

Association of Vitamin D with Moderate to Severe Acne Vulgaris

Tayyaba Iqbal¹, Sadaf Ahmed Asim¹, Sadia Bhatti¹, Madiha Sajid¹, Reema Mirza¹ and Zille Huma²

¹Department of Dermatology, Dow University of Health Sciences, Karachi, Pakistan

²Department of General Medicine, Dow University of Health Sciences, Karachi, Pakistan

ABSTRACT

Objective: To determine the association of vitamin D deficiency in moderate to severe acne.

Study Design: A comparative study.

Place and Duration of the Study: Dermatology OPD at Dow University of Health Sciences, Karachi, Pakistan, from December 2021 to May 2022.

Methodology: Fifty patients with moderate acne, 50 patients with severe acne, and 50 healthy controls were inducted. Information regarding age, gender, and medical and medication history were taken. The severity of acne was rated according to the GAGS (global acne grading system) score. Levels of 25(OH) D were classified as sufficient (>20 ng/mL), insufficient (12-20 ng/mL), or deficient (<12 ng/mL). Significance was taken at p-value <0.05.

Results: The median concentration of vitamin D levels was 7.09 ng/ml in severe acne vulgaris, 13.7 ng/ml in moderate acne vulgaris and 21.6ng/ml in the control group. Serum vitamin D levels were significantly lower (p<0.001) in individuals with acne vulgaris as compared to the healthy controls. However, the decrease in level of vitamin D did not correspond with the severity of acne vulgaris.

Conclusion: Vitamin D deficiency is additionally pronounced in acne vulgaris individuals, but vitamin D levels are not proportional to the severity of acne vulgaris.

Key Words: Acne vulgaris, Vitamin D deficiency, Pilosebaceous unit, GAGS score.

How to cite this article: Iqbal T, Asim SA, Bhatti S, Sajid M, Mirza R, Huma Z. Association of Vitamin D with Moderate to Severe Acne Vulgaris. *J Coll Physicians Surg Pak* 2023; **33(05)**:527-530.

INTRODUCTION

Acne vulgaris is caused by a long-standing inflammatory condition of the pilosebaceous unit, which can affect both males and females. On average, 75 to 95% of all teenagers suffer from acne to some extent.^{1,2} It is globally the eighth most prevalent disease with worldwide prevalence of 9.4%.³ The basic lesions of acne vulgaris are comedones, inflamed papules, pustules nodules, and cysts which are found in severe acne. It is commonly seen in teenagers group but can present in adults too. Pathogenesis of acne is not clearly understood, it may be associated with propionibacterium acnes resulting in hyperkeratinization, increased sebum production and inflammation. The other factors which can influence acne are vitamin D, diet, obesity, and hormonal imbalance.⁴

Vitamin D has several important functions: It plays a major role in calcium metabolism and homeostasis; it also has an impact on T and B lymphocytes, dendritic cells and macrophages through the innate and adaptive immune system.⁵ Many inflammatory diseases are associated with vitamin D deficiency like systemic lupus erythematosus, inflammatory bowel disease and rheumatoid arthritis. It also acts as an immune modulator in cutaneous disorders like psoriasis, atopic dermatitis, vitiligo, urticarial, and alopecia.^{6,7}

Deficiency of this vitamin can result in increased acne formation, as it regulates the sebocytes and keratinocytes proliferation and differentiation, and it also has anti-comedogenic properties.⁸ Vitamin D possesses anti-inflammatory effects through IL-6, IL-8 and matrix metalloproteinase 9. Vitamin D also decreases the expression of IL-17 which was induced by Propionibacterium acnes.⁹ Vitamin D deficiency increases the lipogenesis in the sebaceous glands which causes increase inflammatory lesions of acne. Newer studies show that sebaceous cells were considered as target cells for vitamin D¹⁰, which means calciferol can provide beneficial part in the treatment of acne.¹¹

The current local data regarding the association of vitamin D deficiency with acne is very limited, especially considering the

Correspondence to: Dr. Tayyaba Iqbal, Department of Dermatology, Dow University of Health Sciences, Karachi, Pakistan

E-mail: drtayyaba108@gmail.com

Received: October 25, 2022; Revised: April 03, 2023;

Accepted: April 07, 2023

DOI: <https://doi.org/10.29271/jcpsp.2023.05.527>

climate conditions and long hours of sun exposure. This study will be helpful if an association will be found between vitamin D measures in the body and the severity of the acne, and by correction of calciferol in the affected individual will result in early resolution of acne lesions and also other condition which was affected by vitamin D deficiency. The objective of this study was to determine the association of vitamin D deficiency in moderate to severe acne.

METHODOLOGY

This study was comparative research conducted from December 2021 to May 2022 at Dermatology OPD, Dow University Hospital, Dow University of Health Sciences after approval from the Ethical Committee of the Institute. It comprised a total of 150 patients (50 with severe acne, 50 with moderate acne and 50 controls). The sample size was calculated using PASS version 11 software, two independent sample proportions, 95% confidence interval, 80% power of the test, and 84.6%,¹² among acne and 75% in healthy prevalence of moderate and severe vitamin D deficiency patients.

Patients who fulfilled the inclusion criteria were enrolled. Written consent was taken from the patients. History regarding age, gender, previous history of any illness and medication history was taken. Vitamin D level was determined from all three groups.

Patients with moderate to severe acne vulgaris aged between 18 years to 50 years were included. Nursing and childbearing women, polycystic ovarian syndrome, patients on vitamin D supplements, multi-vitamins, steroids, hormonal treatment, patients on retinoid or history of oral retinoid over the last three months, and patients with chronic systemic diseases were excluded from this research.

Severity of acne was rated by GAGS score.¹³ In this score, forehead, each cheek, nose, chin, and trunk were examined for acne. Each area has its factor (1-3), the factor of forehead, right and left cheeks has a factor of 2 each, 1 each for nose and chin and 3 for trunk. Grade to each area were allotted on the basis of lesions like; comedones, papules, pustules, and nodules as 0, 1, 2, 3, and 4, respectively, then multiplied the factor with the grade score for each area. All the local scores were added. 1-18 score is classified as mild, 19-30 as moderate, 31-38 as severe, and >39 as very severe. Serum levels of 25 (OH) D were measured in both patients and controls. Venesection was done and blood was examined within a day. Vitamin D levels were classified as sufficient (>20 ng/mL), insufficient (12-20 ng/mL), or deficient (<12 ng/mL).^{14,15}

Recorded data were entered and analysed using the IBM SPSS Statistics 21.0 version to report descriptive statistics (Frequency and percentages, mean/SD or median/IQR where appropriate). The normality of quantitative variables (age, vitamin D) was assessed by using the Shapiro-Wilk's test. Associations were assessed between severity of acne vulgaris groups and age by using one way ANOVA test with the post hoc test (LSD) while severity of acne vulgaris groups with Vitamin D by using Kruskal Walli's test with the post hoc test (Mann-Whitney U-

test). Chi-square test was applied for the relation of gender with severity of acne vulgaris patients. A p-value of 0.05 was considered significant.

RESULTS

A total of 150 patients participated in this comparative study. The age group was 18 years to 50 years, mean age being 27.7 ± 7.4 years, 60(40%) patients were male and 90 (60%) were female. The Median concentration of vitamin D levels in patients with severe acne vulgaris was 7.09 ng/ml, in patient with moderate acne vulgaris was 13.7 ng/ml, and in the control group it was 21.6ng/ml. This shows that levels of vitamin D were lesser in individuals with acne vulgaris as compared to the healthy controls, which is statistically significant with p-value of <0.001 (Table I). But there was no relation of serum vitamin D levels with the severity of acne vulgaris.

DISCUSSION

Vitamin D takes a major part in the differentiation and proliferation of keratinocytes and sebocytes. The active vitamin D metabolites target the sebocytes and keratinocytes *via* the nuclear vitamin D receptors. Decreased vitamin D levels causes alteration in the pattern of pilosebaceous follicular keratinization promoting comedogenesis and exacerbation of acne vulgaris.¹⁶

The research was done to assess the relationship of vitamin D levels with acne vulgaris as there is very limited data available. It was observed in this research that the levels of vitamin D in the acne vulgaris patients were lower than the vitamin D levels in the healthy individuals, but its levels are not proportional to the severity of acne vulgaris and these findings are similar with the other study.¹⁷ Factors causing Vitamin D deficiency were not evaluated in this study like sun exposure, psychological impact of acne, and treatment taken for acne, especially isotretinoin. A study conducted in Saudi Arabia by Alhetheli *et al.* concluded that serum levels of vitamin D in controls were significantly higher than those in acne vulgaris patients, and found that there is no relationship between sun exposure and improvement in vitamin D readings in acne vulgaris patients.¹⁷

In this study, the mean age was 27.7 ± 7.4 years and 40% of patients were male, these population were mostly not restricted to home and getting the sufficient amount of sunlight, so despite sufficient sun exposure, patients are vitamin D deficient, and these findings are similar to the findings of Al-Taira *et al.*, who conducted the study in Kuwait and concluded that vitamin D deficiency was detected in adolescents, in presence of hot climates, and sufficient sun-exposure in the Arabian Gulf.¹⁸

In the current study, no significant difference was found in the vitamin D levels between males and females in either control groups or in acne vulgaris patients and this finding is line up with the study which was conducted in 2019 in Egypt by Elmohsen *et al.* who also revealed a decrease concentration of vitamin D in acne patients.¹⁹

Table I: Relationship of age, gender, and vitamin D with groups.

Characteristics	Control N = 50	Moderate N = 50	Severe N = 50	p-value
Age (years), mean ± SD	32.5±8.2	25.3 ^a ±5.2	25.4 ^a ±5.9	<0.001 ^f
Vitamin D (ng/ml), median (IQR)	21.6 (20.3)	13.7 ^b (8.9)	12.5 ^b (7.02)	<0.001 ^a
Gender				
Male	25 (50.0)	15 (30.0)	20 (40.0)	0.125 ^b
Female	25 (50.0)	35 (70.0)	30 (60.0)	

^fOne Way ANOVA, ^aPost-hoc (LSD) test represents no significant mean difference. ^aKruskal Wallis, ^bMann-Whitney test represents no significant mean difference, ^bChi-square test.

A similar study conducted in Turkey by Yildizgören *et al.* concluded that relatively less amount of vitamin D was found in patients with nodulocystic acne.²⁰ This finding was similar with the present study coinciding with the severe variety of acne vulgaris. The study conducted in Korea by Choi *et al.* showed minor differences in the levels of vitamins D in acne vulgaris patients and in healthy population. This is because of the characteristic low vitamin D levels in the Korean population.²¹ Similar research done in Kuwait also concluded that vitamin D supplements are required in acne vulgaris treatment as it regulates the function of sebocytes.²²

The limitation of this study was that the sample size was small, larger numbers of subjects should be included in the study to demonstrate the relation between vitamin D levels and severity of acne.

It is a single-centred study and the factors associated with either vitamin D deficiency or acne vulgaris were not evaluated or excluded.

CONCLUSION

There is a possible association of vitamin D deficiency with acne vulgaris and vitamin D deficiency has the significant impact on the development of acne.

ETHICAL APPROVAL:

The study was conducted in the Dermatology OPD after approval from the Ethical Committee of the Dow University of Health Sciences.

PATIENTS' CONSENT:

Written consent was taken from all the patients.

COMPETING INTEREST:

There were no potential competing interests and no funding from pharmaceutical companies.

AUTHORS' CONTRIBUTION:

TI: Data collection and design of work.

SAA: Final approval of the version.

SB: Drafting the manuscript.

MS, RM: Data analysis and interpretation.

ZH: Critical revision of the manuscript.

All authors have approved the final version of the manuscript to be published.

REFERENCES

- Shamban AT, Narurkar VA. Multimodal treatment of acne, acne scars and pigmentation. *Dermatol Clin* 2009; **27(4)**: 459-6. doi:10.1016/j.det.2009.08.010.
- Yan HM, Zhao HJ, Guo DY, Zhu PQ, Zhang CL, Jiang W. Gut microbiota alterations in moderate to severe acne vulgaris patients. *J Dermatol* 2018; **45(10)**:1166-71. doi: 10.1111/1346-8138.14586.
- Alshammrie FF, Alshammari R, Alharbi RM, Khan FH, Alshammari SK. Epideriology of acne vulgaris and its association with lifestyle among adolescents and young adults in Hail, Kingdom of Saudi Arabia: A community-based study. *Cureus* 2020; **12(7)**:e9277. doi: 10.7759/cureus.9277.
- Contassot E, French LE. New insights into acne pathogenesis: Propionibacterium acnes activates the inflammation. *J Invest Dermatol* 2014; **134(2)**:310-3. doi:10.1038/jid.2013.505.
- Bhalla AK, Amento EP, Clemens TL, Holick MF, Krane SM. Specific high-affinity receptors for 1,25-dihydroxyvitamin D3 in human peripheral blood mononuclear cells: presence in monocytes and induction in T lymphocytes following activation. *J Clin Endocrinol Metab* 1983; **57**:1308-10. PMID:63 13738.
- Cheng HM, Kim S, Park GH, Chang SE, Bang S, Won CH, *et al.* Low vitamin D levels are associated with atopic dermatitis, but not allergic rhinitis, asthma, or IgE sensitization, in the adult Korean population. *J Allergy Clin Immunol* 2014; **133(4)**:1048-55. doi: 10.1016/j.jaci.2013.10.055.
- Bhat YJ, Latif I, Malik R, Hassan I, Sheikh G, Lone KS, *et al.* Vitamin D Level in Alopecia Areata. *Indian J Dermatol* 2017; **62(4)**:407-10. doi: 10.4103/jid.IJD_677_16.
- Lim SK, HaM, Lee YH, Lee Y, Seo YJ, Kim CD, *et al.* Comparison of vitamin D levels in patients with and without acne; A case-control study combined with a randomised controlled trial. *Plos One* 2016; **11(8)**: e0161162. doi:10. 1371/journal.pone.0161162.
- Agak GW, Qin M, Nobe J, Kim MH, Krutzik SR, Tristan GR, *et al.* Propionibacterium acnes Induces an IL-17 Response in acne vulgaris that is regulated by Vitamin A and Vitamin D. *J Invest Dermatol* 2014; **134(2)**:366-73. doi: 10.1038/jid.2013.334.
- Lee WJ, Choi YH, Sohn MY, Lee SJ, Kim DW. Expression of Inflammatory Biomarkers from Cultured Sebocytes was influenced by Treatment with Vitamin D. *Indian J Dermatol* 2013; **58(4)**:327. doi: 10.4103/0019-5154.113959.

11. Reichrath J. Vitamin D and the skin: An ancient friend, revisited. *Exp Dermatol* 2007; **16(7)**:618-25. doi: 10.1111/j.1600-0625.2007.00570.x.
12. Toossi P, Azizian Z, Yavari H, Fakhim TH, Amini SH, Enamzade R. Serum 25-hydroxy vitamin D levels in patients with acne vulgaris and its association with disease severity. *Clin Cases Miner Bone Metab* 2015; **12(3)**:238-42. doi: 10.11138/ccmbm/2015.12.3.238.
13. Doshi A, Zaheer A, Stiller MJ. A comparison of current acne grading systems and proposal of a novel system. *Int J Dermatol* 1997; **36(6)**:416-8. doi: 10.1046/j.1365-4362.1997.00099.x.
14. Institute of medicine committee to review dietary reference intakes for Vitamin D, Calcium. The national academies collection: Reports funded by national institutes of health in: Ross AC, Taylor CL, Yaktine AL, Del Valle HB. editors. *Dietary Reference Intakes for Calcium and Vitamin D*. Washington (DC): National academies press (US) National academy of sciences; 2011.
15. Witkowski JA, Parish LC. The assessment of acne: An evaluation of grading and lesion counting in the measurement of acne. *Clin Dermatol* 2004; **22(5)**:394-7. doi: 10.1016/j.clindermatol.2004.03.008.
16. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. *Lancet* 2012; **379**:361-72; dx.doi.org/10.1016/S0140-6736(11)60321-8.
17. Alhetheli G, Elneam AIA, Alsenaid A, Al-Dhubaibi M. Vitamin D Levels in patients with and without acne and its relation to acne severity: A case-control study. *Clin Cosmet Investig Dermatol* 2020; **13**:759-65. doi: 10.2147/CCID.S271500.
18. Al-Taiar A, AlKhabbaz M, Rahman A, Al-Sabah R, Shaban L, Akhtar S. Plasma 25-hydroxy vitamin D is not associated with acne vulgaris. *Nutrients* 2018; **10(10)**:1525. doi: 10.3390/nu10101525.
19. Elmohsen A, Abd El-Aziz H, AboMohamed N, Dabash A. Assessment of serum level of 25-Hdroxy Vitamin D in patients with Acne Vulgaris. *Egypt J Hosp Med* 2019; **76(3)**:3678-83. doi: 10.21608/ejhm.2019. 39909.
20. Yildizgören MT, Togrul AK. Preliminary evidence for vitamin D deficiency in nodulocystic acne. *Dermatoendocrinol* 2015; **6(1)**:e983687. doi: 10.4161/derm.29799.
21. Choi HS, Oh HJ, Choi H, Choi WH, Kim JG, Kim KM, et al. Vitamin D insufficiency in Korea -- a greater threat to younger generation: The Korea National Health And Nutrition examination survey (KNHANES) 2008. *J Clin Endocrinol Metab* 2011; **96(3)**:643-51. doi: 10.1210/jc.2010-2133.
22. Kramer C, Seltmann H, Seifert M, Tilgen W, Zouboulis CC, Reichrath J. Characterisation of the vitamin D endocrine system in human sebocytes *in vitro*. *J Steroid Biochem Mol Biol* 2009; **113(1-2)**:9-16. doi: 10.1016/j.jsbmb.2008.10.010.

.....