

Serum Vitamin D Levels in Acne Vulgaris and its Relation to Acne Severity: A Case–Control Study

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Abstract

Background: Vitamin D plays an important role in acne vulgaris through its anti-inflammatory, comedolytic, anti-proliferative and antioxidant action. There is paucity of studies about vitamin D status in acne. Hence, we studied serum vitamin D levels in acne and also its association with acne severity and compared them with healthy age, sex, skin phototype matched controls.

Methods: Patients attending our outpatient department with acne vulgaris were included and graded according to Global acne grading system(GAGS). All cases and controls were investigated for serum vitamin D levels using Chemi luminescent Immuno Assay (CLIA).

Results: Forty cases and controls were taken after following inclusion and exclusion criteria. Vitamin D deficiency was observed in 42.5% of patients with acne, but only in 27.5% of the healthy controls and difference was significant. Moreover, an inverse correlation was found between serum vitamin D level and the GAGS score of acne. Pearson's correlation analysis value was -0.362 and the P value = 0.022.

Limitations: The study sample was small.

Conclusions: Serum vitamin D levels were lower in acne patients than in controls, and the levels were inversely correlated with acne severity.

Keywords: Acne vulgaris, Vitamin D, Global acne Grading System.

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Introduction

Acne vulgaris is a common chronic inflammatory disorder affecting the pilosebaceous unit that is seen primarily in adolescents. Most of the acne cases present with pleomorphic lesions consisting of

comedones, papules, pustules, nodules, and cysts of varying extent and severity. Acne occurs in all races worldwide, affecting nearly 90% of people at some point or another in their lifetime.[1] The global

prevalence of acne is 90%. [2] Acne is graded using the Global Acne Grading System Score (GAGS).[3] The major factors contributing to acne development are follicular hyperkeratinization, androgens, sebum, Cutibacterium acnes (C.acnes) and inflammation. [4]

Recently, vitamin D has been attracting attention due to its antioxidant properties in various diseases, including acne vulgaris. It seems that vitamin D facilitates the synthesis of antioxidants like superoxide dismutase (SOD) and glutathione peroxidase. These were found at lower levels in papulopustular cases of acne by a few authors. [5]

Acne induces Th-17 differentiation and, produces IL-17, an inflammatory cytokine, that is increased in acne. Vitamin D inhibits the production of this IL-17, thus reducing the inflammation, reiterating the role of vitamin D in the pathogenesis of acne. [6] Vitamin D regulates the immune system as well as the proliferation and differentiation of keratinocytes and sebocytes. It also has anti-comedogenic properties, along with antioxidant properties. Thus, vitamin D regulates the pathogenesis of acne.[7]

There are few studies reported globally on the relationship between acne vulgaris and vitamin D levels, with varied conclusions. However, there is a dearth of these studies in the Indian population. So, we compared serum levels of vitamin D between cases of acne vulgaris and age, sex, and skin phototype matched controls and also assessed the relation between serum vitamin D levels and severity of acne.

Materials and Methods

A hospital-based case control study was conducted in our outpatient department from October 2019 to June 2021. The study included a total of 40 acne patients of all ages along with 40 age, sex and skin phototype matched healthy controls. Demographic data such as age, sex, body

mass index (BMI), dietary habits, smoking and alcohol history, outdoor activity, menstrual history, history of PCOS, sunscreen usage history of earlier treatment were recorded. Cases receiving therapeutic interventions such as systemic corticosteroids, vitamin D supplements, PUVA and/or NB-UVB, use of oral contraceptive pills (OCP's) in the past three months, patients who used alcohol in the past three months, pregnancy, and lactation were excluded from the study. Clinical photographs of acne patients were taken after informed consent. Ethical approval was obtained prior to the study from the institutional ethical committee (GSLMC/RC:640-EC/640-09/19).

All the acne patients were classified into four categories: mild, moderate, severe, and very severe acne according to the Global Acne Grading System.(Table 1) Baseline venous blood samples (3 ml) were collected from patients and control groups under aseptic conditions. Serum vitamin D levels were estimated within 24 hours of sampling by Chemi Luminescent Immuno Assay (CLIA) using the Roche e411 analyzer at Megsan Diagnostic Centre, Hyderabad. The levels of 25(OH)D were classified as normal (≥ 30 ng/ml), insufficient (21–29 ng/ml), and deficient (≤ 20 ng/ml).

All data were analysed by SPSS statistical software 20.0 Version and MS Excel 2010. Mean, and the standard deviation was calculated. The correlation between the serum vitamin D levels and the severity of acne was evaluated by using Pearson's correlation analysis. P-value < 0.05 was considered statistically significant.

Results

Forty acne patients and forty age, sex and skin phototype matched healthy controls were included in the study. The majority of cases were between 21-30 years (65%) with a mean age distribution of 25.35 ± 5.376 years. Females outnumbered males (F:M =

2.3:1). Among the 40 cases, the majority belonged to mild and moderate grade in equal proportions, i.e., 14 each (35%), followed by severe (7 patients, 17.5%) and very severe (5 patients, 12.5%) grades. Out of 40 acne patients, the maximum number i.e., 35 (87.5%) patients showed decreased serum vitamin D levels. Among them, 18 (45%) patients were insufficient (21–29 ng/ml) and 17 (42.5%) were deficient (≤ 20 ng/ml). However, only 5 (12.5%) patients showed normal serum vitamin D levels (Table 2). The mean serum vitamin D level was lower in cases (22.235 ± 9.227 ng/ml) than controls (27.509 ± 10.954 ng/ml) and the difference was significant (Figure 1). Furthermore, the vitamin D deficiency (≤ 20 ng/ml) was observed

significantly more in acne patients (17 patients, 42.5%) than in healthy controls (11 patients, 27.5%). Serum vitamin D deficiency was more prevalent as the grade of acne progressed from mild to very severe. Moreover, on Pearson's correlation analysis (value = -0.362), a significant inverse correlation was found between serum vitamin D level and the GAGS score of acne, which indirectly depicts the negative relation between serum vitamin D levels and acne severity (P value = 0.022) (Figure 2). No significant correlation was seen between 25(OH)D levels and BMI, truncal acne, history of PCOD, dairy food intake, sunscreen usage, and daily sun exposure factors. (Table 3)

Table 1: The Global Acne Grading System (GAGS)

Location	Factor (F)
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest & Upper back	3

Severity (S)-0=no lesions, 1=comedones, 2=papules, 3=pustules and 4=nodules
Local score=F×S Acne severity: Mild=1-18, Moderate= 19-30, Severe=31-38, Very severe=>39

Table 2 : Distribution of patients with respect to serum vitamin D levels

Serum vitamin D levels (ng/ml)	Number of patients (n = 40)	Percent
Normal (> 30)	5	12.5%
Insufficient (21-29)	18	45%
Deficient (<20)	17	42.5%
Total	40	

Table 3 : Results of vitamin D deficiency according to influencing factors

	Total number of cases	No of patients with Vitamin D deficiency	P-Value
BMI			
< 25 Kg/M ²	30	25 (83.33%)	0.864
≥ 25 Kg/M ²	10	10 (100%)	
Truncal Acne			
Yes	20	11 (55%)	0.174
No	20	6 (30%)	
Sunexposure			
Yes	20	5 (25%)	0.062
No	20	12 (60%)	

Sunscreen Usage			
Yes	21	10 (47.6%)	0.729
No	19	7 (36.8%)	
Acne Severity			
Mild	14	8 (57.14%)	0.022
Moderate	14	8 (57.14%)	
Severe	7	4 (57.14%)	
Very Severe	5	3 (60%)	

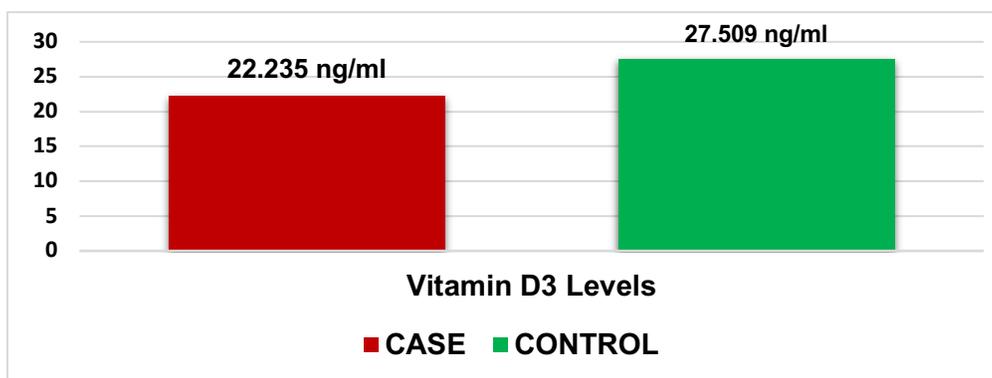


Figure 1: Mean Serum vitamin 25(OH)D level in cases and controls

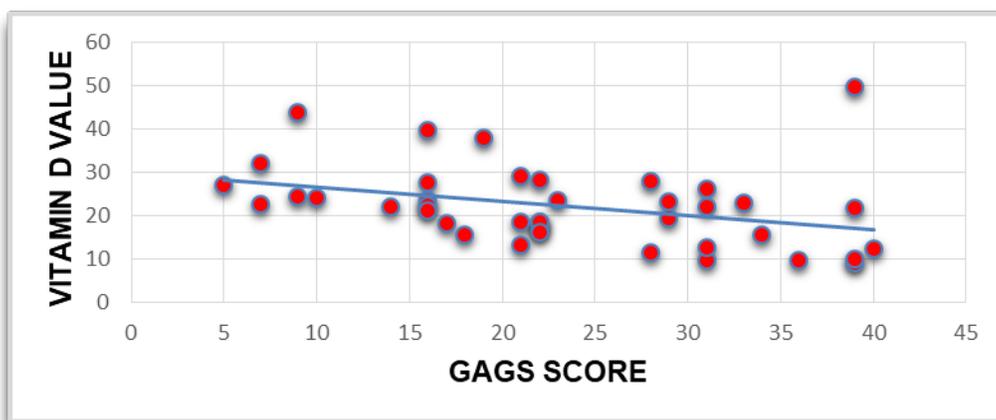


Figure 2: Correlation between serum vitamin D level and acne severity using the Global Acne Grading System (GAGS)

Discussion

Acne results from androgen-stimulated hyperkeratinization and the obstruction of the pilosebaceous follicles, which is secondary to the failure of the normal desquamation of the follicular epithelium, insulin-like growth factor 1 (IGF-1), and androgen-stimulated excessive production of sebum, and subsequent colonization of the follicles by *C.acnes*, along with an immune reaction. [1] In addition to the cosmetic

disfigurement, acne also causes psychological and social impairments in affected individuals. [8]

Vitamin D, originally described in rickets and osteomalacia, has now been shown to play a vital role in various dermatological and medical diseases. The link between acne and vitamin D levels has attracted attention recently. [9] It inhibits the production of IL-17, an inflammatory cytokine produced by

C.acnes, thus reducing the inflammation. Furthermore, its antiproliferative and comedolytic action was due to its effect on FOXO proteins and mTORC1 signalling. In AV, there is increased nuclear extrusion of FOXO1 proteins due to IGF-1 as well as increased mTORC1 signalling. Vitamin D is reported to increase FOXO1 transcriptional activity and downregulate the mTORC1 pathway. This not only shows its role as antiproliferative and comedolytic but also depicts the link between Vitamin D and a western or insulinotropic diet. [1]

In our study, among both cases and controls, the majority of patients belonged to the age group 21-30 years (65%), with a mean age distribution of 25.35 ± 5.376 years. Studies by Seul-Ki Lim et al,[10] Toossiet al,[5] AbdelAal M. et al,[11] Sultana T et al,[12] Yildizgoret al,[1] and El-Hamd MA et al,[8] also showed similar results. Females (70%) outnumbered males (30%), similar to other studies.

We observed lower mean serum vitamin D levels in cases when compared to controls, which were statistically significant. These results were compatible with studies done by Yildizgoret al,[1] and Alhetheli et al.[13] This is because serum vitamin D3 is reported to suppress the proliferation and stimulate the differentiation of keratinocytes. Thus, vitamin D deficiency may have resulted in comedogenics. [14]

In contrast, few studies like those by Seul-Ki-Lim et al,[10] and Singh et al,[14] found no significant difference in the mean serum vitamin D levels between cases and controls. The present study showed a higher prevalence of vitamin D deficiency in patients with acne (42.5%) than in healthy controls (27.5%), a finding that was significant. This was in harmony with previous studies by Seul-Ki-Lim et al,[10] and Singh et al,[14]. However, Toossi et al,[5] not only didn't find any significant difference in serum vitamin D levels

between cases and controls, and there was no significant association between severity of disease and serum vitamin D level as well. This could be due to low serum 25(OH) levels among Iranian population. However, we found a significant negative correlation between vitamin D levels and GAGS scoring of acne which indirectly establishes an inverse relation between vitamin D level and acne severity. AbdelAal et al,[11] Seul – Ki – Lim et al,[10] Singh A et al,[14] and Seul-Ki-Lim et al,[10] specifically found a negative correlation with inflammatory lesions but not with noninflammatory lesions.

Limitations

Limitations include the small number of patients taken into the study.

Conclusions

The present study found that vitamin D deficiency was more prevalent in patients with acne vulgaris and vitamin D levels were inversely correlated with disease severity, suggesting a pivotal role of vitamin D deficiency in acne pathogenesis. We conclude that vitamin D in acne being an intriguing topic nowadays, its importance should not be limited to its epidemiological and pathological role in acne vulgaris. Furthermore, its role in therapeutic management of acne should also be given equal importance and needs to be explored in future research to target multiple interlinked events in its pathogenesis.

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