

The Putative Role of Thyroid Hormones and Vitamin D on Severity and Quality of Life in Psoriasis

Abstract

Introduction: Psoriasis is a chronic immune-mediated inflammatory skin disease. The thyroid hormone receptors are expressed in human skin and the hormones exert their effects on epidermal proliferation and differentiation; they have been hypothesized to play a role in the pathogenesis of psoriasis. Vitamin D is involved in the maintenance of cutaneous barrier homeostasis. Several studies identified an association between polymorphisms of Vitamin D receptor and psoriasis susceptibility. **Subjects and Methods:** Thirty clinically diagnosed psoriasis patients in the age group between 20 and 50 years of both genders attending the outpatient department of dermatology were included as cases. Thirty healthy subjects attending routine health checkup were included as controls. Serum 25 hydroxycholecalciferol was estimated in Mini Vidas autoanalyzer by immunofluorescence technique and Thyroid stimulating hormone (TSH), free T3, and free T4 were estimated by chemiluminescence technology in Cobas e411. Dermatology quality of life index (DLQI) and psoriasis area severity index (PASI) questionnaire was used to assess the quality of life and severity of psoriasis respectively. **Results:** TSH level was significantly increased in psoriasis cases when compared to healthy controls but within reference range ($P < 0.05$). There is a significant negative correlation between PASI and 25-hydroxycholecalciferol and significant negative correlation between PASI and DLQI. **Conclusion:** Our study emphasizes the relationship between biochemical markers, severity of psoriasis, and quality of life. A multimodal holistic approach is needed for the treatment of psoriasis. Psychological support for stress management, drug therapy, and biochemical markers assessment for severity of psoriasis are the need of the hour.

Keywords: Dermatology quality of life index, free T3, free T4, psoriasis area severity index, psoriasis, TSH, Vitamin D

Introduction

Psoriasis is a chronic immune-mediated inflammatory skin disease, with a prevalence of about 2%–3% in the general population.^[1] The primary manifestation of psoriasis is on the skin, although inflammatory processes can occur also in other organs such as cardiovascular system, joints, and eyes.^[2] Psoriasis is a prototypical T-cell-mediated inflammatory disease characterized by activation of antigen presenting cells and activation and expansion of Th-1 and Th-17 cells.^[3] A moderate to large negative impact of the disease on the quality of life with an alteration of everyday activities was reported by a National Psoriasis Foundation Survey in about 75% of patients with psoriasis.^[4]

Skin is the site of synthesis and metabolism of several neuropeptides including

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components of the hypothalamic–pituitary–adrenal (HPA) and hypothalamic–pituitary–thyroid axis and also a source of Vitamin D.^[5] Any derangement of these axes may lead to or may be an indicator of various skin diseases. Since thyroid hormone receptors are expressed in human skin, and the hormones exert their effects on epidermal proliferation and differentiation, they have been hypothesized to play a role in the pathogenesis of psoriasis.^[6] Genetic, environmental, immune defect and hormonal factors take part in the pathogenesis of autoimmune diseases. The role of various hormones such as thyroid-stimulating hormone, cortisol, prolactin, and thyroid hormones in the pathogenesis of psoriasis has been studied previously.^[7] The severity of the disease has been correlated with levels of thyroid hormones, since like prolactin, the thyroid hormone receptors are expressed in the skin^[8] and their levels change during

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the active phase of disease and alleviation of the disease by antithyroid therapy.

Vitamin D is involved in the maintenance of cutaneous barrier homeostasis. Several studies identified an association between polymorphisms of Vitamin D receptor (*VDR*) and psoriasis susceptibility.^[9] 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.^[10] In addition, in psoriatic skin, a decreased expression of *VDR* and reduced tight-junction proteins is associated. Tight junctions are fundamental to regulate adhesion and permeability of keratinocytes, and to polarize cutaneous cell differentiation, to regulate extracellular calcium gradient, interacting with nuclear and cytoplasmic proteins and influencing the regulation of specific genes involved in keratinocytes differentiation and proliferation. The 1,25(OH) D has been shown to exert antiproliferative effects on keratinocytes.^[11] Calcitriol (Vitamin D) has been proposed to work in psoriasis by inhibiting keratinocyte proliferation, repressing growth signals, and T-cell signaling. Calcitriol binds to *VDR* with high specificity which accounts for its biological activity in *VDR* expressing tissues such as skin, muscle, pancreas, pituitary gland, brain, kidneys, reproductive organs, and immune cells. Previous studies have shown that calcitriol arrests cytokine-induced maturation of dermal dendritic cells (DCs) and primes DC to induce regulatory T cells. It has been implicated to inhibit the production of proinflammatory cytokines and stimulate expression of the anti-inflammatory cytokines.^[12]

Hence, the present study was planned to verify the association between Vitamin D status, thyroid profile with the severity, and quality of life in psoriasis.

Subjects and Methods

The present case-control study was conducted in a tertiary health care hospital after getting Institute Human Ethical Committee Approval (ICMR-STS project 2017/05/06). Informed consent was obtained from all the study participants. Thirty clinically diagnosed psoriasis patients in the age group between 20 and 50 years of both genders attending the outpatient department of dermatology were included as cases. Thirty healthy subjects attending routine health checkup were included as controls. Patients suffering from diabetes mellitus, renal disorders, alcoholics, smokers, tobacco chewers, and any other chronic illness were excluded.

Study parameters

After all aseptic precautions, 5 ml of venous blood from the median cubital vein was collected from cases and controls in a plain Vacutainer and serum was separated. All the serum samples were stored at -20°C deep freezer until analysis.

Every day, the quality control samples (Preci control) both level 1 and level 2 were analyzed before analyzing study samples and for any outlier corrective and preventive action was taken appropriately. The biochemical parameter such as serum 25-hydroxycholecalciferol was measured in Mini Vidas autoanalyzer by immunofluorescence technique using a kit manufactured by BioMérieux SA Chemin de l'Orme 69280 Marcy-l'Etoile-France. The measurement range of 25-hydroxycholecalciferol was 8.1–126 ng/ml and health-based reference values were denoted as deficiency <20 ng/ml, insufficiency 21–29 ng/ml, and preferred level is >30 ng/ml.

The thyroid profile (TSH, FT3, and FT4) was analyzed by chemiluminescence technology in Cobas e411. The kits used for thyroid hormones were manufactured by the Roche Diagnostics GmbH, Sandhofer str. 116, D-68305 Mannheim, Germany. The measurement range for FT3 was 0.4–50 pmol/L and for FT4 hormone 0.3–100 pmol/L. The reference ranges for thyroid hormones were: TSH 0.27–4.2 mIU/ml, FT3 2.0–4.4 pg/ml, and FT4 0.93–1.7 ng/dl.

Statistical analysis

Descriptive and inferential statistical analysis was carried out in the present study. Results on continuous measurements were presented as mean \pm standard deviation (minimum – maximum), and results on categorical measurements were presented in number (%). Statistical significance was assessed at a 5% level of significance and $P \leq 0.05$ was considered statistically significant. The total sample size of 60 (30 cases, 30 control) was arrived based on the following formula:

$$n = \frac{Z^2 p (1 - p)}{d^2}$$

In the present study, Student's *t*-test was used for comparison of means between cases and controls. Pearson's correlation analysis was used for the correlation between Vitamin D status, thyroid profile with psoriasis area severity index (PASI), and dermatology quality of life index (DLQI). The statistical software The SPSS 17 (SPSS Inc, Chicago), MedCalc version 9.0.1 (MedCalc Software, Ostend, Belgium), was used for the data analysis. DLQI and PASI questionnaire was used to assess the quality of life and the severity of psoriasis respectively. PASI score is graded from 0 to 10 starting from minimum to maximum severity. DLQI is scored from 0 to 10 starting from minimal to maximum affecting daily life activities.

Results

25-hydroxycholecalciferol levels in psoriasis cases were significantly decreased when compared to the healthy controls ($P < 0.05$). Thyroid-stimulating hormone level was significantly increased in psoriasis cases when compared to healthy controls ($P < 0.05$), but was within reference range [Table 1].

There was significant negative correlation between PASI and Vitamin D3 and between PASI and DLQI. There was no significant association between DLQI and Vitamin D3 [Table 2].

The serum TSH level was significantly associated with the severity of psoriasis [Table 3]. The association of thyroid hormones (FT3 and FT4) with the severity of psoriasis was not significant.

Discussion

Psoriasis is a chronic immune-mediated inflammatory skin disease.^[13] Psoriasis lesions are characterized by hyperproliferation of epidermal keratinocytes associated with the inflammatory cellular infiltrate in both dermis and epidermis.^[14] The epidermis is the natural source of Vitamin D synthesis by sunlight action.

Vitamin D has several important functions and has a significant place in human health. Several studies have showed a high occurrence of Vitamin D deficiency among aged males and females, immature adults, and children.^[15] Studies have established that Vitamin D also exhibits photoprotective, anti-inflammatory, and wound healing effects. The deficiency of Vitamin D has been implicated as an environmental trigger for immune-mediated

disorders including psoriasis and psoriatic arthritis.^[9] There have been many studies conducted to know the association between Vitamin D deficiency and psoriasis. Data published showed a positive correlation between deficiency of Vitamin D and the severity of psoriasis.

Al-Mutairi *et al.*^[16] in their study comparing 100 stable plaque psoriasis patients with 100 age- and sex-matched healthy controls found significantly (29.53 ± 9.38 vs. 53.5 ± 19.6 ng/ml; $P < 0.0001$) lower serum Vitamin D levels in psoriatic patients as compared to the control group. Orgaz-Molina *et al.*^[17] in their study comparing serum 25-hydroxy Vitamin D levels in 43 psoriatic patients with age- and sex-matched 43 healthy controls found that psoriatic patients had lower levels of 25-hydroxy Vitamin D as compared to healthy controls and the difference was statistically significant (24.41 ± 7.80 vs. 29.53 ± 9.38 ng/ml; $P < 0.007$). All the above studies are in accordance with our study in which Vitamin D levels were significantly decreased in psoriasis when compared to controls [Table 1].

It is postulated that the thyroid hormones, T3 and T4, cause an increase in epidermal growth factor (EGF) which leads to epidermal hyperplasia.^[18] In two different studies, Werner *et al.*^[19] reported that T3 stimulates the proliferation of keratinocytes. It is postulated that T3 receptors may play a role in the synthesis of keratin. The existence of T3 receptors on the skin was also proved. Propylthiouracil, which is known to be an antithyroid drug, may affect the keratin synthesis process by binding to nuclear T3 receptors. It is also known that T3 has a major role in the regulation of cell growth and differentiation. Moreover, it has been stated that T3 and T4 have a hyperproliferative effect on the skin by EGF.

The analysis of the US National Health and Nutrition Examination Survey database revealed that patients with thyroid diseases had a significantly increased risk of having psoriasis.^[20] However, after adjusting for confounding variables, this association was not significant. The TSH levels in patients with active psoriasis were significantly lower than those without active disease. Physiological response to stress in healthy individuals is different from that in patients with psoriasis, as demonstrated by alterations in the HPA axis and sympathetic-adrenal-medullary system function.^[21] In our study, serum TSH levels were decreased when compared to controls, but it was within reference range. FT3 and FT4 levels were within limits of reference range.

PASI score is widely used in research and in clinical settings to assess the severity of psoriasis. A score of <10 is considered as mild and a score of more than 10 is considered as moderate-to-severe psoriasis. Ingram *et al.*^[22] found that a significant inverse relationship existed between PASI and 25(OH)D, with an elevation of 25(OH)D by up to 125 nmol/L was associated with mild decreases in PASI (estimated range of decrease, 0–2.6; $P = 0.002$).

Table 1: Biochemical parameters in psoriasis cases and controls

Biochemical markers	Mean±SD		P
	Cases	Controls	
Vitamin D3 (ng/L)	22.761±1.43	30.64±4.33	0.02*
FT3 (ng/dl)	2.77±0.57	2.55±0.92	0.15
FT4 (pg/ml)	1.31±0.43	1.13±0.40	0.03*
TSH (mIU/ml)	3.03±0.96	2.41±1.21	0.05*

* $P \leq 0.05$ significant. SD: Standard deviation; TSH: Thyroid-stimulating hormone

Table 2: Association of psoriasis area severity index and dermatology quality of life index with Vitamin D3

Parameters	r	P
PASI versus Vitamin D3	-0.40	0.02*
DLQI versus Vitamin D3	0.20	0.27
PASI versus DLQI	-0.59	0.00**

$P \leq 0.05$ significant. DLQI: Dermatology quality of life index; PASI: Psoriasis area severity index; TSH: Thyroid-stimulating hormone

Table 3: Association of thyroid profile with psoriasis area severity index score in psoriasis

Parameter	r	P
PASI score versus FT3	0.52	0.32
PASI score versus FT4	0.72	0.08
PASI score versus TSH	0.91	0.04*

* $P \leq 0.05$ significant. PASI: Psoriasis area severity index; TSH: Thyroid-stimulating hormone

Nayak *et al.*^[23] in their study involving 122 psoriasis patients showed no correlation between Vitamin D status and severity of psoriasis. In our study, a significant negative correlation was seen between PASI score and Vitamin D, which indicates the deficiency of Vitamin D increases the severity of psoriasis.

The DLQI is a compact self-reported questionnaire to measure health-related quality of life (HRQoL) over the previous week in patients with skin diseases. It consists of 10 items covering symptoms and feelings (items 1 and 2), daily activities (items 3 and 4), leisure (items 5 and 6), work and school (item 7), personal relationships (items 8 and 9), and treatment (item 10). Each item is scored on a four-point scale, with higher scores indicating greater impairment in HRQoL.^[24] In our study, a negative correlation was seen between PASI and DLQI which states that as the severity of psoriasis increases the quality of life decreases. The patients suffering from severe psoriasis experience difficulty in doing daily activities and mild to moderate psoriasis patients have a social stigma.

In a survey done by the National Psoriasis Foundation, almost 75% of patients believed that psoriasis had moderate to large negative impacts on their quality of life with alterations in their daily activities.^[25] Physical and emotional effects of psoriasis were found to have a significant negative impact on the patient's workplace. Psoriasis patients are more likely to be depressed than the general population with patients' age, education, and disease severity being important predictors of psychological distress. Gupta *et al.*^[26] in their study of 127 psoriasis patients found that 9.7% of patients reported their wish to be dead and 5.5% reported active suicidal ideation at the time of the study.

Conclusion

Our study emphasizes the relationship between biochemical markers, severity of psoriasis, and their impact on quality of life. Vitamin D deficiency increases the severity of psoriasis as supported by our study and other references included in the study. Hence, early treatment of these causative factors will reduce the severity and improves the quality of life. A multimodal holistic approach is needed for the treatment of psoriasis. Psychological support for stress management, drug therapy, and biochemical markers assessment for severity of psoriasis are the need of the hour for psoriasis.

Limitations

The present study is carried out on the limited number of newly diagnosed psoriasis cases in a short duration of 3 months.

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Conflicts of interest

There are no conflicts of interest.

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