





Vitamin D Levels in Patients with and without Acne and Its Relation to Acne Severity: A Case-Control Study

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Background: Vitamin D plays a significant role in the function of the immune system and it influences many dermatological diseases such as psoriasis and atopic dermatitis. The prevalence of vitamin D deficiency is growing globally, with around 30–50% of people are known to have low levels of vitamin D. Acne vulgaris is a common inflammatory disorder of the pilosebaceous unit. Studies about the role of vitamin D in the pathogenesis of acne vulgaris have shown conflicting and nonconclusive results. Thus, the precise purpose of vitamin D has not yet been established.

Objective: First, to evaluate serum levels of vitamin D through a representative sample of patients with acne vulgaris and compare it with matched healthy controls. Second, to investigate if there is a relation between serum vitamin D level and the severity of acne vulgaris.

Materials and Methods: This cross-sectional study included 68 patients with acne vulgaris and 50 matched healthy controls. Serum 25-hydroxyvitamin D [25 (OH) D] levels were measured for both patients and healthy controls.

Results: The study yielded lower levels of serum 25-hydroxyvitamin D in patients with acne vulgaris than its level in healthy controls. This is statistically significant with P-value = 0.003. Regarding age, gender, and sun exposure, there is no significant variation in serum 25-hydroxyvitamin D level. Also, no significant difference between the severity of acne and serum 25-hydroxyvitamin D levels.

Conclusion: This study has shown clearly that vitamin D deficiency is more frequent in patients with acne with P-value = 0.003. However, no significant association between the serum level of 25-hydroxyvitamin D [25 (OH) D] and the severity of acne vulgaris. Further clinical trials on a larger scale are needed to address the importance of vitamin D in acne vulgaris. Specifically, determining whether treatment of acne with both topical vitamin D analogs and vitamin D supplementation is of significant effect.

Keywords: acne vulgaris, vitamin D deficiency, 25-hydroxyvitamin D

Introduction

Acne vulgaris is a chronic inflammatory skin disorder of the pilosebaceous unit, which observed equally in both genders. An estimated 75–95% of all adolescents suffer from acne to some degree.¹ It's characterized by non-inflammatory lesions (white and black comedones), and inflammatory lesions (papules, pustules, nodules, and/or cyst) which can cause negative reflects on patients psychologically and cosmetically by scarring and pigmentations.² It has multi-factorial pathogenesis including hormonal influences, increased sebum secretion, follicular plugs, and

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follicular hyperkeratinization, colonization of *Cutibacterium acnes* (formerly known as *Propionibacterium acnes*) with consequent inflammation.³

Acne vulgaris is localized in areas with the highest density of pilosebaceous units, including mainly the face, back, chest, and shoulders. Classification is essential and guides in the decision of treatment options.⁴ Acne is categorized according to severity into mild, moderate, and severe. Typical lesions of mild acne are characterized by the presence of closed and open comedones with few inflammatory lesions limited to the face. Whereas, in moderate acne, there is an increase in inflammation with papules and pustules on the face. The trunk area could also be affected by mild lesions. Finally, the presence of nodules and cysts are a hallmark of severe acne. Here, widespread lesions of trunk area together with facial lesions are characteristic.⁵

Vitamin D is a fat-soluble steroid hormone derived from dietary intake and its synthesized through the skin via exposure to sunlight. Vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol) are manufactured through solar ultraviolet B radiation. Absorption of UVB irradiation in the skin leads to conversion of provitamin D to pre-vitamin D, followed by the production of vitamin D3.⁶

To evaluate vitamin D deficiency and insufficiency, serum 25 (OH) D concentration is used as a biomarker. Due to short half-life, approximately 15 hours, 1, 25 (OH) 2D levels are not considered a good laboratory test for vitamin D levels. This is in contrast to 25 (OH) D, which is more stable in the blood than 1,25 (OH) 2D. Blood concentrations of 25 (OH) D is 500 to 1000 times higher than 1,25 (OH) 2D levels.⁷ Vitamin D has a regularity effect on the immune system. In addition, it regulates the proliferation and differentiation of keratinocytes and sebocytes. Furthermore, antioxidant and anti-comedogenic properties are features of vitamin D. Thus, vitamin D deficiency may contribute to the pathogenesis of acne.⁸

We aim to evaluate serum levels of vitamin D [25 (OH) D] in patients of acne vulgaris and to investigate the possibility of an existing relationship between low serum vitamin D level and severity of acne vulgaris. Up to our knowledge, this study is considered the first study in the Kingdom of Saudi Arabia that addresses this issue.

Materials and Methods

Subjects

The study was conducted in Outpatient Dermatology Clinics at Qassim University, Saudi Arabia, in the period

between October 2016 and March 2017. It was approved by the Local Medical Ethical committee in the college of medicine at Qassim University and it has complied with the declaration of Helsinki. The study was conducted in the winter season to minimize the effect of seasonal variation on serum vitamin D levels.

A total of 68 acne vulgaris patients (27 male and 41 female) and fifty matched healthy controls (24 male and 26 females) were enrolled. All subjects in the patient group, as well as the control group, had not taken any vitamin D supplementation, and not suffering from any comorbidity or complication of vitamin D deficiency. Both groups had undergone complete physical and clinical examinations and biochemistry tests for serum vitamin D levels. Every subject signed written informed consent upon starting and had received a detailed explanation about the aim and steps of this study.

Acne grading was classified as mild, moderate, and severe. Mild acne marked by (<20 comedones, <15 inflammatory lesions, or total lesion count < 30). Moderate acne characterized by (20–100 comedones, 15–50 inflammatory lesions, or total lesion count 30–125). Severe acne (>5 pseudocysts, Total comedones count >100, Total inflammatory count >50, or total lesion count >125).⁹ All the 68 subjects had filled a data collection sheet for demographics, family history for acne, sun exposure >2 hours/day, age of onset, duration of disease, site of acne (face, chest, and back), past medical history, and other relevant variables.

Inclusion Criteria

Male and female patients with the diagnosis of acne vulgaris according to the global acne grading system (GAGS) score.

Exclusion Criteria

Pregnant, breastfeeding, oral contraceptive pills, postmenopausal, patients on corticosteroids, or any medication that affects vitamin D metabolism (ketoconazole, rifampin, phenytoin, isoniazid). Patients on vitamin D supplementation, patients on multivitamins, patients are suffering from active malignancy or other chronic systemic diseases, patients on regular medication for other diseases, and history of oral isotretinoin over the last 3 months.

Table 1 Baseline Demographics and Clinical Characteristics of Acne Patients and Controls

Characteristic	Acne Patients N (68)	Healthy Control N (50)
Gender		
Male N (%)	27(39.7%)	24(48%)
Female N (%)	41 (60.3%)	26(52%)
Age, year		
Male (mean ± SD)	20.7±3.8	39.8±11.8
Female (mean ± SD)	21.3±3.6	37.7±14.85
Sun – exposure >2 hours per day N (%)	14 (20.5%)	12(24%)
Positive family history of acne N (%)	29(42.65%)	NA
Age at onset of disease, years	16.55±4.99	NA
Duration of the disease, years (mean ± SD)	4.8±0.8	NA
Site of acne		
Face N (%)	68(100%)	NA
Chest N (%)	24(35.3%)	
Back N (%)	40(54.41)	
The severity of the disease		
Mild N (%)	21(30.88%)	NA
Moderate N (%)	26(38.24%)	
Severe N (%)	21(30.88%)	

Abbreviations: N, number; SD, standard deviation; %, percentage; NA, not applied.

Biochemistry and Laboratory Analysis

Patients and controls had their serum 25-hydroxyvitamin D3 [25 (OH) D] concentration measurements. Blood samples were collected from veins and analyzed within 24 h of sampling using the Roche Cobas e411 (Roche Diagnostics System, Switzerland). Following the guidelines of the Food and Nutrition Board of the Institute of Medicine, 25 (OH) D serum levels were categorized into adequate (>20 ng/mL), inadequate (12–20 ng/mL), or deficient (<12 ng/mL).¹⁰

Statistical Analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 SPSS Inc., Chicago, Illinois, USA). Analysis of variance (ANOVA) test between more than two means *t*-test between the means we used to analyses the mean difference, *t*-test between the percentage of analyses percent difference and chi-square. A level of significance with *P*= 0.001 was considered highly significant, and *P*=0.05 was deemed to be insignificant.

Also, Quantitative data were expressed as a mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

Results

This study included 68 patients with acne vulgaris (41 females and 27 males) and 50 healthy controls (26 females and 24 males). Baseline demographics and clinical characteristics of the participants are presented in (Table 1). Patients with acne were younger than healthy controls. Fourteen patients with acne (20.5%) and twelve healthy subjects (24%) were exposed to sunlight longer than two hours per day on average (Table 1).

Biochemical Results of Serum Concentration of Vitamin D [25 (OH) D]

There is a statistical difference between the two groups' serum concentration of vitamin D [25 (OH) D], which was higher in healthy subjects than acne vulgaris patients (*P*-value =0.003) (Table 2). Also, we determined no significant relationship between sun exposure (Figure 1), gender and serum concentration of vitamin D [25 (OH) D] in acne

P-value=0.546

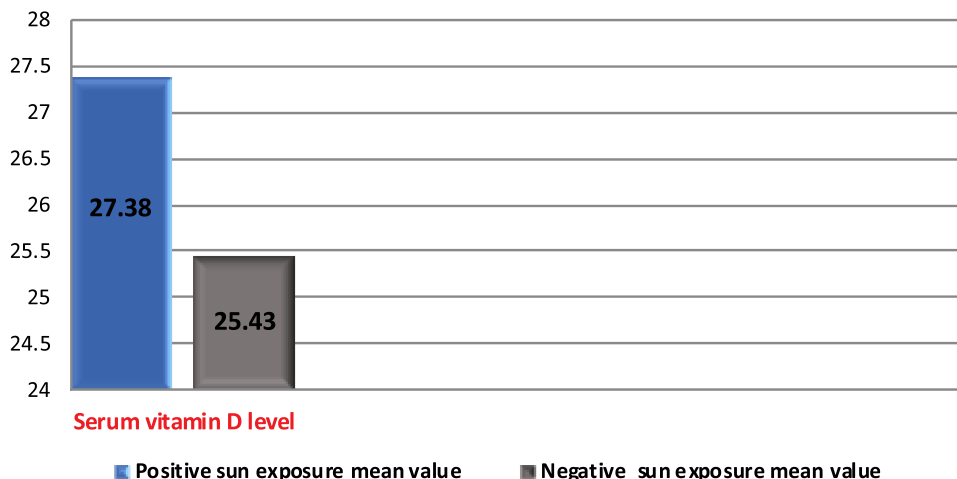


Figure 1 The relationship between serum vitamin D level and sun exposure in acne patients.

Table 2 Comparison of Serum Vitamin D Level Between Acne Patients and Controls

Parameters	Acne Patients (N=68)	Healthy Controls (N=50)	P-value
Serum vitamin D level ng/mL (mean \pm SD)	28.8 \pm 7.9	40 \pm 11.7	0.003**

Note: **Mild significant differences $P \leq 0.005$.

Abbreviations: N, number; SD, standard deviation; %, percentage.

Table 3 The Relationship Between Serum Vitamin D Level and Gender of Acne Patients

Parameters	Acne Patients Male (N=27)	Acne Patients Female (N=41)	P-value
Serum vitamin D level ng/mL (mean \pm SD)	30.39 \pm 7.9	27.8 \pm 7.8	0.199

Abbreviations: N, number; SD, standard deviation.

Table 4 The Relationship Between Serum Vitamin D Level and Gender of Controls

Parameters	Healthy Controls Male (N=24)	Healthy Controls Female (N=26)	P-value
Serum vitamin D level ng/mL (mean \pm SD)	36.3 \pm 10.26	29.3 \pm 12.2	0.042**

Note: **Mild significant differences $P \leq 0.005$.

Abbreviations: N, number; SD, standard deviation.

Table 5 The Relationship Between Serum Vitamin D Level and Acne Vulgaris Severity

Parameters	Acne Patients Mild (N=21)	Acne Patients Moderate (N=26)	Acne Patients Severe (N=21)	P-value
Serum vitamin D level ng/mL (mean \pm SD)	26 \pm 9.4	31.4 \pm 6.9	28.4 \pm 6.7	0.067

Abbreviations: N, number; SD, standard deviation.

Table 6 The Relationship Between Serum Vitamin D Level and Gender of Mild Acne Patients

Parameters	Mild Acne Patients Male (N=8)	Mild Acne Patients Female (N=13)	P-value
Serum vitamin D level ng/mL (mean ± SD)	28.8±7.9	24±8.3	0.349

Abbreviations: N, number; SD, standard deviation.

Table 7 The Relationship Between Serum Vitamin D Level and Gender of Moderate Acne Patients

Parameters	Moderate Acne Patients Male (N=8)	Moderate Acne Patients Female (N=18)	P-value
Serum vitamin D level ng/mL (mean ± SD)	33.6±6.9	30.4±6.8	0.291

Abbreviations: N, number; SD, standard deviation.

Table 8 The Relationship Between Serum Vitamin D Level and Gender of Severe Acne Patients

Parameters	Severe Acne Patients Male (N=11)	Severe Acne Patients Female (N=10)	P-value
Serum vitamin D level ng/mL (mean ± SD)	29.2±5.7	27.5±7.9	0.572

Abbreviations: N, number; SD, standard deviation.

vulgaris patients (P-value = 0.199) (Table 3) while; there was a mild significant relationship between male and female in the healthy control group (P-value= 0.042) (Table 4).

The results of the study showed that there were no significant variations in the vitamin D serum concentrations and acne vulgaris severity (mild, moderate, and severe) (P-value = 0.067) (Table 5).

Also, we do not find significant variation between genders and vitamin D serum concentrations and mild, moderate, and severe acne vulgaris (P-value = 0.349, 0.291, and 0.572 respectively) (Tables 6–8).

Discussion

According to our knowledge, this study is considered the first study in Saudi Arabia concerned with the correlation and assessment of serum vitamin D status and acne vulgaris.

There are several biological mechanisms by which vitamin D induces its anti-inflammatory effects. These mechanisms support the theory of the immune-regulatory function of vitamin D and the anti-inflammatory effects of it in acne patients. Vitamin D inhibits *Cutibacterium acne*-induced Th17 differentiation. Indeed, reducing the expression of IL17 is an inflammatory cytokine that found to be increased in acne patients.¹¹ Vitamin D also reduces the expression of inflammatory

cytokines in cultured sebocytes such as interleukin IL-6, IL-8, and matrix metalloproteinase 9.¹² Other mechanisms are exerting antimicrobial effects by inducing antimicrobial peptides such as LL-37 in human sebocytes.¹³

Our results indicated that serum concentrations of vitamin D in controls were significantly higher than those in acne vulgaris patients (P-value = 0.003). These results are in line with several other studies found that no elevation of serum vitamin D levels in acne patients.^{8,14,15}

Since the aim is to analyze vitamin D status in patients with acne, Our results showed that there was no relationship between sun exposure and improvement in vitamin D readings in patients with acne vulgaris (P-value = 0.546 between positive and negative sun exposure in acne vulgaris patients).

This can be explained by several factors, such as the impact of psychological distress on their avoidance of spending extended periods outdoors. This suggests a possible explanation of low vitamin D levels in patients with acne vulgaris. These results were consistent with Lim et al who revealed that lower level of serum vitamin D in severe acne vulgaris patients might be due to psychological stress.¹⁴

Another factor for deficiency of vitamin D is an environmental factor such as the hot climates in Saudi Arabia and the

Arabian Gulf, especially in the summer. Again, our results are similar to the results of Al-Taiar et al who shed light on the deficiency of vitamin D among adolescents, despite abundant sunshine in the Arabian Gulf.¹⁶ Same results obtained in another study in Egypt by Elmohsen et al. They found no significant relationship between sun exposure and improvement of serum vitamin D levels.¹⁷

This reinforces our point of view that the influence of environmental factors as the high climate's temperature in the Arabian Gulf and Arab countries, might contribute to reduced chances of sun exposure.

Among our patients, we found no significant association between vitamin D deficiency and gender (P-value = 0.199). Our results are similar to those in several studies.^{14,15,17,18} The results of the current study indicated that the mean value of vitamin D was abetted higher in moderate acne (31.4±6.9) than in mild and severe acne. (26±9.4 and 28.4±6.7, respectively). However, this difference was not statistically significant (P-value =0.067), and this can be explained by the small sample size of our study.

Also, we found no significant relationship between vitamin D deficiency and the severity of acne vulgaris. This result is in line with several studies.^{8,19}

Conclusion

This study revealed a statistical significant low serum vitamin D levels in patients with acne vulgaris. This highlights the importance of screening patients with acne for vitamin D insufficiency and deficiency. Further clinical trials on a larger scale are needed to address the importance of vitamin D in acne vulgaris. The authors might suggest a possible role of vitamin D treatment in acne. This necessitating further clinical trials to determine whether treatment of acne with both topical vitamin D analogs and vitamin D supplementation is of significant effect.

Disclosure

The authors report no conflicts of interest in this work.

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