

ORIGINAL ARTICLE

Evaluation of 25-hydroxy vitamin D levels and disease severity in patients with acne vulgaris

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Abstract

Acne vulgaris is a multifactorial skin disorder. Many etiological factors are speculated to contribute to the pathogenesis of acne, one of these is vitamin D deficiency. Previous studies reported contradictory results about serum 25 hydroxy vitamin D (25-OH vitamin D) levels, its association with acne, some claimed that acne lesion might improve with vitamin D supplementation. We aimed to assess serum 25-OH vitamin D levels in acne patients, identify their relation with disease severity in a larger study group. The study included 134 acne patients, 129 controls. Acne disease severity was identified with Global Acne Grading Scale (GAGS) scores. Serum 25-OH vitamin D levels were measured in all groups. Serum 25-OH vitamin D levels were significantly lower in acne patients than in controls ($P < .001$). The prevalence of vitamin D deficiency was significantly higher in acne group than in control group (77.6% vs 63.9%; $P = .041$). There was a negative-strong statistically significant correlation detected between serum 25-OH vitamin D levels and GAGS scores in patient group ($P < .001$; $r = -.910$). According to these results, we claim that evaluating serum 25-OH vitamin D levels in acne patients, vitamin D supplementation as a treatment option may be a consideration for further studies.

KEYWORDS

acne, disease severity, vitamin D

1 | INTRODUCTION

Acne vulgaris, is the most common skin disorder globally. Approximately 9.4% of the world's population is affected by acne vulgaris.¹⁻³ It is a chronic inflammatory disease of the pilosebaceous unit and is clinically characterized by seborrhoea, comedones, papules, pustules, and various degrees of scarring. Acne distribution is higher in areas with the highest density of pilosebaceous units, such as face, upper chest, neck, back, and shoulders.⁴ The disease onset usually occurs during early adulthood.⁵ Many etiological factors that may underlie the pathogenesis of acne have been proposed, including abnormal follicular keratinization, hormonal dysfunction, *Propionibacterium acnes* colonization and inflammation, increased levels of sebum secretion.⁶

Vitamin D is a fat-soluble vitamin that regulates the immune system and proliferation, differentiation of sebocytes and keratinocytes.

It also has anticomedogenic and antioxidant effects. Thus, vitamin D deficiency may have a role in the pathogenesis of acne.^{6,7}

Few studies have been reported on the association of acne vulgaris with vitamin D levels. In this study, we aimed to investigate the serum 25-OH vitamin D levels in acne vulgaris patients and the relationship of 25-OH vitamin D levels with the severity of the disease.

2 | MATERIALS AND METHODS

2.1 | Sample

The study was a single-centered, prospective and controlled study and undertaken between April 2019 and May 2019. Herein, we included 134 patients aged 18-65 years clinically diagnosed as having acne vulgaris and 129 gender- and aged-matched healthy individuals

without acne vulgaris. Patients with no acne therapy, patients without hormonal dysfunction that can cause acne such as polycystic ovary syndrome (PCOS), patients who do not use drugs that can cause acne lesions such as vitamin B12, halogens and hormonal therapy were included. Patients and controls with disorders that affect the serum level of vitamin D, such as renal, hepatic, hormonal, and bone metabolism dysfunctions, and those taking vitamin D and calcium supplements and drugs which may affect vitamin D levels, including bisphosphonates, systemic corticosteroids during the last six months and regular sunscreen users were excluded from the study.

The study was approved by the local clinical and laboratory research ethics committee and participants were enrolled in the study only after they provided written informed consent.

2.2 | Measures

The severity of acne vulgaris was assessed using Global Acne Grading Scale (GAGS) in patients. Based on GAGS, the body was divided into six areas—forehead, nose, each cheek, chin and back—with a factor assigned to each area according to the surface area and density of the pilosebaceous unit. In these areas, each type of lesion is given a value: zero for no lesion, one for comedones, two for papules, three for pustules and four for nodules. The local score for each area is calculated as factor \times grade (lesion type). All local scores are added to reach a global score. Acne severity based on the global score is grouped as mild (1-18), moderate (19-30), severe (31-38) and very severe (≥ 39).

Serum 25-OH vitamin D concentrations were measured for patients and controls. Blood samples were taken from the veins. The samples were analyzed within 24 hours of sampling using Roche Cobas E601 Modular Diagnostic System. Vitamin D status was categorized⁸ as vitamin D deficiency (≤ 20 ng/mL), vitamin D insufficiency (21-29 ng/mL), and vitamin D sufficiency (≥ 30 ng/mL) using the aforementioned acceptable cut-off points.

2.3 | Statistical analysis

Statistical analysis was performed using the SPSS (Statistical Package for the Social Sciences) software for Windows (v23.0; SPSS Inc.,

Chicago, Illinois). The normality of the data distribution was evaluated using the Shapiro-Wilk test. Student's *t*-test was used to compare the means of numeric variables between the two groups. Pearson correlation analysis was used to estimate the linear relationship between continuous variables. *P*-values were considered statistically significant at $\leq .05$.

3 | RESULTS

The patients diagnosed with acne vulgaris ($n = 134$) in this study were 51 men (38.1%) and 83 women (61.9%). The mean age of the patients was 20.11 ± 2.92 years. Fifty-two individuals (40.3%) of the control group ($n = 129$) were men and 77 (59.7%) were women. The mean age of the control group was 20.27 ± 3.17 . There were no statistically significant differences according to the age and gender between groups ($P > .05$). The mean body mass index (BMI) score was 21.46 ± 1.37 in the acne group and 21.23 ± 1.23 in the control group. No statistically significant difference in the BMI was found between the groups ($P > .05$). There were statistically significant differences in the serum 25-OH vitamin D levels between groups ($P < .001$). There was no significant correlation between age, sex, BMI and serum 25-OH vitamin D levels ($P > .05$). We compared acne and control groups according to the 25-OH vitamin D status. Vitamin D deficiency was significantly more prevalent in the acne group compared with the control group (77.6% vs 63.9%; $P = .041$) (Table 1.).

Patients with acne vulgaris were divided into four groups according to GAGS as having mild (1-18), moderate (19-30), severe (31-38), and very severe acne (≥ 39). No correlation was found between severity of the disease and age ($P > .05$). The very severe acne group comprised 43 (32.1%) patients, the severe acne group comprised 64 (47.8%) patients, the moderate acne group comprised 15 (11.2%) patients, and the mild acne group comprised 12 (9%) patients.

Vitamin D deficiency was found to be significantly higher in severe acne group and very severe acne group than other groups (93.8% and 100%, respectively) (Table 2).

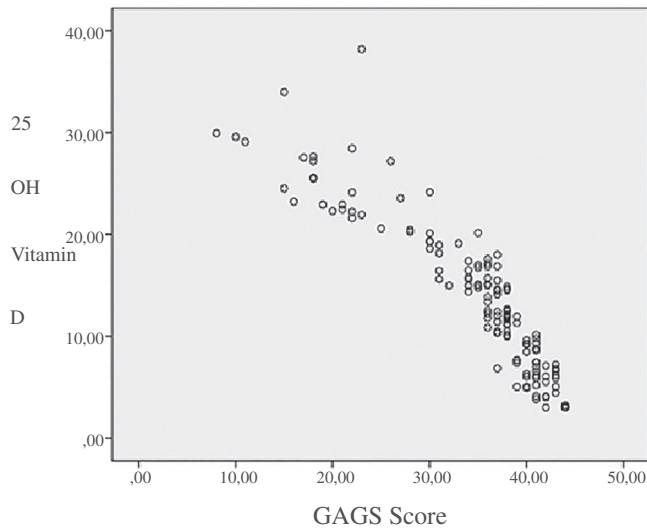
There was a negative-strong statistically significant correlation detected between serum 25-OH vitamin D levels and GAGS scores in patients with acne vulgaris ($P < .001$; $r = -.910$) (Figure 1.).

TABLE 1 Comparison of patients and control group according to demographical, clinical and 25-OH vitamin D levels

	Acne Group (n = 134)	Control Group (n = 129)	P value
Age (years)	20,11 \pm 2,92	20,27 \pm 3,17	>.05
Sex (Female/Male) (%)	61,9 / 38,1	59,7 / 40,3	>.05
BMI (kg/m ²)	21,46 \pm 1,37	21,23 \pm 1,23	>.05
25-OH vitamin D levels (ng/ml)	14,17 \pm 7,42	20,27 \pm 3,17	.000
Classification of 25-OH vitamin D status			
Vitamin D deficiency n(%)	104 (77,6)	82 (63,9)	.041
Vitamin D insufficiency n(%)	28 (20,9)	43 (33,3)	>.05
Vitamin D sufficiency n(%)	2 (1,5)	4 (3,1)	>.05

TABLE 2 The comparison of 25-OH vitamin D status in patients with acne according to the severity of the disease

	Severity of disease				Total
	Mild 12 (9)	Moderate 15 (11.2)	Severe 64 (47.8)	Very severe 43 (32.1)	
Classification of 25-OH vitamin D status					
Vitamin D deficiency (≤ 20) n(%)	0 (0)	1 (6,7)	60 (93,8)	43 (100)	104 (77,6)
Vitamin D insufficiency (21–29) n(%)	11 (91,7)	13 (86,7)	4 (6,3)	0 (0)	28 (20,9)
Vitamin D sufficiency (≥ 30) n(%)	1 (8,3)	1 (6,7)	0 (0)	0 (0)	2 (1,5)

**FIGURE 1** Correlation of GAGS Scores and 25-OH vitamin D levels

4 | DISCUSSION

Acne vulgaris is a common, multifactorial, and complex skin disorder that affects the quality of social life in patients.^{6,9–11}

Vitamin D has many functions, such as regulating innate and adaptive immune systems and modulating calcium metabolism and homeostasis. It is reportedly associated with so many diseases, including systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, and some dermatological diseases, such as psoriasis, vitiligo, alopecia areata, and atopic dermatitis.^{12–16}

Some of previous studies about acne pathophysiology with vitamin D suggest a fictional role of vitamin D in acne development.

In Cramer et al's study; it was found that sebocytes, which play an important role in the pathogenesis of acne vulgaris expressed VDR and the enzymatic machinery to synthesize and metabolize biologically active vitamin D analogues and claimed that vitamin D endocrine system was of high importance for sebocyte function and physiology.¹⁷ On the other hand, inflammatory cytokines are the key factor in the pathophysiology of acne. Keratinocytes and sebocytes synthesize some inflammatory cytokines such as interleukin-1 β (IL-1 β), IL-6, IL-8, and tumor necrosis factor- α (TNF- α), both cell types can be activated by *P. acnes* via Toll-like receptors (TLRs), CD14, and CD1 molecules¹⁸ and it was found that expression of inflammatory biomarkers is influenced

by treatment with vitamin D in cultured sebocytes.¹⁹ Vitamin D regulates the growth and differentiation of keratinocytes and other cells as its bioactive form, 1,25-Dihydroxyvitamin D₃. Sebocytes were identified as bioactive vitamin D-responsive target cells, indicating that vitamin D analog may be effective in the treatment of acne.²⁰ Acne vulgaris is a multifactorial disorder of the pilosebaceous follicles of human skin and its pathogenesis has not been yet completely understood but the disease progress with chronic inflammation resulting from the immune response targeting *Propionibacterium acnes* plays a significant role in its pathogenesis. In one study, it was suggested that *P. acnes* induces strongly T helper-17 and T helper-1 and they evaluated whether Th17 cells are involved in the inflammatory response against *P. acnes*, they found both all-trans retinoic acid and 1,25-Dihydroxyvitamin D₃ suppressed Th17 generation, they suggested a role for retinoids and vitamin D in regulating the expression of genes required for Th17 differentiation.²¹

In our study we found significantly lower 25-OH vitamin D levels in the acne patient group than in the control group and a negative-strong statistically significant correlation detected between serum 25-OH vitamin D levels and GAGS scores in patients with acne vulgaris with a larger number of participants. There was no any result about relationship between PCOS and 25-OH vitamin D levels in our study due to absence of patients with PCOS.

As compared with similar studies in published data, in an Iranian study with 39 acne patients and 40 controls, no difference was reported in the median levels of 25-OH vitamin D between acne patients and controls, no correlation was found between the disease severity and 25-OH vitamin D levels unlike our results; however, 12 patients and 3 controls had PCOS in the study.²² Yildizgoren et al compared 25-OH vitamin D levels between 43 nodulocystic acne patients and 46 controls, it was found that patients with nodulocystic acne had lower 25-OH vitamin D levels compared to the individuals in the control group.⁶ In addition to Yildizgoren's study, we compared the disease severity with 25-OH vitamin D levels with a larger number of participants and studied acne patients with different stages. Similar to the study we detected lower 25-OH vitamin D levels in the very severe and severe acne group. In a South Korean study, 80 acne vulgaris patients were compared with 80 controls, and significantly higher prevalence of vitamin D deficiency (<12 ng/mL) was reported in the acne group. They also observed that oral vitamin D supplementation significantly resolved acne inflammation in a randomized controlled trial of 39 vitamin D-deficient acne patients.¹⁵ In a controlled study with 453 acne patients and 250 controls, authors also reported significantly higher prevalence of vitamin D

deficiency (<50 nmol/L) in acne vulgaris patients than in controls.²³ However, in three of the studies that mentioned above, correlation of the disease severity and 25-OH vitamin D levels were not assessed as our study.^{6,15,23} In a study from Egypt, El-Hamd et al compared 90 patients with acne vulgaris with 60 age- and sex-matched healthy individuals. They found that the serum levels of 25-OH vitamin D were significantly lower in patients with acne vulgaris than in healthy individuals, and there was a significant inverse relation between the levels of 25-OH vitamin D and severity of acne as our results. They also found that the serum levels of 25-OH vitamin D were significantly increased after systemic isotretinoin treatment in patients with acne vulgaris.²⁴

In a cross-sectional study from Kuwait, Al-Taiar et al observed 479 acne patients [379, mild acne (79.1%); 100, moderate acne (20.9%)], and no significant association was found between 25-OH vitamin D levels and acne vulgaris different from our results. In this study, the mean age was 12.28 years, and the patients had mild and moderate acne vulgaris; no participant had severe acne vulgaris.²⁵ Participants from our study group were older (the mean age was 20.11 ± 2.92 years) than participants from this study group. Disease severity in patients was higher in our study (patient group consisted of 32.1% very severe, 47.8% severe, 11.2% moderate, 9% mild) than in this study. And there was no evaluation the correlation of 25-OH vitamin D levels and disease severity.

Published data about 25-OH vitamin D levels and its association with acne vulgaris seems to be conflicting. We observed that vitamin D deficiency was seen in all patients of the very severe group, 93.8% patients of the severe group, and 6.7% of the moderate group.

Our study has some limitations. We could not observe whether the acne lesions in patients responded to vitamin D supplementation or not. In addition, we did not evaluate the status of vitamin D after systemic acne treatment with a case-control study with long-term period follow-up.

5 | CONCLUSION

In outpatient dermatology clinics, performing serum 25-OH vitamin D levels in especially severe acne patients may be considered as a routine laboratory work. With further studies, vitamin D supplementation may be considered as an alternative or co-treatment option.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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