol; at 37°C pre D3 is converted to D3.[6]

Keratinocytes are the only cells in the body containing the previous pathway. Vitamin D is biologically inert and must undergo two hydroxylation processes in the body to be activated. Keratinocytes are not only capable of producing D3, but of metabolizing D3 via the vitamin D 25 hydroxylase (CYP27A) to 25 hydroxycholecalciferol in the liver and 25OHD 1α hydroxylase (CYP27B1) to its active metabolite 1,25(OH)2D3 in the kidney.[7]

MATERIAL AND METHODS

This is a prospective, observational and case-control study was conducted in the Department of Dermatology, American International Institute of Medical Sciences.

Clinically diagnosed 186 patients of chronic plaque psoriasis and 63 healthy controls were studied. A detailed history was inquired and clinical examination was done with evaluation of serum vitamin D levels.

Inclusion Criteria: Clinically diagnosed chronic plaque psoriasis patients and healthy controls of age > 15 years of any sex.

Exclusion Criteria: Other types of psoriasis patient and those on treatment, which might influence vitamin D status.

Detailed demographic and clinical data of cases were recorded in a pre-structured proforma. Special emphasis was given to the patient's job (indoor/outdoor) and the menopausal status as both parameters may influence the level of vitamin D.

In group A, the duration of psoriasis, disease severity according to psoriasis area and severity index (PASI), the nail psoriasis severity index (NAPSI), and treatment history were also recorded. PASI scores were graded as mild (PASI <7), moderate (PASI 7–12), and severe (PASI >12).

Patients having any concomitant infection, chronic inflammatory disease, primary or iatrogenic immuno-suppression, or malignancy were excluded. Additionally, patients receiving any medication which could influence the level of vitamin D in the body, namely, systemic steroids, bisphosphonates, systemic corticosteroids, calcium supplements, or vitamin D3 supplements were excluded. We also excluded psoriasis patients from treatment with phototherapy and/or topical vitamin D analogues. In order to avoid any differences in sun exposure and oral vitamin D intake in the diet, all study participants were from the same topographic region. Cases were subjected to routine investigations including haemogram, renal and liver profile, and erythrocyte sedimentation rate (ESR) level.

Statistical Analysis

Microsoft Office Excel and SPSS version 25 were used to examine the data. Categorical variables were expressed as absolute numbers, proportions, and percentages, and continuous variables were expressed as ranges, means, and standard deviations. Unpaired T test was employed to compare quantitative continuous variables.

RESULTS

We studied 160 patients (73 males and 67 females) with chronic plaque psoriasis. The mean age was 45.93 ± 15.282 years and the median age 41.50 years. The duration of disease ranged from 1 month to 38years with a mean duration of 5.69 years. The mean age at onset of disease was 37.05 years. A family history of psoriasis was mentioned by 16 (15.4%). The mean PASI was 1.93 (± 0.706). The majority of cases (61, 50%) had moderate disease while 35 (29.2%) and 25 (20.8%) had mild and severe disease respectively. Among 120 patients with psoriasis, scalp involvement was seen in 59 (49.2%), nail involvement was seen in 42 (35%), and palmoplantar involvement was seen in 18 (15%) cases. Flexural and genital involvement was seen in 5 (4.2%) and 2 (1.7%) of total cases only. Among those with nail involvement, pits were present in 26 (39.4%), subungual hyperkeratosis in 20 (30.3%), and onycholysis in 13 (19.7%). Other nail signs included oil droplet sign in 2 (3.03%), transverse ridging in 3 (4.54%), and leukonychia in 2 (3.03%) cases.

The control group subjects enrolled comprised 60 outpatient (32 males and 28 females) healthy volunteers who were the attendants of patients other than psoriasis. The two groups did not significantly differ in age, sex, Fitzpatrick skin phototype, sun exposure per day, history of smoking and alcohol intake, DBP, FBS, TAG, HDL, calcium (Table 1). But they significantly varied in BMI (OR 2.142, 95% CI 1.025–4.477, P= 0.043), SBP (OR 5.745, 95% CI, P= 0.022) and metabolic syndrome (OR 4.634, 95% CI 1.020–21.058, P=0.047).

Abbreviations: Kg/m^2, kilograms per square meter; mm of Hg, millimeters of Mercury; mg/dl, milligram per decilitres.

The mean serum 25(OH) D concentration in cases was 19.57 ± 6.85 ng/mL and the mean level of serum 25(OH) D level in control group was 23.63 ± 6.40 ng/mL and was statistically significant (p=

0.001) (Table 2). Vitamin D deficiency (<20 ng/dl) was observed in 57.5% of patients with psoriasis versus 30% of control subjects (P<0.001, OR 3.720, 95% CI 1.890–7.322). Regarding vitamin D insufficiency (<30 ng/dl), it was observed among 87.5% of patients with psoriasis and 83.3% of control subjects. Multivariate studies with binary logistic regression showed a strong association between the presence of psoriasis and vitamin D deficiency (<20 ng/dl) even after adjusting for age, sex, BMI, sun exposure, physical exercise and Fitzpatrick skin phototype (OR 2.929, 95% CI 1.376–6.230, P<0.005). [Table 1]

Among the cases with severe PASI, 26 (97%) had vitamin D deficiency and 1 normal vitamin D level. With moderate disease, 42 (71.9%), 13 (22.1%), and 5 (6%) had deficient, insufficient, and normal levels of vitamin D respectively. Ten (28%), 25 (65.9%), and 4 (8.2%) had a normal, insufficient, and deficient vitamin D in mild disease. A significant negative correlation was found between serum 25(OH) D level and PASI (r= −0.6289, P= 0.01). A receiver operating characteristic curve was performed and an optimal cutoff PASI value of 4.05 (AUC=0.889, P<0.001) was obtained. Above this value, patients had a high risk of vitamin D deficiency with the sensitivity of 84.1% and specificity of 82.4%. No significant differences were found in occupation, duration of sun exposure, history of smoking and alcohol intake, age at onset, duration of disease, associated comorbidities, BMI, presence of metabolic syndrome, SBP, DBP, FBS, TAG and serum calcium even after conducting a binary logistic regression model for vitamin D deficiency.

Table 1: Summary of Demographic Characteristics and Biochemical Parameters of Cases and Controls

Characteristics	Cases n (%)	Controls n (%)	P value
Age in Years			
Mean ± SD	45.93 ± 14.282	41.62 ± 14.465	0.566
Gender			
Male	64(52.6)	33 (53.4)	0.920
Female	59(47.7)	29 (46.8)	
Body Mass Index			
Normal/ under (<23 kg/m^2)	44 (35.9)	39 (63.5)	**<0.001**
Preobese (23–27.5 kg/m^2)	43(36)	21 (33.4)	
Obese (≥27.5 kg/m^2)	36 (29.3)	3 (3.4)	
Dietary Habit			
Vegetarian	13 (11)	5 (6.78)	0.330
Mixed	109 (91)	57 (94.3)	
Duration of Sun Exposure			
< 30 minutes	63 (44.2)	32 (53.3)	0.246
≥ 30 minutes	67 (55.8)	28 (46.7)	
Physical Exercise			
Yes	31 (25.8)	20 (33.3)	0.293
No	89 (74.2)	40 (66.7)	
History of Smoking			
Yes	33 (27.5)	10 (16.7)	0.108
No	88 (72.5)	51 (83.3)	
History of Alcohol Intake			
Yes	41(33.4)	20 (31.8)	0.794
No	81 (66.8)	41 (68.3)	
Presence of Comorbidities			
Yes	48 (40)	14 (23.3)	**0.027**
No	72 (60)	46 (76.7)	
Skin Group			
III/IV	81 (67.5)	35 (58.3)	0.226
V/ VI	39 (32.5)	25 (41.7)	
Metabolic Syndrome			
Yes	41 (34.2)	6 (10)	**<0.001**
No	79 (65.8)	54 (90)	
Systolic Blood Pressure			
Normal (<120 mm of Hg)	87 (72.5)	55 (91.7)	**0.003**
Elevated/ High (≥120 mm of Hg)	33 (27.5)	5 (8.3)	
Diastolic Blood Pressure			
Normal (<80 mm of Hg)	86 (71.7)	49 (81.7)	0.144
Elevated/ High (≥80 mm of Hg)	34 (28.3)	11 (18.3)	
Fasting Blood Sugar			
Normal (<100 mg/dl))	84 (70)	55 (91.7)	**0.001**
Pre/Diabetes (≥100 mg/dl)	36 (30)	5 (8.3)	
Triglycerides			
Normal (<150 mg/dl)	76 (63.3)	45 (75)	0.166
High (≥150 mg/dl)	44 (36.7)	15 (25)	
High Density Lipoproteins			
Normal	100 (83.3)	54 (90)	0.230
Low	20 (16.7)	6 (10)	

Serum Calcium			
Low (<8.6 mg/dl)	18 (15)	8 (13.3)	0.939
Normal (8.6–10.2 mg/dl)	95 (79.2)	48 (80)	
High (≥10.2 mg/dl)	7 (5.8)	4 (6.7)	

Note: Bold values signify significant value.

Table 2: Mean Vitamin D Level in Cases and Controls

Characteristics	Cases Mean ± SD	Controls Mean ± SD	*t*-test	p value
25OH Vitamin D (ng/dl)	19.58 ± 6.86	31.63 ± 6.40	0.433	<0.001

Table 3: Multivariate Analysis of Cases and Controls

Category	Adjusted Odds Ratio (95% CI)	P value
History of Smoking	1.245 [0.497–3.110]	0.642
History of Comorbidities	0.026 [0.399–2.180]	0.873
Body Mass Index	2.142 [1.025–4.477]	0.043
Metabolic Syndrome	4.634 [1.020–21.058]	0.047
Systolic Blood Pressure	5.745 [1.228–25.615]	0.022
Diastolic Blood Pressure	0.269 [0.072–0.996]	0.049
Fasting Blood Sugar	2.902 [0.845–9.960]	0.09
Triacylglycerides	0.813 [0.343–1.928]	0.639
Serum 25OH Vitamin D level	2.931[1.377–6.230]	0.006

DISCUSSION

Our study showed that the association between serum vitamin D and psoriasis might be modified by central obesity, indicated by WHR. Inconsistent with the findings in the majority of previous studies,[8] our results showed that there was no significant difference in serum vitamin D level between the psoriasis patients and healthy controls. However, a significant interaction between the serum vitamin D level and obesity was identified. This is the first time that the serum vitamin D level in Chinese psoriasis patients was reported. Our results also showed that, interestingly, serum 25(OH)D deficiency was associated with a higher risk of psoriasis only in the subgroup of abnormal WHR. This inconsistent finding suggested that the impact of decreased vitamin D on psoriasis pathogenesis might be related to central obesity, a well-acknowledged comorbidity of psoriasis.

Unfortunately, no previous study has explored the modification effects of WHR on the association between serum vitamin D and psoriasis. Nevertheless, vitamin D deficiency has been multi-dimensionally confirmed to correlate with obesity (9, 24–27), especially central obesity. The reported relationship between psoriasis and decreased serum Vitamin D may be mediated by the shared mechanism of the coexistence of psoriasis and central obesity.[9-14]

Another explanation for our result lies in the specialty for the studied population. After a long time of poverty, the Chinese population has been increasingly experiencing a non-communicable tsunami, especially for central obesity and diabetes,[15] since the opening-and-reform-up from the 1980s. Within the past four decades, the number of psoriasis patients has been significantly increased,[16] and the epidemic of psoriasis has shifted from a genetic-dominated to a comorbidity-driven epidemic in China. The climbing prevalence of central obesity among Chinese psoriasis patients might help us distinguish the relationship among psoriasis, central obesity, and serum vitamin D. Besides, the average serum vitamin D level in the healthy Chinese population has been reported to be lower than that in the western population.[17,18]

A multi-center research in 2013 showed that the average serum vitamin D level in the general Chinese population was around 25 nmol/L, lower than the reported average according to the western standard.[19] The fact that vitamin D insufficiency in the Chinese population is too common to show any difference between the psoriasis patients without central obesity and the healthy controls might be another explanation for the inconsistent finding.

One limitation of this study is selection bias. The healthy controls were recruited from an ongoing cohort, and the participants who received vitamin D test were mostly the elderly people (generally >40 years). Another significant limitation of our study is that the participants were recruited across a 1-year period, which cannot erase the confounding effect from the seasonal change of serum vitamin D status owing to the difference in exposure to sunlight. However, all participants in our study resided in Hunan province, and the difference due to latitude can be ignored.

CONCLUSION

To date, the successful treatment based on adequate dietary intake of vitamin D or oral vitamin D supplementation in psoriasis represent an unmet clinical need and the evidence of its beneficial effects remains still controversial. Nevertheless, the Nutritionists should consider a general vitamin D supplementation in populations at high risk for vitamin D deficiency, such as psoriatic patients. This information is important either for Dermatologists and Nutritionists to increase the knowledge on the potential usefulness of vitamin D in psoriasis with the aim to reduce not only its clinical severity, but also cardiac risk factors and

psoriasis co-morbidities. Future well-designed dietary intervention trials with vitamin D supplementations on large population samples are needed to define the specific dose of vitamin D supplementations for psoriasis.

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