The Egyptian Journal of Hospital Medicine (July 2019) Vol. 76 (3), Page 3678-3683

Assessment of Serum Level of 25-Hydroxy Vitamin D in Patients with Acne Vulgaris

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ABSTRACT

Background: acne vulgaris is a common chronic inflammatory disease of the pilosebaceous unit, characterized by the formation of non-inflammatory comedones and inflammatory papules, pustules, nodules and cysts.

Objective: the aim of this study was to evaluate serum levels of vitamin D in a group of Egyptian patients with acne vulgaris in comparison to controls, in order to shed more light on its possible role in the pathogenesis and detect any relation between vitamin D and acne severity.

Patients and Methods: the study recruited 90 subjects, 60 acne vulgaris patients and 30 age and sex matched healthy controls. All patients were subjected to detailed history taking and examination to detect extent and severity of acne vulgaris. Blood samples were taken from all participants to assess serum 25 OH D level.

Results: revealed lower serum vitamin D levels in acne patients in comparison to controls, with statistically significant p value (0.009). Serum 25 OH D level showed no significant difference in females than in males in both patients ($p = 0.726$) and controls in comparison to patients ($p = 0.794$). There was no significant difference in level of 25 OH D between participants reporting adequate sun exposure and those reporting inadequate sun exposure in patients ($p = 0.804$) but it was statistically significant p value in controls in comparison to patients ($p < 0.001$).

Conclusion: the present study revealed lower, statistically significant, serum vitamin D levels in acne patients, suggesting a possible role for vitamin D supplementation in acne treatment.

Keywords: 25-Hydroxy Vitamin D, Acne Vulgaris

INTRODUCTION

Acne vulgaris is a common chronic inflammatory disease of the pilosebaceous unit, characterized by the formation of non-inflammatory comedones, inflammatory papules, pustules, nodules or cysts **(1).**

Acne vulgaris is a multifactorial disease involving androgen-induced increased production of sebum, together with altered keratinization, inflammation and bacterial colonization of hair follicles by propionibacterium (P.) acnes **(1).** In addition, nutritional factors such as vitamins and minerals may be involved in the pathogenesis of acne **(2).**

Specific dietary agents and supplements are known to enhance the health and appearance of the skin, by improving immune function at the skin level and providing therapeutic bioactive agents that assist in the treatment of many skin conditions, such as psoriasis, eczema and acne **(3).**

Vitamin D is a fat-soluble steroid hormone, which plays an important role in calcium homeostasis, immune system regulation as well as cell growth and differentiation. The main source of vitamin D is the skin upon sun exposure and a small proportion is obtained from dietary sources **(4).**

Sebocytes are identified as bioactive vitamin D-responsive target cells, suggesting a possible role for vitamin D in acne **(5).** In addition, vitamin D has multiple effects on innate and adaptive immune responses through its actions on T and B lymphocytes, macrophages and dendritic cells, all of which express vitamin D receptors (VDR)**(6).**

AIM OF THE WORK

The aim of this study is to evaluate serum levels of 25(OH)D in a group of Egyptian patients with acne vulgaris in comparison to controls, in order to shed more light on its possible role in the pathogenesis and detect any relation between 25(OH)D and acne severity.

PATIENTS AND METHODS

Patients:

This study was conducted on 90 adult individuals.

The subjects were recruited from Dermatology Outpatient Clinics in Al-Azhar University Hospitals.

The 90 adult individuals were divided into 4 groups:

- **Group (1):** included 30 apparently healthy not suffering from any manifestations of acne.
- **Group (2):** included 20 patients with mild acne vulgaris.
- **Group (3):** included 20 patients with moderate acne vulgaris.
- **Group (4):** included 20 patients with severe acne vulgaris.

Ethical consideration:

An informed consent was taken from all subjects before enrollment in the study **after approval of the Medical Research Ethics Committee.**

Received:17/4/2019
Accepted:16/5/2019

Case inclusion criteria:

Male and female patients with active acne (mild, moderate and severe) according to the global acne grading system (GAGS) score.

Age: from 18 to 30 years old.

Case exclusion criteria:

1- Patients receiving or who had received any systemic therapy or phototherapy in last 3 months.
2- Acute and chronic kidney disease patients.
3- Acute and chronic liver disease patients.
4- Pregnancy.
5- Post menopausal women.
6- Medication that affect vitamin D metabolism/its absorption (phenytoin, rifampin, isoniazid, ketoconazole).

Participants were subjected to the following:

1. **Detailed History Taking:**

- Personal history including name, age, sex, occupation and indoor versus outdoor sun exposure.
- Frequency and duration of sun exposure:

2. **Dermatologic Examination:**

- Site: face, chest or back
- Type of lesions: comedones, papules, pustules, nodulocystic lesions or scars.
- Severity of acne vulgaris which was graded into mild, moderate or severe according to the global acne grading system (GAGS) score.

3. **Sampling for assessment of serum 25 OH D level:**

Three milliliters of peripheral venous blood were collected from each participant under sterile conditions for detection of serum levels of 25 OH D, the most indicative form of vitamin D level in the body [(7)].

4. **Assessment of vitamin D status:**

Vitamin D status was defined as one of the following:
Deficiency: 25 OH D concentration <20 ng/ml.
Insufficiency: 25 OH D concentration 20-29 ng/ml.
Sufficiency: 25 OH D concentration >29 ng/ml [(8)].

Laboratory Methodology:

25 OH D was measured in sera of all patients and controls using Human 25 OH DELISA kit provided by E A198 Bioassay England, China.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
  - P-value <0.05 was considered significant.
  - P-value <0.001 was considered as highly significant.
  - P-value >0.05 was considered insignificant.

RESULTS

Descriptive analysis:

This case control study was conducted on 60 patients with acne vulgaris and 30 controls. Clinical and laboratory data of all participants are presented in table (1).

Table (1): Clinical and laboratory data of the studied groups

Variables	Acne patients N=60	Controls N=30
Age (years)		
Range	18.0 – 25.0	18.0 – 30.0
Mean ±SD	20.12 ± 2.04	26.6±3.27
Median	20.0	27.50
Sex		
Males N (%)	28 (46.7%)	13 (43.3%)
Females N (%)	32 (53.3%)	17 (56.7%)
Adequate Sun exposure		
Positive N (%)	40 (66.7%)	25 (83.3%)
Negative N (%)	20 (33.3%)	5 (16.7%)
Site of lesions		
Face	60 (100%)	
Chest	22 (36.7%)	
Back	30 (50%)	
Severity of disease		
Mild N (%)	20 (33.3%)	
Moderate N (%)	20 (33.3%)	
Severe N (%)	20 (33.3%)	
Duration of disease (months)		
Range	1 –120	
Mean ±SD	18.08±23.62	
Family history		
Positive N (%)	6 (10%)	
Negative N (%)	54 (90%)	
Serum vitamin D (ng/ml)		
Range	17.9 - 85.3	12.1 - 88.1
Mean ±SD	28.7±10.65	32 ± 18.15
Vitamin D status		
Sufficient	8 (13.3%)	10 (33.3%)
Insufficient	25 (41.7%)	13 (43.3%)
Deficient	27 (45%)	7 (23.3%)

N= number, SD= standard deviation

B- Comparison between the studied groups:

Table (2): Comparison between the two studied groups according to demographic data.

	Control (n= 30)		Patient (n= 60)		p
	No.	%	No.	%	
Sex					
Male	13	43.3	28	46.7	0.765
Female	17	56.7	32	53.3	
Age (years)					
Min. – Max.	18.0 – 30.0		18.0 – 25.0		<0.001*
Mean ±SD	3.27±26.63		20.12 ± 2.04		
Median	27.50		20.0		

*: Statistically significant at $p \leq 0.05$

There was no significant difference between male and female between the 2 groups.

While according to age there was significant difference between the 2 groups.

Table (3): Comparison between the two studied groups according to adequate sun exposure.

Adequate sun exposure	Control (n=30)		Patient (n= 60)		p
	No.	%	No.	%	
Negative	5	16.7	20	33.3	0.096
Positive	25	83.3	40	66.7	

As regard comparing between patient and control according to adequate sun exposure there was no significant difference.

Table (4): Comparison between the two studied groups according to Serum vitamin D level

Serum Vitamin D level	Control (n=30)		Patient (n= 60)		P
	No.	%	No.	%	
Deficient	7	23.3	27	45.0	0.039*
Sufficient	10	33.3	8	13.3	
in sufficient	13	43.3	25	41.7	

*: Statistically significant at $p \leq 0.05$

In comparison between the two studied groups according to serum vitamin D status there was significant difference.

Table (5): Comparison between the studied groups according to serum vitamin D level

Serum Vitamin D level	Control (n=30)		Patient						P
			Mild (n=20)		Moderate (n=20)		Severe (n=20)		
	No.	%	No.	%	No.	%	No.	%	
Deficient	7	23.3	4	20.0	9	45.0	14	70.0	0.009*
Sufficient	10	33.3	3	15.0	3	15.0	2	10.0	
In sufficient	13	43.3	13	65.0	8	40.0	4	20.0	

As regard comparing between control and patient (mild, moderate and sever) according to serum vitamin D status, there was significant difference.

Comparison between acne vulgaris patients with mild, moderate and severe acne regarding demographic data:

Table (6): Comparison between acne vulgaris patients with mild, moderate and severe acne regarding age and sex:

	Patients						P.
	Mild (n = 20)		Moderate (n = 20)		Severe (n = 20)		
	No.	%	No.	%	No.	%	
Sex							0.626
Male	11	55.0	8	40.0	9	45.0	
Female	9	45.5	12	60.0	11	55.0	
Age (years)							0.818
Mi.-Max.	18.0-24.0		18.0-25.0		18.0-25.0		
Mean±SD	19.95±1.88		20.35±2.23		20.05±2.09		
Median	20.0		20.0		20.0		

Table (7): Comparison between acne vulgaris patients with mild, moderate and severe acne regarding family history:

Family history	Patient						P
	Mild (n=20)		Moderate (n=20)		Severe (n=20)		
	No.	%	No.	%	No.	%	
Negative	19	95.0	17	85.0	18	90.0	0.863
Positive	1	5.0	3	15.0	2	10.0	

In comparison between acne vulgaris patient with mild, moderate and severe according to family history there was no significant difference.

Table (8): Comparison between acne vulgaris patients with mild, moderate and severe acne regarding adequate sun exposure:

Adequate sun exposure	Patient						p
	Mild (n=20)		Moderate (n=20)		Severe (n=20)		
	No.	%	No.	%	No.	%	
Negative	3	15.0	4	20.0	13	65.0	0.001*
Positive	17	85.0	16	80.0	7	35.0	

*: Statistically significant at $p \leq 0.05$

In comparison between acne vulgaris patients with mild, moderate and severe according to adequate sun exposure there was significant difference.

Table (9): Comparison between acne vulgaris patients with mild, moderate and severe acne regarding vitamin D serum level:

Serum Vitamin D level	Patient						P
	Mild (n=20)		Moderate (n=20)		Severe (n=20)		
	No.	%	No.	%	No.	%	
Deficient	4	20.0	9	45.0	14	70.0	0.023*
Sufficient	3	15.0	3	15.0	2	10.0	
in sufficient	13	65.0	8	40.0	4	20.0	

*: Statistically significant at $p \leq 0.05$

In comparison between acne vulgaris patient with mild, moderate and severe according to serum vitamin D status there was significant difference.

DISCUSSION

The results of the study revealed significant lower serum vitamin D levels in acne patients in comparison to controls. In comparison between acne vulgaris patient with mild, moderate and severe according to serum vitamin D status there was significant difference.

These results are in accordance with a study reporting that vitamin D deficiency significantly potentiates the inflammatory process in young men with severe acne [(9)], as well as, animal studies suggesting a therapeutic effect of vitamin D analogues in acne through demonstrating comedolytic effects on pseudocomedones in rhino mouse [(10)].

Further support is also shown by previous reports suggesting a possible beneficial role for vitamin D in acne, where incubation of the human sebaceous gland cell line with vitamin D resulted in a dose-

dependent suppression of cell proliferation. In addition, using real-time polymerase chain reaction (PCR), it was demonstrated that key components of the vitamin D system (VDR, 25 hydroxylase, 1α hydroxylase and 24 hydroxylase) are strongly expressed in such cells [(5)].

In addition, vitamin D decreases the production of inflammatory biomarkers, especially IL-6, IL-8 and MMP-9 by cultured sebocytes [(11)]. Moreover, **Zhang *et al.*** [(12)] demonstrated that vitamin D inhibits monocyte/macrophage proinflammatory cytokine production by targeting mitogen-activated protein kinase (MAPK) phosphatase-1.

Furthermore, vitamin D has antimicrobial as well as immuno-modulatory actions [(13)]. Vitamin D inhibits the proliferation of Th1 lymphocytes [(14)], which play a key role in the inflammation observed in acne [(15)]. In addition, **Agak *et al.*** [(16)] reported that IL-17 is induced by action of P. acnes on peripheral blood mononuclear cells, an effect abolished by vitamin D.

Regarding vitamin D status, only 40% of patients and 33.3% of controls had sufficient levels of vitamin D in this study. This may be attributed to social and cultural factors as the conservative dress code of Egyptians, which blocks exposure to sunlight. Added to that, the reduction in outdoor leisure time and the rise in office-based work have led to an increased lack of sunlight exposure.

The study also showed no significant difference in serum 25 OH D level - the best clinical index of vitamin D status - between males and females in either patients or controls groups. This is supported by another study, which reported that serum levels of 25 OH D and 1, 25 (OH) 2D were similar in men and women with multiple sclerosis [(17)].

On the other hand, several studies showed that females are at higher risk of vitamin D deficiency. **Al-Kindi *et al.*** [(18)] investigated serum 25 OH D levels among apparently healthy Omani women of childbearing age and reported vitamin D deficiency in all participants. In addition, **Al-Kindi *et al.*** [(18)] reported vitamin D deficiency in 33% and vitamin D insufficiency in 67% of pregnant Omanis. These studies conducted in Oman give a warning that subclinical vitamin D deficiency may be prevalent among females and indicate the need for vitamin D supplementation especially during pregnancy and lactation.

In this study, there was a controversy as regards the relation between vitamin D status and sun exposure, where no relation was found in the patient group ($p=0.804$), whereas, a significant decrease in serum 25 OH D level was noted in controls reporting inadequate sun exposure as compared with those reporting adequate exposure ($p<0.001$).

This controversy suggests the presence of factors in patients with acne vulgaris that may affect the cutaneous photosynthesis of vitamin D or its further activation in the liver by 25 hydroxylase enzyme. In addition, it appears that sun exposure alone cannot alter the vitamin D status in patients of acne vulgaris and vitamin D supplementation is required for the treatment of vitamin D deficiency in those patients.

Previous studies conducted by **Clemens *et al.*** [(19)] **and Need *et al.*** [(20)] proved that intentional unprotected sun exposure to increase vitamin D photosynthesis is not only unnecessary, but also inefficient for populations at highest risk of vitamin D deficiency. In addition, other studies have proved that sun exposure is not the only determinant of vitamin D status, as individuals living at lower latitudes in relatively sunny environments are also at risk of vitamin D insufficiency [(21)].

Conversely, **Giovannucci *et al.*** [(22)] reported that increased duration of sun exposure was positively correlated with vitamin D concentrations.

In conclusion, the present study revealed lower, significant, serum vitamin D levels in acne patients, suggesting a possible role for vitamin D supplementation in acne treatment.

Nevertheless, it remains speculative whether vitamin D deficiency primarily contributes to disease pathogenesis or merely represents a consequential event to the inflammatory processes involved. According to a recent systematic review, one solid fact is emphasized; vitamin D deficiency appears to be a marker of ill health regardless of being an actual cause or an association [(23)].

CONCLUSIONS

In conclusion, the present study revealed lower, statistically significant, serum vitamin D levels in acne patients, suggesting a possible role for vitamin D supplementation in acne treatment.

RECOMMENDATIONS

- Further studies on a larger scale are needed to shed more light on the importance of vitamin D in acne.
- Controlled studies to determine whether treatment of acne vulgaris patients with topical vitamin D analogues, as well as vitamin D supplementation is of significant effect would represent an attractive area of research.

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