

# Prevalence of Vitamin D insufficiency and deficiency among seborrheic dermatitis patients: a cross-sectional study at Makati Medical Center

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## ABSTRACT

**INTRODUCTION** Seborrheic dermatitis is a chronic and recurrent inflammatory dermatosis affecting different age groups with a prevalence rate of 1-5% among Asian adults. Due to its immune-modulatory and anti-inflammatory properties, vitamin D has been correlated with inflammatory dermatoses such as seborrheic dermatitis.

**OBJECTIVES** To determine the prevalence of vitamin D insufficiency, deficiency and severe deficiency among Filipino adult patients with moderate to severe seborrheic dermatitis.

**METHODS** A single-center, analytical, cross-sectional study at Makati Medical Center, which included Filipino patients aged 18-60 years, diagnosed with moderate-to-severe seborrheic dermatitis based on Investigator's Static Global Assessment (ISGA) with serum vitamin D levels classified as normal, insufficient, deficient and severely deficient.

**RESULTS** We included 61 patients, 5 patients (8%) of whom presented with normal Vitamin D levels. Twenty-one patients (34%) presented with vitamin D insufficiency, 32 patients (52%) presented with vitamin D deficiency, while 3 patients (5%) presented with severe deficiency. Vitamin D insufficiency and deficiency were more prevalent among patients in the younger age group ( $p = 0.001$ ), with predominant scalp lesions ( $p = 0.006$ ), and those who are single ( $p = 0.015$ ). There was no statistically significant difference in the prevalence of vitamin D insufficiency and/or deficiency based on seborrheic dermatitis severity as per ISGA scale ( $p = 0.126$ ).

**CONCLUSION** Seborrheic dermatitis in Filipinos has been associated with vitamin D insufficiency, deficiency and severe deficiency. The prevalence of vitamin D deficiency is seen in almost half of patients while vitamin D insufficiency is seen in almost one-third of patients with seborrheic dermatitis. While topical and oral medications have been the treatment of choice for seborrheic dermatitis, the role of oral vitamin D supplementation as adjunct treatment may be studied.

**KEYWORDS** seborrheic dermatitis, vitamin D deficiency, vitamin D insufficiency

## INTRODUCTION

Seborrheic dermatitis is one of the most common dermatoses affecting infants, adolescents, and adults. It is a chronic inflammatory dermatologic condition that usually appears on areas of the body with a large density of sebaceous glands, such as the scalp, face, chest, back, axilla, and groin. Cheong et al. in 2015 estimated seborrheic dermatitis prevalence rate in Asian adults to be 1-5%.<sup>1</sup> Although it can be associated with nutritional deficiency, a weakened immune system (e.g., human immunodeficiency virus infection), and neurologic disease (e.g., cardiovascular event, Parkinson's disease), seborrheic dermatitis typically occurs in healthy persons. It has a bimodal distribution, with peaks at two to twelve months of age and in adolescence and early adulthood. It is more severe in cold and dry

climates and during periods of increased stress.<sup>2</sup>

Adult seborrheic dermatitis present most often on the face and/or scalp as ill-defined erythematous patches associated with fine scaling, involving one or more sites of predilection. Although the etiology of adult seborrheic dermatitis is not definitely known, there are three principal factors that appear to play a role: sebaceous gland secretion, alteration in colonization and metabolism of cutaneous microflora (*Malassezia* species), and individual susceptibility and host response.<sup>3</sup>

Studies have shown that vitamin D has effects on the sebaceous gland. It has been reported that incubation of the human sebaceous gland cell line with 1,25-dihydroxyvitamin D results in a dose-dependent suppression of cell proliferation.<sup>4</sup> This led to the conclusion that local synthe-

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sis or metabolism of vitamin D metabolites may be of importance for growth regulation and various other cellular functions in sebaceous glands and that sebaceous glands represent promising targets for therapy with vitamin D analogs.<sup>4</sup>

Vitamin D is a fat-soluble nutrient that humans obtain through the diet and by synthesis in the skin upon exposure to ultraviolet B. It is then converted by the liver to 25-hydroxyvitamin D, which is the easily measurable and major circulating form, hence the best indicator of vitamin D nutritional status. Under the influence of parathyroid hormone, the kidney then converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D, the biologically active, hormonal form of importance in the metabolism of calcium and phosphorus. Outside of the skeletal system, many cell types, including various cells in the skin, also express the vitamin D receptor.<sup>5</sup>

According to a study by Dimitrova in Bulgaria, the preferred level of serum 25-hydroxyvitamin D for adults is 30–70 ng/mL. The value of 21–29 ng/mL is interpreted as insufficiency and a level less than 20 ng/mL as deficiency. Serum 25-hydroxyvitamin D levels under 10 ng/mL is evaluated as a severe deficiency based on the electrochemiluminescence immunoassay (ECLIA) method analyzer.<sup>6</sup>

In the Philippines, Tanchee-Ngo et al. studied vitamin D levels among admitted Filipino elderly patients and noted that serum 25-hydroxyvitamin D levels were as follows: > 30 nmol/L (adequate), 20–30 nmol/L (inadequate/insufficient), and < 20 nmol/L (deficient).<sup>7</sup>

According to a review by Mostafa et al., vitamin D deficiency appears to be a marker of ill health regardless of being an actual cause or an association. His review highlighted the most commonly studied dermatological diseases that were associated with vitamin D, namely: skin cancer, psoriasis, vitiligo, scleroderma, systemic lupus erythematosus, atopic dermatitis, acne vulgaris and alopecia.<sup>8</sup>

Palmer et al. indicated in their study a link between vitamin D and eczema outcomes and showed that lower serum vitamin D levels is associated with increased incidence and severity of eczema symptoms.<sup>9</sup> The study concluded, however, that current available evidence does not allow firm conclusions to be made on whether vitamin D status affects the development of atopic eczema.<sup>9</sup> In a recent study, noted spontaneous remission of seborrheic dermatitis in summer, and the therapeutic effects of vitamin D on other papulosquamous dermatosis such as psoriasis.<sup>6</sup>

Of late, studies have demonstrated that keratinocytes possess vitamin D receptors that inhibit the proliferation and stimulate the differentiation of the epidermal cells. Furthermore, vitamin D receptor ligands diminish the expression of proinflammatory cytokines, exerting therapeutic effect in many autoimmune and skin diseases.<sup>6</sup>

Despite several studies showing a correlation of vitamin D

with inflammatory skin conditions, there is a lack of published articles showing a correlation between vitamin D levels and seborrheic dermatitis among Filipinos.<sup>11,12</sup>

The primary objective of this study is to determine the prevalence of vitamin D insufficiency, defined as laboratory values between 20–30 nmol/L, vitamin D deficiency, defined as laboratory values < 20 nmol/L, and severe vitamin D deficiency, defined as laboratory values < 10nmol/L, among seborrheic dermatitis patients in Makati Medical Center, Makati, Philippines.

Furthermore, this study aims to identify the prevalence of vitamin D insufficiency, deficiency, and severe deficiency among patients with moderate and severe seborrheic dermatitis as classified according to the Investigator's Static Global Assessment (ISGA) scale, as well as its correlation to age, sex, civil status, duration of illness, previous treatment for seborrheic dermatitis, past illnesses, allergies, and physical examination findings.

## MATERIALS AND METHODS

This is a single-center, analytical cross-sectional study conducted at the outpatient dermatology clinics and inpatient facilities of Makati Medical Center, Makati City, Philippines, from 2016 to 2018.

We included the following patients: Filipino aged 18 to 60 years with Fitzpatrick skin phototype III and IV; clinically diagnosed with moderate to severe scalp, facial, and scalp with facial seborrheic dermatitis with a baseline seborrheic dermatitis severity score of three (moderate: coarse scale with moderate red coloration/moderate plaque thickness) or four (severe: thick tenacious scale with deep coloration/severe plaque thickness) as determined by an Investigator's Static Global Assessment (ISGA) specific for seborrheic dermatitis (Table 1); and with signed informed consent.

We excluded patients with: other active eczemas or psoriasis on the same location of the seborrheic dermatitis (face and/or scalp); active, localized, or systemic infection diagnosed before determination of vitamin D levels; untreated cutaneous

**Table 1.** Seborrheic Dermatitis-specific Investigator's Static Global Assessment (ISGA scale).

| Score | Interpretation | Description   |
|-------|----------------|---|
| 0     | Clear          | Clear, except for minor residual discoloration                            |
| 1     | Faint          | Occasional fine scale, faint erythema/barely perceptible plaque thickness |
| 2     | Mild           | Fine scale with light coloration/mild plaque elevation                    |
| 3     | Moderate       | Coarse scale with moderate red coloration/moderate plaque thickness       |
| 4     | Severe         | Thick tenacious scale with deep coloration/severe plaque thickness        |

malignancies on the face; and compromised immune system.

The sample size was computed based on a previous study of Dimitrova J,<sup>6</sup> which showed that the estimated proportion of vitamin D insufficiency in patients with seborrheic dermatitis is 90%. With a margin of error of 8% and a 95% confidence interval, the computed sample size was 55. To account for the possibility of 10% attrition rate and/or missing data, the final sample size was amplified to 62.

For all patients included in the study, after baseline history and physical examination, clinical photography, and determination of overall skin condition severity through the ISGA scale, vitamin D assay determination using the Abbott Architect Chemiluminescent Microparticle Immunoassay (CMIA) analyzer method was done at Makati Medical Center Laboratory Department by a registered medical technologist who underwent proper training given by the tertiary hospital.

Blood extraction was done on an accessible vein on the forearm (antecubital vein). Proper calibration of the machine was ensured and done multiple times in a year coinciding with the change and/or refill of the reagent. The prevalence of vitamin D insufficiency, defined as values between 20–30 nmol/L, vitamin D deficiency, defined as values < 20 nmol/L, as well as severe vitamin D deficiency, defined as values < 10nmol/L, were determined. The clinical profile of the patients was determined based on age, sex, body mass index, duration of lesions, as well as past illnesses.

A descriptive summary of the demographic and clinical characteristics of the patients was done using frequency and proportion for categorical variables, median and interquartile range (IQR) for non-normally distributed continuous variables, and mean and standard deviation for normally distributed continuous variables. Shapiro-Wilk was used to test the normality of the continuous variables. One-way analysis of variance (ANOVA) and Fisher's exact test was used to determine the difference of mean and frequency, respectively. Missing values were neither replaced nor estimated. Null hypotheses were rejected at less than 0.05  $\alpha$ -level of significance. STATA version 13.1 was used for data analysis. The study commenced upon the approval of the Institutional Review Board.

Upon knowledge of patients' vitamin D levels, those with elevated levels were referred to the appropriate Internal Medicine specialist for further evaluation and management, while those with deficient and insufficient levels were treated with daily oral vitamin D3 (cholecalciferol) supplementation at a dose of 6,000 IU per day for eight weeks. All patients were given appropriate management for their seborrheic dermatitis, in the form of topical corticosteroids and/or calcineurin inhibitors, topical anti-fungal agents, moisturizers, oral antihistamine drugs, and/or oral anti-fungal agents, independent of their vitamin D levels.

No adverse events related to blood extraction were noted upon follow up of the patients with their attending dermatologist after 1–2 weeks. No subject withdrew during the duration

of the study.

## RESULTS

A total of 61 patients were enrolled to this study (Table 2). The mean age was 46.5 years (SD 13.7). Forty-three percent (26) of the participants were males while 57% (35) were females; 59% (36) were single while 41% (25) were married. For the duration of illness, 21% (13) of the participants had lesions for less than a month, 54% (33) had lesions for less than a year, while 25% (15) had lesions for more than a year. Fifty-four percent (33) of all study patients had previous treatment for seborrheic dermatitis. A total of 46% (28) had illnesses such as hypertension and diabetes mellitus while 5% (3) had known allergies. For ISGA scale, 95% (58) were classified as moderate, while 5% (3) were classified as severe. A total of 16% (10) were seen as inpatients that were referred to Dermatology Service for the management of seborrheic dermatitis, while 84% (51) were seen as outpatients. Majority (52%, 32) presented with lesions on the scalp, 36% (22) had lesions on the face, while 11% (7) had lesions on both the face and scalp.

Only five patients (8%) presented with normal vitamin D levels (median 47.8 nmol/L, IQR 34.6 to 53.2). Twenty-one patients (34%) had insufficient vitamin D levels (median 23.1 nmol/L, IQR 21.6 to 24.3), 32 (52%) had deficient vitamin D levels (median 17.8 nmol/L, IQR 12.0 to 17.7), while 3 (5%) had severely deficient vitamin D levels (median 8.5 nmol/L, IQR 6.0 to 8.7) (Table 2).

A test of significance showed a statistically significant difference in the mean age between the groups ( $p = 0.001$ ), with patients with insufficient and deficient vitamin D levels belonging to the younger age group.

All subjects with normal vitamin D levels were married (Table 2). For participants with normal vitamin D levels, 60% (3) presented with lesions on the face while 40% (2) presented with lesions on both the face and scalp (Table 2). For participants with insufficient vitamin D levels, 71% (15) had lesions on the scalp and 29% (6) had lesions on the face. For participants with deficient vitamin D levels, 53% (17) had lesions on the scalp, 34% (11) had lesions on the face, and 13% (4) had lesions on both the face and scalp. Results showed that those with lesions on the scalp primarily have lower vitamin D levels ( $p = 0.006$ ). There is no sufficient evidence to conclude that the distribution of patients according to vitamin D status is significantly different as to sex ( $p = 0.77$ ), duration of illness ( $p = 0.60$ ), previous treatment for seborrheic dermatitis ( $p = 0.23$ ), history of past illnesses ( $p = 0.32$ ) and allergies ( $p = 0.17$ ), ISGA scale ( $p = 0.13$ ) and whether the patient is an in-patient or out-patient ( $p = 0.06$ ) (Table 2).

## DISCUSSION

This study showed that majority of patients with seborrheic dermatitis have vitamin D insufficiency or deficiency, consistent with the study of Dimitrova in 2013.<sup>6</sup> The majority of the patients with vitamin D insufficiency or deficiency had lesions

Table 2. Demographic and clinical characteristics of patients with seborrheic dermatitis (N = 61).

| Variable                                     | Total     | Vitamin D Status |                       |                    | P-value |
|--|-----------|------------------|-----------------------|--------------------|---------|
|  |           | Normal<br>N (%)  | Insufficient<br>N (%) | Deficient<br>N (%) |         |
| Age (yrs.), Median (IQR)                     |           | 55 (55, 60)      | 27 (26, 33)           | 32 (25, 52)        | 0.0045* |
| Gender                                       |           |                  |                       |                    |         |
| Female                                       | 35 (57.4) | 2 (40.0)         | 11 (52.4)             | 22 (62.9)          | 0.532 † |
| Male   | 26 (42.6) | 3 (60.0)         | 10 (47.6)             | 13 (37.1)          |         |
| Status                                       |           |                  |                       |                    |         |
| Married                                      | 25 (41.0) | 5 (100.0)        | 6 (28.6)              | 14 (40.0)          | 0.014 ‡ |
| Single                                       | 36 (59.0) | 0 (0.0)          | 15 (71.4)             | 21 (60.0)          |         |
| Duration of illness                          |           |                  |                       |                    |         |
| 1 month or less                              | 14 (22.9) | 1 (20.0)         | 6 (28.6)              | 7 (20.0)           | 0.646 ‡ |
| 1 year or less                               | 32 (52.5) | 2 (40.0)         | 12 (57.1)             | 18 (51.4)          |         |
| More than a year                             | 15 (24.6) | 2 (40.0)         | 3 (14.3)              | 10 (28.6)          |         |
| Previous treatment for seborrheic dermatitis | 33 (54.1) | 4 (80.0)         | 11 (52.4)             | 18 (51.4)          | 0.535 ‡ |
| Physical exam                                |           |                  |                       |                    |         |
| Face   | 22 (36.1) | 3 (60.0)         | 6 (28.6)              | 13 (37.1)          | 0.011 ‡ |
| Face and scalp                               | 7 (11.5)  | 2 (40.0)         | 0 (0.0)               | 5 (14.3)           |         |
| Scalp  | 32 (52.5) | 0 (0.0)          | 15 (71.4)             | 17 (48.6)          |         |

\*Kruskal Wallis test; †Chi-square test; ‡ Fischer's exact test

Table 3. ISGA scale and vitamin D status (N = 61)

| ISGA scale | Total     | Vitamin D Status |                       |                    | P-value |
|------------|-----------|------------------|-----------------------|--------------------|---------|
|            |           | Normal<br>N (%)  | Insufficient<br>N (%) | Deficient<br>N (%) |         |
| Moderate   | 58 (95.1) | 5 (100.0)        | 18 (85.7)             | 35 (100.0)         | 0.532E  |
| Severe     | 3 (4.9)   | 0 (0.0)          | 3 (14.3)              | 0 (0.0)            |         |

located predominantly on the scalp, consistent with the study of Rahimi et al. in 2021, which noted that scalp disease severity was associated with lower serum vitamin D level citing a possible role of vitamin D in the pathogenesis of seborrheic dermatitis, as the scalp region presents with increased number and activity of sebaceous glands where vitamin D has been identified to have effects.<sup>4,12</sup> Furthermore, our study have shown that majority of the patients with vitamin D insufficiency or deficiency were in their 30s, and according to a study by Byung et al. in 2005, sebaceous gland activity increases through teenage years, as well as the second and third decades of life, before it starts to decline.<sup>13</sup>

The correlation of vitamin D deficiency and insufficiency and civil status were not identified by the previous studies of Dimitrova, Rahimi and Byung. Factors like stress levels, diet and lifestyle may have a factor and these may be further elucidated by more studies.

Inadequate vitamin D levels in patients with seborrheic

dermatitis may be related to isoenzyme alteration involved in vitamin D metabolism as stated by Rahimi et al.<sup>12</sup> As such, topical vitamin D analogues such as calcipotriol has already been used for years to treat inflammatory skin diseases such as psoriasis vulgaris. However, data are still conflicting with regards to its effects on seborrheic dermatitis. Oral vitamin D supplementation, like topical vitamin D analogues, may have therapeutic effects on seborrheic dermatitis, which is under the spectrum of inflammatory skin diseases.

This study only included data of seborrheic dermatitis patients in a private institution setting in the Philippines, which is a tropical country. We included only adults aged 18–60 years with Fitzpatrick skin types III and IV. The investigators recommend a multicenter study with a bigger sample size, which may include the pediatric age group, and comparison with healthy control subjects with and without other dermatologic diseases and of different Fitzpatrick skin types. Mild seborrheic der-

matitis, defined as fine scales with light coloration and/or mild plaque elevation by the (iSGA) scale, were excluded from the study to be able to focus on patients presenting with exacerbated seborrheic dermatitis such as those with moderate and severe seborrheic dermatitis based on the (iSGA) scale.

One of the limitations of this study is the absence of participant measures such as diet, lifestyle and UV history, which could have been possible sources of bias and imprecision. These were not taken into account and were not added in the inclusion criteria, as those who are on certain diet with vitamin D supplementation, as well as those with active lifestyles with sufficient sun exposure, may be a confounding factor on the vitamin D levels of the participants.

With the current global pandemic, vitamin D has been widely studied by researchers not only for its role in calcium metabolism, but also for its immune-modulatory, anti-proliferative and pro-differentiative properties.<sup>6</sup> Physicians are becoming more aware of the promising effects of vitamin D, hence vitamin D level determination has been an integral part of work-

up for most patients. To the best of our knowledge, this is the first study in the Philippines to assess the vitamin D status of patients with seborrheic dermatitis.

## CONCLUSION

Vitamin D insufficiency and deficiency have been associated with numerous medical conditions, and its association with skin diseases, particularly inflammatory skin diseases like seborrheic dermatitis, is still to be further elucidated. Seborrheic dermatitis, being identified as one of the most common, recurrent, and infrequently debilitating skin disease when severe, has been treated with topical and oral medications (anti-inflammatories, antifungals, and antihistamines) to address its etiology. The role of oral vitamin D supplementation as an adjunct treatment in helping improve disease severity and recurrence may be studied in the future. The investigators believe that the results of this study will serve as a pivot and inspiration for further studies between seborrheic dermatitis and vitamin D in the Philippines.

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