

## Effect of Vitamin D Supplementation on Patients with Acne Vulgaris: An Intervention Study

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### Abstract:

**Background:** Acne is chronic inflammatory disease with formation of papules, pustules, and nodules. Vitamin-D is fat soluble vitamin with immunomodulatory function, helps reducing inflammation. **Objectives:** assess frequency of serum vitamin-D deficiency among acne vulgaris patients and the effect of vitamin-D supplementation on acne grading. **Method:** the study was conducted on two phases, phase I was a cross-sectional study included measuring serum vitamin D level for 80 acne patients attending dermatology clinic at Menoufia University Hospital. Phase II was an interventional case control study where studied acne patients with vitamin-D deficiency (66 patients) were randomly divided into two groups; one group (33 patients) were treated with free Oral vitamin-D 2000IU/ tablet daily for two months in addition to regular acne treatment. The other group (33 patients) received traditional treatment for acne without vitamin-D supplementation and both groups were followed up clinically for two months. **Results:** frequency of vitamin-D deficiency among studied patients was 82.5%, there was statistically significant relation between vitamin-D deficiency and severity of acne as 27.3% and 9.1% of them had grade 3& 4 acne respectively versus 7.1% and zero% among acne patients with normal vitamin D. Vitamin-D deficiency is significantly prevalent among female patients (98.4%), there was significant improvement in acne grading after vitamin-D supplementation. **Conclusion:** There is a significant relation between vitamin-D deficiency and severity of acne vulgaris and vitamin -D has a good role in management of acne. So. It is recommended to evaluate the serum level of vitamin D in acne patients and provide vitamin D supplementation to vitamin D deficient patients beside topical treatments for acne.

**Keywords:** Acne, Vitamin-D Supplements, Topical Treatment

### Introduction:

Acne Vulgaris is a common skin disorder worldwide, affecting all ages and races, considered as a long term chronic inflammatory disease of the skin.<sup>(1)</sup> It affects nearly 85% of adolescents <sup>(2)</sup> and about 30% of adults which is known as post- adolescent acne that often occurs in individuals aged 25 years or older particularly women.<sup>(3)</sup> Acne lesions, which may be papules, pustules, or nodules commonly affecting face, chest and back therefore acne patients may suffer from emotional distress due to its chronicity and potential outcomes which include physical scars and persistent hyperpigmentation.<sup>(4)</sup>

Some medical conditions predispose acne vulgaris like polycystic ovaries (PCO), congenital adrenal hyperplasia and depression. Acne is characterized by pimples, scaly red skin, blackheads, whiteheads, pinheads, and large papules. The most distressing form of acne is called cystic acne, which develops internally beneath the skin, whereas most other forms of acne are more superficial.<sup>(5)</sup> Although multiple factors contribute to acne development, chronic inflammation is an important mechanism. Several inflammatory mediators such as cytokines, defensins have been identified in acne lesions.<sup>(6)</sup>

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Vitamin D plays a role in regulating immune system, proliferation, and differentiation of keratinocytes and sebocytes. It has antioxidant and anti-comedogenic properties.<sup>(7)</sup> So, vitamin D deficiency has a positive role in pathogenesis of acne vulgaris.<sup>(8)</sup>

Vitamin D is fat-soluble substance that is synthesized in human body when the skin is exposed to ultraviolet (UV) light and it can be obtained exogenously through dietary intake. Vitamin D has an important impact on skin health, its deficiency is associated with many dermatological disorders.<sup>(9)</sup> Acne vulgaris appears to be seasonal, with the winter months seeing the most severe form of disease, however in summer months (when vitamin D levels are higher), there is significant improvement in acne lesions.<sup>(10)</sup>

Vitamin D is considered as antioxidant agent that has positive effect on acne vulgaris. It seems that vitamin D makes superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) which were found at lower levels in papulo-pustular cases of acne.<sup>(11)</sup>

Since the antimicrobial role of vitamin D is the new issue to be raised by many authorities and social cultures and focused on now as a treatment. This study was conducted to highlight the effect of vitamin D supplementation on treating acne patients. The study aimed to assess frequency of serum vitamin-D deficiency among studied acne patients and the effect of vitamin-D supplementation on acne grading.

## Methods:

This study was conducted on acne patients who were recruited from dermatology outpatient clinics, Menoufia University Hospital, Egypt in the time frame from May 2019 to April 2020. The sample size was calculated to be 78 acne patients using Raosoft online sample size calculator with power of 80%, confidence interval of 95% based on the prevalence of acne vulgaris in adult patients from the previous literatures (93.2%),<sup>(10)</sup> the sample was increased to 90 to compensate for the dropout and data loss.

Ten patients withdrew from the study during the follow up stage and the study was conducted finally on 80 acne vulgaris patients. Based on their previous medical history; certain acne patients were excluded from the study e.g., those with topical or systemic treatment with steroids, diabetes mellitus, thyroid disorders (increased comedogenesis), hepatic enzyme inducers (accelerated vitamin D metabolism), Chronic liver or renal diseases (metabolic disturbances), females with PCO (hyperandrogenism and increased comedogenesis) and acne patients receiving vitamin D or calcium supplementation.

The studied acne patients who accepted to participate in the study and fulfilled the exclusion criteria were selected from a total of 230 acne patients who attended the dermatology clinic during period of data collection. The study was conducted on two phases; the first phase

was cross-sectional study to assess frequency of vitamin D deficiency among the studied group.

The severity of acne vulgaris was assessed by clinical examination according to: Tutakne<sup>(12)</sup> grading system for acne which classifies acne vulgaris into four grades as follows: **Grade 1:** Comedones, occasional papules, **Grade 2:** Papules, comedones, few pustules (1-3), **Grade 3:** Predominant pustules >3, nodules, abscesses, **Grade 4:** Mainly cysts, abscesses, widespread scarring.

Blood samples (2 ml ) withdrawn once to assess vitamin D level in the studied acne patients after having their consent where normal vitamin D level is > 30 ng/dl, level 20 ng-30 ng/dl is insufficient, level < 20 ng/dl is deficient.<sup>(13)</sup> Then the acne patients with vitamin D deficiency (66 patients) were randomly divided into two groups using computer-based randomization to start the second phase of the study as a case control study. The case group (33 patients) were treated with maintenance dose of free oral vitamin D 2000IU per tablet daily<sup>(14)</sup> for 2 months besides regular treatments of acne. The control group (33 patients) received traditional treatment for acne vulgaris without vitamin D supplementation. Both groups were followed up clinically after two months.

The control group received vitamin D supplementation after the follow up stage of the study for ethical considerations. Digital photos for acne lesions before and after treatment were obtained from participants after having their written consent.

**Data Management:** Statistical presentation and analysis of the present study was conducted with SPSS V.20, X2 (*Chi 2 test*): for comparison between two independent qualitative variables normally distributed. *F test*: for comparison of two statistical models that have been fitted to a data set, P value > 0.05 was considered statistically non-significant, P value < 0.05 was considered statistically significant, P value < 0.001 was considered statistically highly significant.

**Ethical consideration:** The study was approved by the ethical committee of the Faculty of Medicine, Menoufia University. All participants were volunteers, written consents were taken from patients after explaining the purpose of the study and assuring confidentiality.

### Results:

This study shows that frequency of vitamin D deficiency among the studied acne patients was 82.5% (**Figure 1a**). Vitamin D deficiency was significantly more prevalent among female acne patients (98.4%) (**Figure 1b**). There was a significant negative correlation between acne grade and serum level of vitamin- D (**Figure 2**). A statistically significant relationship was found between serum vitamin D level and severity of acne vulgaris as 27.3% and 9.1% of vitamin D deficient group had grade 3& 4 acne respectively versus 7.1% and 0 % among acne patients with normal vitamin D (**Table 1**).

Also, there was statistically significant relationship between the mean level of vitamin-D and grade of acne vulgaris among the studied

group, where the mean serum vitamin D level was the lowest among patients with 4th grade acne ( $5.2 \pm 1.7$ ) (**Table 2**). After vitamin D supplementation, there was significant improvement in acne grading where about 60% of acne patients treated with vitamin D supplementation reached stage zero of acne versus 9% among those treated with topical treatments only without supplementations. Also no patients treated with vitamin D supplementation have acne grade III or IV versus 9% of those treated only with topical treatments still have acne stage III (**Table 3**).

#### Discussion:

The results of this study revealed increased frequency of vitamin D deficiency among the studied acne patients (82.5%). This comes in accordance with a study conducted in Turkey<sup>(15)</sup> where prevalence of vitamin D deficiency was 95.3% among 43 acne patients. Lim et al<sup>(16)</sup> study in Southeast Asia reported that the prevalence of vitamin D deficiency was significantly higher among patients with acne (48.8%) in comparison to healthy controls (22.5%).

Further support for these results showed by recent studies conducted in Egypt<sup>(17)</sup> and in Saudi Arabia<sup>(18)</sup> on acne patients versus matched healthy controls and reported that Serum levels of 25-hydroxy-vitamin D was significantly lower in acne patients than in healthy control. The same results were obtained from Elmohsen et al study<sup>(19)</sup> which was performed on 60 Egyptian acne vulgaris patients

and 30 healthy controls and found significantly lower serum levels of vitamin D in acne patients than in the healthy controls. These findings from different studies indicate that there is a significant relation between vitamin D levels and acne vulgaris and this is contributed to the potent anti-inflammatory effect of vitamin D. However, a cross-sectional study<sup>(20)</sup> conducted on 714 Kuwaiti adolescents showed no significant association between 25-OH-Vitamin D level and clinically assessed acne vulgaris.

This study reported increased frequency of vitamin D deficiency among female acne patients (98% -  $p$  value  $< 0.001$ ) in comparison to males. A study in Italy<sup>(21)</sup> investigated the impact of gender difference on vitamin D and they found that female gender was associated with severe vitamin D deficiency (41.9% vs. 30.4%,  $p < 0.001$ ). However, a study<sup>(22)</sup> conducted on adult Saudi population found that males had a higher prevalence of vitamin D deficiency (72.0% vs. 64.0%) when compared to female participants and Puspita et al study<sup>(23)</sup> conducted in Indonesia reported higher mean serum vitamin D level in females (18.5 ng/mL) than males (16.68 ng/mL).

This difference may be attributed to the increased prevalence of obesity among Egyptian females in comparison to males according to WHO report<sup>(24)</sup> and since vitamin D is a fat-soluble vitamin it's highly stored in body fat with low peripheral serum level<sup>(22)</sup>.

As regard the relationship between serum vitamin D level and severity of acne vulgaris;

this study revealed that 27.3% and 9.1% of vitamin D deficient group had grade 3& 4 acne respectively and the mean vitamin D level was the lowest among patients with 4th grade acne ( $5.2 \pm 1.7$ ). In accordance with this finding, Lim et al study<sup>(16)</sup> done on 80 acne patients showed that the level of serum vitamin D was inversely associated with the severity of acne, and there was a significant negative correlation with inflammatory lesions.

Furthermore, a cross sectional study<sup>(25)</sup> conducted on 60 Sudanese patients suffering from acne vulgaris showed significant decrease in serum vitamin D levels with the increase in acne grading, where the mean vitamin D level was ( $16.8 \pm 3.42$  ng/mL) among mild acne patients however severe acne cases had the lowest mean vitamin D level ( $10.4 \pm 1.64$  ng/mL).

On the other hand, Alhetheli et al study<sup>(18)</sup> conducted on Saudi acne patients attending Outpatient Dermatology Clinics at Qassim University Hospital reported that the mean value of vitamin D was higher in moderate acne ( $31.4 \pm 6.9$ ) than in mild and severe acne ( $26 \pm 9.4$  and  $28.4 \pm 6.7$ , respectively). However, this difference was not statistically significant. In addition, Toossi et al study<sup>(26)</sup> conducted on 39 Iranian patients with acne vulgaris, revealed no significant associations between severity of acne and serum vitamin D. This difference may be due to their small sample size.

In the present study there is a significant negative correlation between acne stage and

serum level of vitamin D ( $r = -0.313$ , P value  $< 0.05$ ). These results are in concordance with a study done<sup>(20)</sup> in Indonesia which reported a strong negative correlation between serum vitamin D level and acne vulgaris severity ( $r = -0.792$ ;  $p < 0.05$ ). Also, Kemeriz et al study<sup>(27)</sup> done on 134 acne patients revealed a strong statistically significant negative- correlation between serum vitamin D levels and acne severity ( $r = -0.910$ ;  $P < 0.001$ ).

A significant improvement in acne grading after vitamin D supplementation for two months was the most important finding in the current study where about 61% of treated patients with vitamin D and regular acne treatments reached grade 0 of acne vulgaris. This comes in agreement with Lim et al study<sup>(16)</sup> conducted in Korea that proved significant improvement in inflammatory lesions after supplementation of vitamin D 1000 IU/day for 2 months for acne patients with vitamin D deficiency where significant improvement and down grading of acne lesion were noted. Mohamed et al<sup>(17)</sup> study in Egypt reported improved acne and significant higher serum level of vitamin D among cases treated with vitamin D supplementation compared to placebo group.

In contrast to these findings, Tehrani et al study<sup>(28)</sup> conducted in Iran on 80 women with acne and polycystic ovaries (PCO) treated with metformin and vitamin D for 4 months found no significant effect of vitamin D supplementation on acne lesions. This may be attributed to the

prevalent hyperandrogenism and increased comedogenesis among PCO female patients.

**Conclusion:** There's significant relation between vitamin-D deficiency and severity of acne vulgaris. Treatment of acne vulgaris with vitamin D supplementation to vitamin D deficient patients will give better results than topical treatments only. So, it is recommended to evaluate the serum level of vitamin D in acne patients and provide vitamin D supplementation to vitamin D deficient patients beside topical treatments for acne.

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**Conflict of interest:** there is no conflict of interest.

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**Table (1): Relationship between Serum Vitamin D and Grading of Acne Vulgaris among the Studied Group**

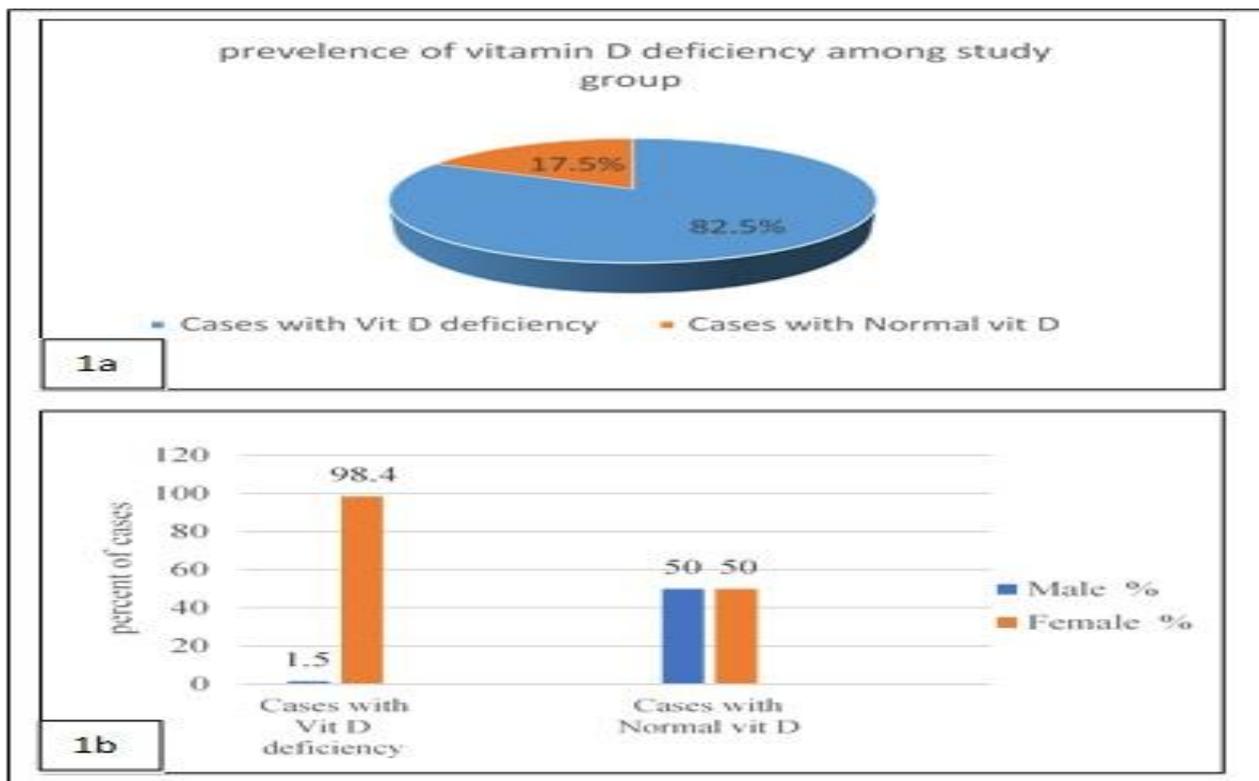
Acne stage	Vitamin D deficiency group		Normal vitamin D Group		Total		X <sup>2</sup>	P value
	N(66)	%	N(14)	%	N(80)	%		
▪ Grade 1	18	27.3	9	64.3	27	33.8	8.1	0.043
▪ Grade II	24	36.4	4	28.6	28	35		
▪ Grade III	18	27.3	1	7.1	19	23.8		
▪ Grade IV	6	9.1	0	0	6	7.5		

**Table (2): Serum Vitamin D Level and Severity of Acne Vulgaris**

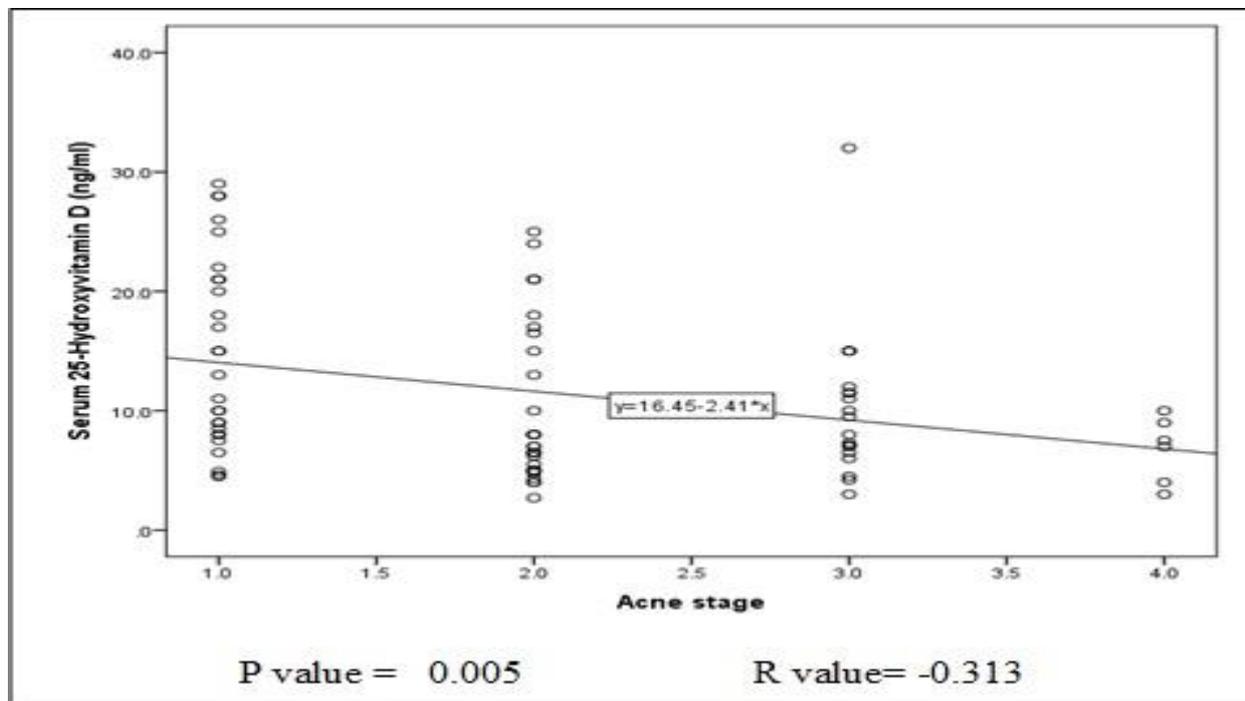
	<b>Grade I N 27</b>	<b>Grade II N 28</b>	<b>Grade III N 19</b>	<b>Grade IV N 6</b>	<b>F test</b>	<b>O value</b>
Vit D	15.8±4 9-32	11.02±6.6 8.5-25	8.2±2.9 3-15	5.2±1.7 2.7-7.5	7.6	<0.001

**Table (3): Grading of Acne Vulgaris among Both Groups at the End of Follow-up Period**

<b>Acne grade</b>	<b>Group I with Vitamin D supplementation</b>		<b>Group II without Vitamin D supplementation</b>		<b>X<sup>2</sup></b>	<b>P value</b>
	<b>N=33</b>	<b>%</b>	<b>N=33</b>	<b>%</b>		
0	20	60.6	3	9.1	39.8	<0.001
I	12	36.4	16	48.5		
II	1	3	11	33.3		
III	0	0	3	9.1		
IV	0	0	0	0		



**Figure (1): Prevalence of Vitamin D Deficiency Among Study Group (1a), Vitamin Deficiency among Male and Female Acne Patients (1b)**



**Figure (2): Correlation between Acne Grade and Serum Level of Vitamin D**

**Figure (3a):** A case of grade II acne vulgaris where there are multiple comedones , few papules and a pustule after treatment with topical acne treatments and oral vit D 2000IU for two months ; the patient downgraded to grade 0 where there's no comedones or papules only post inflammatory hyperpigmentation is found.



**Figure (3b):** A case of grade II acne vulgaris where there's multiple comedones, a papule and a pustule treated with topical treatment for acne for two months and downgraded to grade I acne where there's remaining comedones and macules



**Figure (3): Acne Vulgaris Improvement with Different Treatment Protocols**

### الملخص العربي

#### تأثير مكملات فيتامين د على مرضى حب الشباب: دراسة تداخلية

ولاء محمود عبد العزيز ، تغريد محمد فرحات ، هالة مصيلحي شاهين ، محمد عبد الواحد جابر ، نورا عبد الهادي خليل  
**الخلفية:** حب الشباب مرض جلدي مزمن ، فيتامين د هو فيتامين يذوب في الدهون ، يساعد على تقليل الالتهاب الجلدي. **الأهداف:** تحديد تأثير استعمال فيتامين (د) على تحسين درجة حب الشباب . **الطريقة:** دراسة حالة أجريت على 80 مريضاً بحب الشباب في عيادة الجلدية بالمستشفى الجامعي. 66 من 80 مريضاً يعانون من نقص فيتامين د. تم توفير حبوب من فيتامين د 2000 وحدة دولية لكل قرص كالتالي: 33 مريضاً عولجوا فوراً بالفيتامين مع علاج حب الشباب. 33 حاله الاخرى تم علاج حب الشباب دون مكملات ومتابعتها سريريا لمدة شهرين ثم تم اعطاء فيتامين د عن طريق الفم لدواعي اخلاقيه . **النتائج:** هناك علاقة كبيرة بين مستوى فيتامين د ودرجة حب الشباب. حيث ان حوالي 9 ٪ من المرضى الذين يعانون من نقص فيتامين (د) يعانون من حب الشباب من الدرجة الرابعة ، 27 ٪ من المرضى الذين يعانون من نقص فيتامين (د) لديهم حب الشباب من الدرجة 1 وحوالي 64 ٪ من المرضى الذين كان مستوى فيتامين د لديهم طبيعى كانوا يعانون من حب الشباب من الدرجة 1. كما كان هناك تغير كبير في درجة حب الشباب بعد العلاج بفيتامين د: حيث وصل حوالي 35٪ من مرضى حب الشباب الذين يعانون من نقص فيتامين د إلى المستوى صفر من حب الشباب . **الخلاصة:** يفضل إعطاء فيتامين (د) عن طريق الفم في علاج حب الشباب للمرضى الذين يعانون من نقص فيتامين د للحصول على نتائج أفضل.