

Original Research Article

Serum 25-hydroxyvitamin D level in psoriasis patients: a case-control study

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ABSTRACT

Background: Sufficient level of vitamin D in blood is required for proper regulation of cell differentiation and proliferation. Unchecked proliferation of cells leads to various disease states. Vitamin D also has immunomodulatory effects in the body. Psoriasis is a chronic inflammatory and hyperproliferative disease with vitamin D having an impact on it. This case – control study was done to judge the levels of vitamin D in patients of psoriasis compared to age and sex matched controls.

Methods: A case control study was conducted including 50 patients (35 females and 15 males) of chronic plaque psoriasis from dermatology outpatient department of Maharaja Agrasen Medical College (MAMC), Agroha, Haryana, representing patients from north India and 50 healthy controls. Both urban and rural background patients were included.

Results: The mean serum 25-hydroxyvitamin D (25-OHD) level in psoriasis patients was 22.865±11.386 ng/ml, whereas in controls it was 35.116±11.048 ng/ml ($p < 0.001$). Serum level of 25-OHD in psoriatic patients was deficient (<20 ng/ml) in 26 (52%), insufficient (20-30 ng/ml) in 8 (16%) psoriatic patients.

Conclusions: High prevalence of low vitamin D level was found in this study. We infer that vitamin D does play a role in the pathogenesis, precipitation, exacerbation, or treatment resistance of psoriasis.

Keywords: Psoriasis, Vitamin D level, Pathogenesis

INTRODUCTION

Psoriasis is a chronic inflammatory disease associated with many complications, co-morbidities and adverse quality of life.¹ The prevalence is quite high, about 2-3% in general population.² Now-a-days, psoriasis is considered a systemic pathology which includes arthritis, obesity, metabolic disease with increased cardiovascular risks.³⁻⁵ Biological mechanism of psoriasis is still not well-understood but seems to be multifactorial.⁶ Studies

on immunopathogenesis and genetics in psoriasis hypothesize a systemic inflammatory process rather than a single organ disease.^{3,7}

A large number of research studies have demonstrated higher risk of cardiovascular diseases in psoriasis.⁸⁻¹² So it is imperative to search for all the factors responsible for adverse quality of life, cardiovascular events, aggravation and treatment resistance of disease in psoriasis. Vitamin D level in serum is one such factor which has been found to be relevant in psoriasis.

The role of vitamin D as a regulator of skin physiology is very complex and the process of epidermal differentiation from basal layer to stratum corneum and ultimate shedding of stratum corneum is a sequential, tightly regulated process.¹³ 7-dehydrocholesterol, a precursor of vitamin D, is located in membranes of basal and spinous layers.¹⁴ By UVB's photochemical reaction, 7-dehydrocholesterol is converted to pre-vitamin D₃ known as cholecalciferol, which is then converted first to 25-hydroxy vitamin D (25-OHD) and then to 1,25-hydroxyvitamin D (calcitriol) which is the active form of vitamin D. This active form and its receptor (Vitamin D Receptor - VDR) regulate the differentiation and proliferation of keratinocytes. This active form exerts antiproliferative effects on keratinocytes.¹⁵ In-vitro studies have shown a clear inhibitory effect of high pharmacological doses of vitamin D on keratinocytes.^{16,17} Calcitriol does regulate the cell proliferation in epidermis, increases keratin synthesis, regulates barrier integrity and permeability of stratum corneum.^{13,16,17} These effects are due to its capacity to regulate intercellular calcium levels.^{18,19} A decrease in calcitriol level, or loss of function of VDR disrupts the differentiation of epidermis resulting in hyperproliferation of basal layer.^{13,20,21}

Therapeutic effects of topical vitamin-D analogues have been used in psoriasis for quite some time now. There has to be a combination of effects, i.e., reduced cellular proliferation, increased cellular differentiation and immunomodulatory effect of vitamin D in psoriasis.

Immunomodulatory effect of vitamin D is through production of cathelicidins and defensins in keratinocytes, by inhibition of cell proliferation, and through cytokines.²²

The keratinocyte growth and differentiation is through vitamin D receptors (VDR). There has been many studies, that show the deficiency of vitamin D in psoriasis leading us to think that it may play a key role in the pathogenesis of psoriasis. It may cause precipitation, exacerbation and treatment resistance also.

In this study, we planned to evaluate the serum levels of 25-OHD in patients of psoriasis in North India and to compare it with controls.

METHODS

This case-control study was carried out in the dermatology outpatient department of Maharaja Agrasen Medical College (MAMC), Agroha in the year 2018 (September to November). The study was approved by ethical committee of the institution.

50 patients with clinical diagnosis of chronic plaque psoriasis, attending outpatient department of dermatology, and 50 age and gender matched controls were enrolled in our study. Severity of psoriasis was

measured by internationally accepted Psoriasis Area and Severity Index (PASI) score. Details like age, sex, duration, daily sunlight exposure, body mass index (BMI), PASI score, family history, drug history and personal history (smoking, alcohol use) were recorded in a standard proforma. An informed signed consent was taken from all participants of the study. The patients were divided into urban and rural categories.

Criteria for selection was age (18-70 years) and duration of chronic plaque psoriasis (more than 6 months), who had not received any specific anti psoriatic treatment (like phototherapy, topical vitamin D) in the last 2 months. Patients and controls who were pregnant, smokers, alcoholics, having other autoimmune diseases, malignancy, bowel disease, on oral vitamin supplements were excluded from the study.

A 5 ml venous blood sample was obtained and serum 25-OHD level was measured using chemiluminescent immunoassay (CLIA). Values <20 ng/ml were considered deficiency, from 20 to <30 ng/ml insufficiency and ≥30 ng/ml sufficiency.

Data were analyzed by using SPSS (Statistical package for Social Science) version 17.0 software. 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. Pearson's correlation coefficient (r) was used for correlation of continuous variables. In all assessments for statistical significances, level of significance was confidence interval at 95% level of confidence (p<0.05).

RESULTS

The mean age of psoriatic patients was 39.22±10.78 years, and the mean age of control group was 39.28±10.73 years, there was no significant difference between the two groups. Both groups were similar in terms of sex, urban/rural background, BMI and daily sunlight exposure (Table 1).

The mean duration of disease was 4.52±3.24 years. The mean PASI score was 16.09±6.85. The mean body surface area (BSA) in% was 33.91±15.16. The mean 25-OHD level in patients was 22.865±11.386 ng/ml (minimum being 6.66 ng/ml and maximum being 40.70 ng/ml), whereas in controls it was 35.116±11.048 ng/ml (minimum being 8.10 ng/ml and maximum being 51.02 ng/ml). There was a statistically significant difference between cases and controls (p<0.001). Serum level of 25-OHD in psoriatic patients was deficient (<20 ng/ml) in 26 (52%), whereas in controls it was deficient in only 8 (16%). Serum level of 25-OHD was found to be insufficient (20-30 ng/ml) in 8 (16%) psoriatic patients and in 5 (10%) of controls (Table 2).

Table 1: Comparison of demographic variables between psoriasis patients and controls.

| Variables | Psoriasis patients (n=50) | Controls (n=50) | P value |
|---|---------------------------|-----------------|---------|
| Age (mean±SD) (years) | 39.22±10.78 | 39.28±10.73 | 0.978 |
| Sex | | | |
| Male (n) (%) | 35 (70%) | 35 (70%) | 1.000 |
| Female (n) (%) | 15 (30%) | 15 (30%) | |
| Background | | | |
| Urban (n) (%) | 27 (54%) | 27 (54%) | 1.000 |
| Rural (n) (%) | 23 (46%) | 23 (46%) | |
| BMI (mean±SD) (kg/m ²) | 24.34±1.95 | 23.98±1.79 | 0.336 |
| Daily sunlight exposure (mean±SD) (minutes) | 227.80±151.34 | 234.20±149.99 | 0.832 |

Table 2: Comparison of serum 25-OHD levels between psoriasis patients and controls.

| 25-OHD Level | Psoriasis patients (n=50) | Controls (n=50) | P value |
|------------------------------------|---------------------------|-----------------|----------|
| Mean±SD (ng/ml) | 22.865±11.386 | 35.116±11.048 | <0.001** |
| Minimum (ng/ml) | 6.66 | 8.10 | |
| Maximum (ng/ml) | 40.70 | 51.02 | |
| Deficient (n) (%) (<20 ng/ml) | 26 (52%) | 8 (16%) | <0.001** |
| Insufficient (n) (%) (20-30 ng/ml) | 8 (16%) | 5 (10%) | |
| Sufficient (n) (%) (30-100 ng/ml) | 16 (32%) | 37 (74%) | |

**p<0.001; Highly significant

Serum 25-OHD level did not correlate with the duration of disease ($r=0.077$, $p=0.597$), but it correlated with higher BSA ($r=-0.384$, $p=0.006$) and PASI score ($r=-0.438$, $p=0.001$).

DISCUSSION

Main finding of our study was vitamin D deficiency or insufficiency in psoriasis as compared to controls. Lower vitamin D level (deficient and insufficient) was very frequent in psoriasis patients as much as in 68%, whereas in controls it was only 26%. Low vitamin D levels have been associated with osteoporosis, easy fall and fractures in elderly, in parathyroid diseases, chronic kidney diseases, vitiligo and rosacea. Several studies of the efficacy of narrow-band ultraviolet-B (NB-UVB) rays have shown positive effect of increased vitamin D level in these patients which has improved our opinion regarding role of systemic vitamin D therapy in psoriasis.²³⁻²⁸

Since 1930, relationship of low vitamin D levels in psoriasis has been studied. In 1985, Morimoto found out that a few cases of psoriasis improved with vitamin D.²⁹ In 2012, Orgaz-Molina et al found lower vitamin D levels in psoriasis patients as compared to control group.³⁰ In another study, Gisondi reported that psoriatic patients had 2.5 times higher risk of vitamin D deficiency than controls.³¹ Ricceri and others found a prevalence of vitamin D insufficiency in 97% and deficiency in 68% of patients as compared to 53% and 10% in controls, respectively.³²

Srirama reported vitamin D deficiency in 76% of psoriasis patients as compared to 26% in controls.³³ Her study showed deficiency independent of age, gender, BMI and PASI score. Pavlov from Bulgaria reported vitamin D deficiency in a large percentage of psoriatic patients (48.9% insufficient and 47.82% deficient).³⁴

Ricceri et al reported prevalence of 25.6% of vitamin D deficiency (<20 ng/ml) in chronic plaque psoriasis.³² In our study, vitamin D insufficiency (level between 20-30 ng/ml) was 16% and deficiency (less than 20 ng/ml) was 52%, whereas in controls, the corresponding values were 10% and 16% respectively. So, our study was in concordance with these studies.

Systemic vitamin D administration has been found to regress the severity of psoriasis as described by Castro et al in adalimumab – induced psoriasis, and Perez et al reported oral vitamin D induced improvement in psoriasis patients.^{35,36} Topical treatment of psoriasis with vitamin D analogues is well established and documented.³⁷

Vitamin D deficiency in psoriasis may be because of changes in isoenzymes needed for vitamin D synthesis. A few studies have reported vitamin D Receptor (VDR) polymorphism difference in psoriasis patients and general population.³⁶ Vitamin D deficiency in psoriasis may also be secondary to inflammatory milieu in the body, as c-reactive protein (CRP) was found to be negatively correlated with vitamin D deficiency.³⁰ Majority of psoriasis patients in the present study were found to have either deficiency or insufficiency of vitamin D, which

could contribute to precipitation, aggravation, treatment resistance and evolution of the disease.

In conclusion, serum vitamin D levels are significantly lower in large number of psoriatic patients as compared to normal healthy subjects. We support the idea of intervention studies with vitamin D in psoriasis and we propose that serum levels of 25-OHD should be tested in psoriasis patients and it should be supplemented in appropriate doses to those patients to prevent exacerbation, precipitation and resistance to treatment.

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