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Original Article

Correlation between the severity and type of acne vulgaris lesions with serum vitamin D levels: A cases control study of HIT Hospital, Taxila

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Abstract

Objective Vitamin D plays a crucial role in various physiological processes, including immune regulation, inflammation, and sebaceous gland function, all of which are relevant to acne pathogenesis. The objective of the study is to determine association between Severity and Type of Acne Lesions with Serum Vitamin D Levels.

Methods This case control study included 162 unmarried females of 12-30 years of age entitled to HIT hospital treatment were enrolled through random sampling technique, out of which 71 females with acne were taken as cases and 91 matching healthy controls were enrolled. History of vitamin supplementation in the last 6 months, acne treatment, systemic steroids or any chronic inflammatory disease were not included. GAG score was used to grade the acne and Vit. D levels were sorted as deficient (<30 nmol/L), inadequate (30-75nmol/L) and adequate (>75nmol/L). The data was entered and analyzed using SPSS-28. t-test was used for comparing Vitamin D levels among cases and controls. To correlate the sub groups of acne and vitamin D among cases and controls, chi square test was performed, p-value, when <0.05 was considered statistically significant.

Results Mean age of participants with acne vulgaris was 19.23±7.42 while the mean age of controls was 21.4±6.97. Statistically significant association was found between mean vitamin D levels among cases and controls (p-value=0.024). Moreover, a statistically significant relation was found between acne vulgaris severity and vitamin D levels (p-value= 0.047).

Conclusion This study showed Vitamin D deficiency is evident in acne vulgaris patients and a statistically significant association with the severity of acne lesions.

Key words
Acne Vulgaris; Vitamin D; GAG score.

Introduction

Acne vulgaris is a prevalent inflammatory disorder affecting pilosebaceous unit among the young population globally. Currently, the research has highlighted four key steps that contribute to acne development; blockage of follicular ostium, entrapment of Propionibacterium acnes (P. acnes), increase in

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sebum production stimulated by androgen, and very essentially, inflammation.[1,2]

Vitamin D, a fat-soluble seco-steroid, is primarily synthesized in the basal layer of the skin. When exposed to UVB radiation for 15-20 minutes, the skin can produce approximately 250 micrograms (10,000 IU) of vitamin D, assuming minimal erythema occurs.[3,4] The precursor of vitamin D, 7-dehydrocholesterol, is present in the plasma membranes of epidermal basal keratinocytes and fibroblasts. Upon UVB exposure, it is converted to pre-vitamin D3, which is then released into the systemic circulation and binds to vitamin D-binding protein (DBP). Subsequently, vitamin D undergoes hepatic hydroxylation to form 25-hydroxyvitamin D (calcidiol), and finally, in the kidney, it is further transformed into its active form, 1,25-dihydroxy vitamin D (calcitriol).[3-5]

Vitamin D and it`s VDR (vitamin D receptor) play significant roles in the skin biology. The presence of calcium and vitamin D3 influence the differentiation process of keratinocyte, leading to various interconnected functions.[5] These include keratinocyte envelope formation, promote differentiation, and inhibit proliferation.[6,7] Moreover, the innate immune response is regulated by inducing toll like receptor 2 [TLR2] and its co-receptor [CD14].[4]

It has been stated that the vitamin D system [25OHase, 24OHase, 1aOHase, and, VDR] is strongly expressed in sebaceous glands. It has been established that the synthesis and metabolism of vitamin D can be of significance for growth regulation and cellular functions in sebaceous glands.[4,6]

Propionibacterium acnes (P. acnes) induces inflammation through the Th17 pathway. Vitamin D [1,25OH2D} prevents P. acnes-induced Th17 differentiation, and therefore, it can be considered effective to modulate acne. Moreover, sebocytes are identified as vitamin D [1,25OH2D] target cells, and alteration in inflammatory biomarkers is indicative that vitamin D (analogs) can be effective for acne treatment.[7]

Study in Saudi Arabia reported 40% of patients with AV had deficiency in serum 25(OH)D level, but only 28.8% of the healthy control with no significant variation between gender and sun exposure.[8] Study in Iran also reported serum 25(OH) level in patients with AV lower than healthy control.[9] While study in Kuwait reported there is no significant correlation between serum 25(OH) level with AV severity.[10]

These days, studies about correlation between serum vitamin D level and Acne Vulgaris severity are still debated, so we evaluate correlation between serum vitamin D and Acne vulgaris severity.

Methods

After formal ethical approval from IRB of HITEC-IMS Taxila. This case control study was done in outpatient Dermatology Department of HIT hospital from Jan 23 to June 23. Sample size was calculated using.[11]

$$\frac{r+1}{r}\frac{SD(Z\beta+Z\alpha/2)^2}{d^2}$$

A total of 162 unmarried females aged 12-30 years, entitled to HIT hospital were enrolled in the study using random sampling technique. Among them 71 females with acne were selected as cases and 91 healthy matching controls were enrolled. Females with history of vitamin supplementation in the last 6 months, acne treatment, systemic steroids or any chronic inflammatory disease were not included.

Informed written consent was obtained from all

participants, and examination was done by Dermatologist. Demographic information like age, height and weight, sunscreen use was noted. Acne was graded using Global Acne Grading System (GAGS) score (0=None, 1-18= Mild, 19-30=Moderate, 31-38= Severe, >39= Very severe).

Serum 25-hydroxyvitamin D3 (25(OH)D) levels of both cases and control were measured. Blood samples were collected from veins and analyzed within 24 h of sampling using the Elecsys and Cobas e analyzer (Roche Diagnostics System, Switzerland). Levels of 25(OH)D were categorized as adequate=>75 nmol/L, inadequate= 30-75 nmol/L and deficient =<30 nmol/L.[12]

The data was entered and analyzed using SPSS-28. t-test was used for comparing Vitamin D levels among cases and controls. To correlate the sub groups of acne and vitamin D among cases and controls, chi square test was performed, p-value, when <0.05 was considered statistically significant.

Results

In our study 71 females with acne vulgaris between 13-30 years of age, 14 (19.7%) out of 71 cases have vitamin D deficiency while 16 (17.5%) out of 91 matching controls had vitamin D deficiency. The age range was 12-30 years with mean age of participants with acne vulgaris was 19.23±7.42 while the mean age of controls was 21.4±6.97. Only 11.26% (8) out of 71 cases and 19.7% (18) out of 91 controls were using sunscreen as shown in **Table 1**.

Table 1 Clinical and Lab Data of Studied Groups

Variables	*Cases (n= 71)*	*Control (n=91)*
Age (range)	12-30 year	12-30 years
Mean	19.23	21.4
SD	± 7.42	± 6.97
Use of sun screen		
Positive N%	11.26%	19.7%
Negative N%	88.74%	80.3%
Acne severity		
Mild	18 (25%)	
Moderate	38 (54%)	
Severe	12 (17%)	
Very severe	3 (4%)	
Vitamin D levels		
Mean	43.14	52.63
SD	± 17.954	± 31.244
Vitamin D status		
Adequate	7 (9.85%)	18 (19.78%)
Inadequate	50 (70.4%)	57 (62.63%)
Deficient	14 (19.71%)	16 (17.58%)

Table 2 Comparison of Vitamin D levels among Cases and Control.

	N	*Mean*	*SD*	*p-value*
Cases	71	43.14	17.954	0.024
Control	91	52.63	31.244	

Statistically significant association was found between mean vitamin D levels among cases and controls (p-value= 0.024) as shown in **Table 2**. Regarding the relationship between severity of acne vulgaris and vitamin D levels statistically significant positive association was observed among cases as shown in **Table 3**.

Frequency distribution of severity of acne vulgaris is shown in **Figure 1**.

Discussion

Vitamin D is also called "sunshine vitamin" because of its synthesis in keratinocytes after

Table 3 Relationship between Acne severity and Vitamin D levels.

		Vitamin D levels				*p-value*
		Adequate	*Inadequate*	*Deficient*	*Total*	
Acne severity	Mild	1	12	5	18	0.047
	Moderate	3	31	4	38	
	Severe	3	4	5	12	
	Very severe	0	3	0	3	
Total		7	50	14	71	

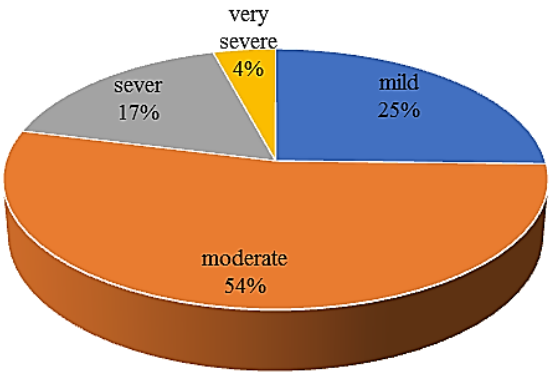

Figure 1 Frequency distribution of acne vulgaris severity.

sun exposure. Not only is it produced in the skin but it also regulates the keratinization process. Its influence on sebaceous gland cannot be overlooked. Several exogenous and endogenous factors involved in the pathogenesis of acne have already been studied but the data on the role of vitamin D in acne vulgaris is limited. Keeping in mind the anti-inflammatory and antimicrobial properties of vitamin D we anticipated finding its relationship with acne vulgaris. An adequate level in the body may help address the inflammatory lesion of acne.

The results of this case control study revealed that the mean age of participants with acne vulgaris was 19.23±7.42 while the mean age of controls was 21.4±6.97 which is similar to a case control study done by Elmohsen *et al.* in Egypt and Kemeriz *et al.* in Turkey.[13,14]

In our study, we found that vitamin D levels in acne vulgaris patients were lower than in controls, a statistically significant association was revealed. These findings align with a comparative study done in Pakistan (2023) by T Iqbal *et al*.[15] Another cross-sectional study done in Saudi Arabia by Alhetheli also showed vitamin D deficiency in acne vulgaris in comparison to healthy controls and added that there is no relation between sun exposure and an increase in vitamin D levels in acne patients (p-value=0.546 among +ve and -ve sun exposure in acne patients).[8] A Korean study reported that vitamin D level was significantly and negatively associated with inflammatory lesions of acne patients ($P< 0.05$ and $r=-0.512$), at the same time, no such relation was established between the non-inflammatory lesion and vitamin levels indicating a connection between the severity of inflammation with the degree of vitamin D deficiency.[12]

However, it`s important to note that the literature on this topic is diverse and show difference of opinion regarding the association of the severity of acne with vitamin D levels is concerned. In our study, a statistically significant relation was found between acne vulgaris severity and vitamin D levels which is consistent with the study done in Turkey (2020) by Kemeriz *et al.* and in Indonesian study stating a strong -ve correlation ($P= <0.05$, $r= –0.719$) between serum Vit D levels and severity of AV.[14,16] This is further supported by the clinal trial done in Eygpt (2023) by Abdelaziz *et al.* evaluating the impact of vit. D supplements which showed 60% of acne vulgaris patients when treated with vitamin D supplements downgrade to stage zero as compared to 9% of the patients treated with topical treatment.[17] Similarly, a study done in Saudi Arabia by Al-Dhubaibi evaluating the role of vitamin D found a significant rise in plasma levels of vit D three months after starting isotretinoin.[18] However, studies done by T Iqbal and Alhetheli showed no significant association between acne severity and Vit. D levels.[8,15] A Turkish study evaluated C- reactive protein and vit. D levels among cases and control showed no significant association.[19]

We found that only 19.7% of the controls and 9.8% of the cases have adequate levels of vitamin D which is probably to the dress code practices in Pakistan. In this study we do not evaluate factors the effect Vit. D levels like

psychological stress or morbidities, dietary factors, sun exposure duration that in one way or the other effect serum levels. Moreover, the small sample size, lack of multicenter involvement and we have not evaluated vit. D levels in cases after treatment are the limitations of this study.

Conclusion

In conclusion, while our study suggests a significant association between lower vitamin D levels and acne vulgaris severity. Addressing the limitations and conducting well-designed studies will contribute to a better understanding of the potential role of vitamin D in the management and treatment of acne vulgaris.

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