



Original Research Article

Correlation between Vitamin-D and Calcium levels with severity of nail involvement in psoriasis: An observational study from Northern India

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ABSTRACT

Introduction: Psoriasis is a common chronic autoimmune inflammatory multisystem disease mainly involving skin, nails and joints. Several studies have reported lower levels of vitamin D and calcium in psoriasis. But there is paucity of literature regarding levels of vitamin D and calcium in nail psoriasis.

Objective: To study the level of Vitamin D and calcium in psoriasis patients with nail involvement and to correlate their levels with nail severity using Nail Psoriasis Severity Index (NAPSI).

Materials and Methods: A total of 60 psoriasis patients with nail changes were recruited for the study. The severity of nail changes was calculated using Nail Psoriasis Severity Index (NAPSI). All non-specific nail changes which were present in the psoriasis patients were noted as well. Apart from routine investigations, blood calcium level and serum vitamin D levels were also sent for investigation.

Results: Majority of the participants were male with male: female ratio of 2.75:1. The mean age at onset of nail involvement was 42.87 ± 17.19 years. About three-fourth of the patients were hypocalcaemic and vitamin D deficient or insufficient. There was a moderate negative correlation between NAPSI and blood calcium (mg/dL), and it was statistically significant ($\rho = -0.33$, $P = 0.011$). There was a weak positive correlation between NAPSI and S. Vitamin-D (ng/mL), and this correlation was not statistically significant ($\rho = 0.11$, $P = 0.402$). However, on multivariate regression analysis of NAPSI, significant association was found between nail psoriasis severity index (NAPSI) with blood calcium level and serum vitamin D levels ($P=0.01$).

Conclusion: Blood calcium and serum vitamin D levels were found low in patients of nail psoriasis. Hence, oral vitamin D and calcium supplementation may aid in the earlier response to standard nail psoriasis treatment and further studies are required to prove the therapeutic effect of calcium and vitamin D in nail psoriasis.

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1. Introduction

Psoriasis is a common chronic autoimmune inflammatory multisystem disease mainly involving skin, nails and joints. Complex fine tuning and intricate interaction between cells of adaptive immune system (T helper lymphocytes that is Th1, Th17 and Th22) and innate immune system (macrophages, dendritic cells) contribute to keratinocyte hyperproliferation and epidermal hyperplasia, skin inflammation and infiltration of T cells, dendritic cells,

macrophages and neutrophils and also leads to dendritic cell maturation, acquired immune response amplification and T regulation inhibition.^{1,2}

The role of Vitamin D in various autoimmune diseases (like systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, diabetes melitus, primary biliary cirrhosis) blaming the vitamin D receptor polymorphism in the pathogenesis of these autoimmune diseases has been suggested.³ Vitamin D receptors are also present in cells of immune lineages such as T lymphocytes, B lymphocytes, antigen presenting cells and synthesize active metabolite of vitamin D. Vitamin D modulates innate and

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adaptive immune response in an autocrine manner in local immunological environment. Vitamin D inhibits B cell proliferation, T cell proliferation (leading to shift in Th1 to Th2 phenotype) and decreases the inflammatory Th17 phenotype. Besides, vitamin D also inhibits production of inflammatory cytokines by monocytes and also inhibits dendritic cells differentiation and maturation.⁴ In innate immunity, vitamin D acts by triggering Toll-like receptors on macrophages leading to induction of antimicrobial peptide cathelicidin.

Calcium and vitamin D have a very important role in growth, differentiation and metabolism of nail unit. In autoimmune diseases, apart from modulating immune responsive cells, vitamin D supplementations also aids in calcium homeostasis and absorption for growth and development of nails and bones.

Nail involvement is very common in psoriasis and can present in up to 92% patients.^{5–12} Specific nail changes in psoriasis includes nail bed signs (subungual hyperkeratosis, onycholysis, oil drop dyschromia and splinter haemorrhage) and nail matrix signs (pitting, crumbling, leuconychia and red spots in lunula).

Several studies have reported lower levels of vitamin D and calcium in psoriasis.^{13–16} Calcium and vitamin D have role in proper growth and differentiation of nail unit. But there is paucity of literature regarding levels of vitamin D and calcium in nail psoriasis.

2. Objective

To study the level of Vitamin D and calcium in psoriasis patients with nail involvement and to correlate their levels with severity using Nail Psoriasis Severity Index (NAPSI).

3. Materials and Methods

This cross-sectional study was conducted in 60 psoriasis patients with nail changes who were aged more than 18 years attending the outpatient department of dermatology. The duration of study was 3 months from 16th September 2019 to 15th December 2020. Detail history was taken and all the 20 nails were thoroughly examined and photographed.

The severity of nail changes was calculated using Nail Psoriasis Severity Index (NAPSI) where each nail is divided into 4 quadrants and scoring is done on the basis of presence of nail bed or nail matrix signs in each quadrant of the nail. So, the total score is 8 for 1 nail, 80 for all fingernails and 160 for both finger as well as toe nails. Two different persons agreed on the NAPSI scoring of the patients.

Apart from nail signs which are specific for psoriasis and included in NAPSI scoring, all non-specific nail changes which were present in the psoriasis patients were also included and their frequency was noted. Besides routine investigations, blood calcium level and serum vitamin D

levels were sent as well. Patients who were already on oral calcium and vitamin D supplementation, pregnant and lactating females or patients suffering from any other chronic disease which could affect calcium and vitamin D levels were excluded from our study. Written and informed consent were obtained from all patients.

Patients were categorised as having normal calcium (blood calcium level ≥ 8.2 mg/dl) or having hypocalcaemia (blood calcium level < 8.2 mg/dl). On the basis of serum vitamin D levels, they were categorised as vitamin D deficient (< 20 ng/ml), insufficient (20–30 ng/ml) and having normal vitamin D (> 30 –100 ng/ml).

After completion of the study the data was compiled and double checked in the Statistical Package for Social Sciences (SPSS 11.5, SPSS Inc., Chicago, IL, U.S.A.). Chi square test, student's t-test and Wilcoxon Mann Whitney U test were used to analyse the data. Statistical significance was considered at $p < 0.05$.

4. Results

We collected data of 60 psoriasis patients with nail changes. Of these, majority that is 44 (77.3%) were males and 16 (22.7%) were females with male: female ratio of 2.75:1. The age of patients ranged from 18 to 85 years with mean age of 44.67 ± 16.81 years. The age at of onset of nail involvement in psoriasis ranged from 15 to 85 years with a mean of 42.87 ± 17.19 years.

Amongst specific nail signs included in NAPSI, the most frequent nail sign observed was subungual hyperkeratosis present in 44 (73.3%) patients, followed by onycholysis in 22 (36.6%), pitting in 32 (53.3%), crumbling in 31 (51.6%), oil drop dyschromia in 16 (26.6%), splinter haemorrhage in 15 (25%), leuconychia in 5 (8.3%) patients. Red spots in lunula was not present in any of the patients.

Apart from these, various non-specific signs were also prevalent, most common being longitudinal ridging found in 32 (53.3%) patients, followed by beau's line in 13 (21.6%), clubbing in 4 (6.6%), onychodystrophy in 3 (5%), pterygium in 3 (5%), longitudinal melanonychia in 2 (3.3%) and koilonychia in 2 (3.3%) patients.

The mean NAPSI was 38.03 ± 27.05 with range from 0 (in patients with nail signs not involved in NAPSI) to 99. Of these, only 8 (13.3%) of the patients had NAPSI ≤ 10 , while majority that is 52 (86.7%) patients had severe nail involvement having NAPSI > 10 .

The blood calcium level ranged from 7.1 to 10.9 mg/dl with a mean of 9.26 ± 1.12 mg/dl. Of these 16 (26.7%) were having normal calcium (≥ 8.2 mg/dl) while majority that is 44 (73.3%) were having hypocalcaemia (< 8.2 mg/dl).

The serum vitamin D levels of the patients ranged from 3.8 to 72 ng/ml with a mean of 24.65 ± 13.72 ng/ml. Of these, 24 (40%) were vitamin D deficient (< 20 ng/ml), 22 (36.7%) were vitamin D insufficient (20–30 ng/ml) and 14 (22.3%) were having normal vitamin D (> 30 –100 ng/ml).

Table 1: Association between NAPSI ≤ 10 and >10 with calcium and vitamin D

Parameters	NAPSI Category		P value
	≤ 10 (n = 8)	>10 (n = 52)	
Blood Calcium (mg/dL)	9.80 \pm 0.87	9.18 \pm 1.14	0.069 ¹
Blood Calcium			0.095 ²
<8.2 mg/dL	0 (0.0%)	16 (30.8%)	
≥ 8.2 mg/dL	8 (100.0%)	36 (69.2%)	
Serum Vitamin-D (ng/mL)	18.23 \pm 8.73	25.63 \pm 14.13	0.167 ¹
Serum Vitamin-D			0.272 ²
<20 ng/mL	4 (50.0%)	20 (38.5%)	
20-30 ng/mL	4 (50.0%)	18 (34.6%)	
>30 ng/mL	0 (0.0%)	14 (26.9%)	

***Significant at $p < 0.05$, 1: Wilcoxon-Mann-Whitney U Test, 2: Fisher's Exact Test

4.1. Association between NAPSI ≤ 10 and >10 with calcium and vitamin D (Table 1)

The mean blood calcium level in patients with NAPSI ≤ 10 was 9.80 \pm 0.87 mg/dl and NAPSI >10 was 9.18 \pm 1.14 mg/dl and it was not significant (W = 292.000, $p = 0.069$). In patients with NAPSI ≤ 10 , (100%) had blood calcium level < 8.2 mg/dL while in patients with NAPSI >10 , 16 (30.8%) patients had blood calcium < 8.2 mg/dL while 36 (69.2%) patients had blood calcium ≥ 8.2 mg/dL and it was not significant ($\chi^2 = 3.357$, $P = 0.095$).

The mean serum vitamin D level in patients with NAPSI ≤ 10 was 18.23 \pm 8.73 mg/dl and NAPSI >10 was 25.63 \pm 14.13 mg/dl and it was not significant (W = 144.000, $p = 0.167$). In patients with NAPSI ≤ 10 , 4 (50%) patients were vitamin D deficient, 4 (40%) patients were vitamin D insufficient and none had normal vitamin D while in patients with NAPSI >10 , 20 (38.5%) patients were vitamin D deficient, 18 (34.6%) patients were vitamin D insufficient and 14 (26.9%) had normal vitamin D levels and it was not significant ($\chi^2 = 0.832$, $P = 0.272$).

4.2. Correlation between NAPSI and blood calcium

There was a moderate negative correlation between NAPSI and blood calcium (mg/dL), and this correlation was statistically significant ($\rho = -0.33$, $P = 0.011$). For every 1-unit increase in NAPSI, the blood Calcium (mg/dL) decreases by 0.01 units.

4.3. Comparison of Calcium < 8.2 mg/dl and ≥ 8.2 mg/dl in terms of NAPSI

The mean NAPSI in the S. Calcium: < 8.2 mg/dL group was 47.38 \pm 23.80 and in the serum calcium: ≥ 8.2 mg/dL group was 34.64 \pm 27.60. There was a significant difference between the 2 groups in terms of NAPSI (W = 472.000, $P = 0.045$).

4.4. Comparison of Vitamin D deficiency/insufficiency in terms of NAPSI

The mean NAPSI in the vitamin D deficient group was 37.08 \pm 23.36, in the vitamin D insufficient group was 29.36 \pm 23.06 and in patients having normal vitamin D was 53.29 \pm 33.40 and it was not significant ($P = 0.086$).

4.5. Correlation between NAPSI and serum Vitamin-D (ng/mL)

There was a weak positive correlation between NAPSI and S. Vitamin-D (ng/mL), and this correlation was not statistically significant ($\rho = 0.11$, $P = 0.402$).

4.6. Correlation between S. Calcium (mg/dL) and S. Vitamin-D (ng/mL)

There was a weak positive correlation between S. Calcium (mg/dL) and S. Vitamin-D (ng/mL), and this correlation was statistically significant ($\rho = 0.29$, $P = 0.023$).

For every 1-unit increase in S. Calcium (mg/dL), the S. Vitamin-D (ng/mL) increases by 3.96 units.

4.7. NAPSI univariate and multivariate regression

On univariate analysis, no correlation was found between NAPSI and age of psoriasis patients, age of onset of nail involvement and blood calcium levels. Positive correlation was found between NAPSI and male gender, serum vitamin D levels ($P < 0.05$) (Table 2).

On multivariate regression analysis of NAPSI with only selected variables in model, there was significant association between NAPSI and male gender, blood calcium level and serum vitamin D levels ($P < 0.05$) (Table 3).

5. Discussion

Since ages we have utilised the beneficial effect of vitamin D production in skin by sunlight in psoriasis treatment. There is a possible bidirectional relationship between lower levels of vitamin D and psoriasis.¹⁴ Various vitamin D

Table 2: Univariate Analysis of NAPSI

Dependent: NAPSI		unit	value	Total	P
Age (years)	[18.0,85.0]	Mean (SD)	38.0 (27.0)	60 (100.0)	0.299
Gender	Male	Mean (SD)	32.5 (22.9)	44 (73.3)	0.007
	Female	Mean (SD)	53.4 (32.0)	16 (26.7)	
Age of onset (years)	[8.0,83.0]	Mean (SD)	38.0 (27.0)	60 (100.0)	0.885
Blood calcium (mg/dl)	[7.1,10.9]	Mean (SD)	38.0 (27.0)	60 (100.0)	0.119
Serum vitamin D (ng/ml)	[3.8,72.0]	Mean (SD)	38.0 (27.0)	60 (100.0)	0.009

Table 3: Regression of NAPSI with selected variables in model

Dependent: NAPSI		unit	Value	Coefficient (univariable)	Coefficient (multivariable)
Age (years)	[18.0,85.0]	Mean (SD)	38.0 (27.0)	0.22 (-0.20 to 0.64, P=0.299)	-
Gender	Male	Mean (SD)	32.5 (22.9)	-	-
	Female	Mean (SD)	53.4 (32.0)	20.92 (5.96 to 35.88, P=0.007)	22.76 (9.03 to 36.50, P=0.002)
Age of onset (years)	[8.0,83.0]	Mean (SD)	38.0 (27.0)	0.03 (-0.43 to 0.49, P=0.885)	-
Blood calcium (mg/dl)	[7.1,10.9]	Mean (SD)	38.0 (27.0)	-4.90 (-11.09 to 1.30, P=0.119)	-10.36 (-15.99 to -4.72, P=0.001)
Serum vitamin D (ng/ml)	[3.8,72.0]	Mean (SD)	38.0 (27.0)	0.66 (0.17 to 1.14, P=0.009)	0.77 (0.32 to 1.23, P=0.001)

MODEL FIT: F (3,56) = 9.94, p = <0.001 Number in dataframe = 60, Number in model = 60, Missing = 0, Log-likelihood = -269.68AIC = 549.4, R-squared = 0.35, Adjusted R-squared = 0.31

receptor polymorphism have been shown to affect the skin barrier and development of psoriatic lesions.¹⁵ There is also decreased expression of vitamin D receptor in psoriatic skin.¹⁷ Vitamin D analogues have been used very frequently as first line modality in the treatment of psoriasis. Many studies have depicted lower levels of vitamin D in psoriasis.^{18–20} In our study also, vitamin D levels were found low with mean of 24.65 ± 13.72 ng/ml in psoriasis patients with nail involvement with more than three-fourth of the patients being either vitamin D insufficient or vitamin D deficient. Vitamin D levels also significantly correlated with severity of nail psoriasis measured via NAPSI on multivariate analysis (P=0.001).

Hypocalcaemia is known risk factor for severe psoriasis, pustular psoriasis and erythrodermic psoriasis. In our study, the mean blood calcium was 9.26 ± 1.12 mg/dl and around three-fourth of the patients were hypocalcaemic. There was a moderate negative correlation between NAPSI and blood calcium (mg/dL), and this correlation was statistically significant ($\rho = -0.33$, P = 0.011). Several other studies have also shown calcium levels to be low in patients of psoriasis.^{21,22}

To the best of our knowledge, no study has been done regarding levels of vitamin D and calcium in nail psoriasis. This study highlights the deficiency of vitamin D and calcium in nail psoriasis and how this deficiency correlates

with the severity of nail involvement in psoriasis.

6. Conclusion

Blood calcium and serum vitamin D levels were found low in patients of psoriasis. Hence, oral vitamin D and calcium supplementation may aid in the earlier response to standard nail psoriasis treatment and further studies are required to prove the therapeutic effect of calcium and vitamin D in nail psoriasis.

7. Source of Funding

None.

8. Conflict of Interest

None.

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