Serum Level of Vitamin D &Beta-2-Defensin In Patients with Acne Vulgaris

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Abstract

Objective: The aim of this study was to detect the role of vitamin D and hBD-2 in pathogenesis of acne vulgaris.

Background: Vitamin D deficiency may facilitate the pathogenesis of acne. Colonization of *P. acnes* is suggested to increase hBD-1 and hBD-2 release and thereby leading to inflammatory cells to accumulate at infection site.

Patients and methods: The present study was conducted as a case-control study included 60 individuals who were divided into 2 groups; case group: which included 30 acne vulgaris patients and control group: which included 30 healthy individuals. Each patient underwent; complete history taking, full physical examination and dermatological examination. Laboratory assessment: measurements of vitamin D and beta-2-defensin were done for all participants by enzyme linked immunosorbent assay (ELISA).

Results: Serum level of vitamin D was signifcantly lower in the case group when compared to the control group (p-value < 0.05). Serum level of BD-2 was significantly higher in the case group when compared to the control group (p-value < 0.05) between patients and controls. There was a statistically significant negative correlation with p-value <0.05 between BD-2 and vitamin D level among cases.

Conclusion: Vitamin D deficiency was more frequent in patients with acne indicating a potential role of vitamin D deficiency in acne pathogenesis. The up-regulation of beta-defensins in acne vulgaris patients when compared to controls although this comparison still non-significant suggests that beta-defensins may be involved in the pathogenesis of acne vulgaris.

Keywords: Acne Vulgaris, beta-Defensins, Kratinocytes, Vitamin D

Introduction

It is estimated that 9.4% of the world's population is affected by acne vulgaris (AV) with the highest prevalence among adolescents. It is the most common skin disease globally and ranked as the eighth most common disease worldwide. Although isolated skin diseases are unlikely to be fatal conditions, during 2013 skin diseases were the fourth leading cause of disability worldwide [1].

Sebaceous glands have an important role in the innate immunity. They secrete antimicrobial peptides, antibacterial lipids and neuropeptides. There are many factors which regulate sebaceous glands functions including androgen stimulation, vitamin D and insulin-like growth factor one. Sebaceous follicles that have microcomedones provide an anaerobic and lipid-rich environment which is ideal for P. acnes activity. Propionibacterium acnes trigger cytokine activation by Toll-like receptors, indicating the role innate immunity in acne development [2].

Vitamin D regulates the immune system, the proliferation and the differentiation of keratinocytes and sebocytes. Furthermore, it has antioxidant and anti-comedogenic properties.Hence, vitamin D deficiency

may facilitate the pathogenesis of acne [3].

Defensins, a small antimicrobial peptide family, are cationic proteins which are expressed in all human epithelial tissues and are excreted as a response to microbial infections; include 28–42 amino acids and contain three disulfide bonds. *P. acnes* whose colonization is increased in AV is suggested to increase hBD-1 and hBD-2 release beside chemokines from keratinocytes and mononuclear cells and thereby leading to inflammatory cells to accumulate at infection site [4]. The aim of this study was to detect the role of vitamin D and hBD-2in pathogenesis of acne vulgaris.

Patients and methods

The present study was conducted as a case-control study in the Dermatology, STDs and andrology department of Fayoum University Hospital, during the period from January 2017 to June 2017. Laboratory investigations were performed at the Clinical Pathology Department of Fayoum University Hospital, after approval of the Dermatology Research Ethics Committee. Participant's names were kept on a password-protected database and linked only with a study identification number for this research. Written informed consent was obtained from each patient before his or her enrollment in the study. The present study included 60 individuals who were divided into 2 groups; case group: which included 30 acne vulgaris patients and included 7 males and 23 females and control group: which included 30 healthy individuals and included 14 males and 16 females. Inclusion criteria were: age >18 years old. Exclusion criteria were: patients with organic diseases that may affect level of vitamin D and beta-2-defensin. Patients with primary skin diseases other than acne.

Each patient underwent; complete history taking: including name, age and sex. Full physical examination: to exclude any systemic illness associated with vitamin D and beta-2-defensins' level such as; cachexia, anorexia nervosa and obesity. Dermatological examination was done to exclude any dermatological diseases associated with increased vitamin D and beta-2

defensin level such as; psoriasis.. Laboratory assessment: Measurements of vitamin D and beta-2-defensin were done for all participants by enzyme linked immunosorbent assay (ELISA).

The statistical analysis was conducted using statistical package for social science (SPSS) version20 on IBM compatible computer (SPSS Inc., Chicago IL, USA). Quantitative data were described using mean, standard deviation and median. The statistical tests used were: Chi-square test (χ^2), Student t-test and pearson correlation. The results were considered statistically significant for $p<0.05$.

Results:

The patient group ages ranged from 19 to 35 years (23.7±2.8). The control group ages ranged from 18 to 34 years (24.7±4.5). There was no statistically significant difference between the two groups regarding age (p-value= 0.3). There was no statistically significant difference between the two groups regarding BMI (p-value = 0.47). There was no statistically significant difference between the two groups regarding sex (p-value= 0.06). There was no statistically significant difference between the two groups regarding positive family history (p-value=0.78) **(Table 1)**. Serum level of vitamin D was lower in the case group (23.2±11.7) when compared to the control group (33.8±17.3) with a statistically significant difference (p-value < 0.05) between patients and controls (**Table 2**). Data analysis showed no statistically significant relation between serum BD-2 and serum Vitamin D and severity of acne vulgaris (**Table 3**). There was a statistically significant negative correlation with p-value <0.05 between BD-2 and vitamin D level among cases which indicated increasing in BD-2 will be associated with decreasing in Vit D (**Figure 1**). There was a statistically significant positive correlation with p-value <0.05 between vitamin D level and age among controls which indicated increasing in age will be associated with increasing in Vit D (**Figure 2**).

Discussion:

In the present study majority of the case group are females. This is in

accordance with a previous study which found that among adults, female sex was more prevalent, with 385 (85%) female patients versus 69 (15%) male patients. In the adolescents, female patients numbered 378 (53%) versus 335 male patients (47%). The pathogenesis of adult female acne is very complex and remains incompletely elucidated. Similar to adolescent acne, the pathogenesis of adult female acne involves aninterplay of excess sebum production, abnormal keratinization within the follicle and bacterial colonization of the pilosebaceous duct by Proponibacterium acnes. Furthermore, hormones, the use of cosmetics and/or drugs and chronic stress have been put forward as possible etiological factors [5].

In the current study there was a statistically significant difference between cases and controls as regards vitamin D level with low mean of vitamin D were found among cases. Our findings are in accordance with **El-Hamd and his colleagues** as they found; significant low serum levels of 25 hydroxy vitamin D in patients with acne vulgaris compared with controls [6].

In the present study there was no significant difference between cases and controls regarding family history. The current study supported is different from previous studies. **Al Hussein and his colleagues** observed that positive family history was significantly more frequent among patients than controls [7].

In the current study positive family history was evident in 63.3% of cases. **El-Tonsy and Attia** reported that 34% of our patients had positive family history of acne [8].

Another study by **Al-Hammadi and his colleagues** concluded that the severity of acne in adolescence is associated with a positive history of severe acne in first-degree relatives, especially the mother. The risk of inflammatory acne, although slight, was greater among adolescents whose siblings had the disease, which is consistent with the literature and probably related to genetic factors. The same pattern was observed in relation

to lower educational levels of parents, which may mean less concern with the disease or greater difficulty in accessing early treatment [9].

This is in contrast to **Al-Hilali and Al-Anssari** who found that negative family history was more prevalent in patients with acne vulgaris [10].

In the present study we found lower levels of serum vitamin D were found in severe acne group. This is in agreement with a previous study which found a significant lower vitamin D level in patients with acne than normal subjects. Vitamin D levels were inversely correlated with acne severity especially in patients with more inflammatory lesions [11].

Also, serum level of 25 hydroxy vitamin D was found to be inversely related with acne severity suggesting that there is a connection between low vitamin D and acne [6]

It is hypothesized that the impact of vitamin D on AV is due to the possible anti-inflammatory effect. The presence of *Propionibacterium acnes* in AV lesion leads to secretion of various inflammatory cytokines, including IL-8 and IL-12 in addition to the recruitment of activated T helper 1 (Th1) and T helper 17 (Th17) lymphocytes to the site of early AV lesions. Vitamin D modulates both the innate and adaptive immune responses by governing lymphocyte activation, survival, differentiation and maturation in addition to inhibition of the expression of interferon and pro-inflammatory cytokines in monocytes (IL-1, IL-6, TNF-α, IL-8 and IL-12) [12].

In the present study, we found no significant association between BMI and vitamin D in acne vulgaris. However, previous study denoted that Vitamin D deficiency has been shown to occur at higher rates in obesity compared with controls, possibly because of decreased bioavailability from dietary and cutaneous sources due to deposition in body fat compartments. Also the authors suggested that any effect of vitamin D deficiency on acne pathogenesis appears to be independent of BMI [13].

Regarding serum BD-2, it was found to be significantly increased in the case group when compared with the control group. Our current study is in an accordance with a previous observation that antimicrobial peptides, hBD-1 and hBD-2, which had antimicrobial activity and immunological properties, were expressed in pustular lesions of acne patients and were significantly higher when compared with that of the healthy controls [14]. This finding, together with the existing data, supported the role of hBD-1 and hBD-2 in acne pathogenesis [4].

Conclusion:

We found that vitamin D deficiency was more frequent in patients with acne indicating a potential role of vitamin D deficiency in acne pathogenesis. The up-regulation of beta-defensins in acne vulgaris patients when compared to controls although this comparison still non-significant suggests that beta-defensins may be involved in the pathogenesis of acne vulgaris.

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Table 1: Comparison of demographic characters in different studied groups

Variables		**Cases** (n=30)		**Control** (n=30)		**p-value**	**Significance**
Age (years)		23.7	2.8	24.7	4.5	0.3	NS
BMI (kg/m^2)		22.8	2.2	23.3	2.8	0.47	NS
Sex	Male	7	23.3%	14	46.7%	0.06	NS
	Female	23	76.7%	16	53.3%		
y history	Negative	19	63.3%	21	70%	0.78	NS
	Positive	11	36.7%	9	30%		

BMI: Body mass index

CRP: C-reactive protein

NS: Non significant difference (P-value >0.05)

Table (2): Comparisons of BD-2 and vitamin D level in different study groups

Variables	**Cases** (n=30)	**Control** (n=30)	**p-value**	**Significance**
BD-2 (median)	129.8	179.9	0.0344	S
Vit D (median)	15.6	24.6	0.005	S

BD-2: Beta 2 defensine

S: Significant difference (P-value <0.05)

Vit D: Vitamin D

Table 3: Association between different degrees of disease severity among case group with BD-2 and vitamin D

Degree of severity	**BD-2**	**Vit D**
	Median	Median
Mild	229.1	24.7
Moderate	313.7	21.3
Sever	432.5	15.4
p-value	0.321	0.226
Significance	NS	NS

BD-2: Beta 2defensine

S: Significant difference (P-value <0.05)

Vit D: Vitamin D

Figures:

Figure 1: Correlation between BD-2 and vitamin D among the case group

Figure 2: Correlation between vitamin D level and age among controls.

Figure 1:

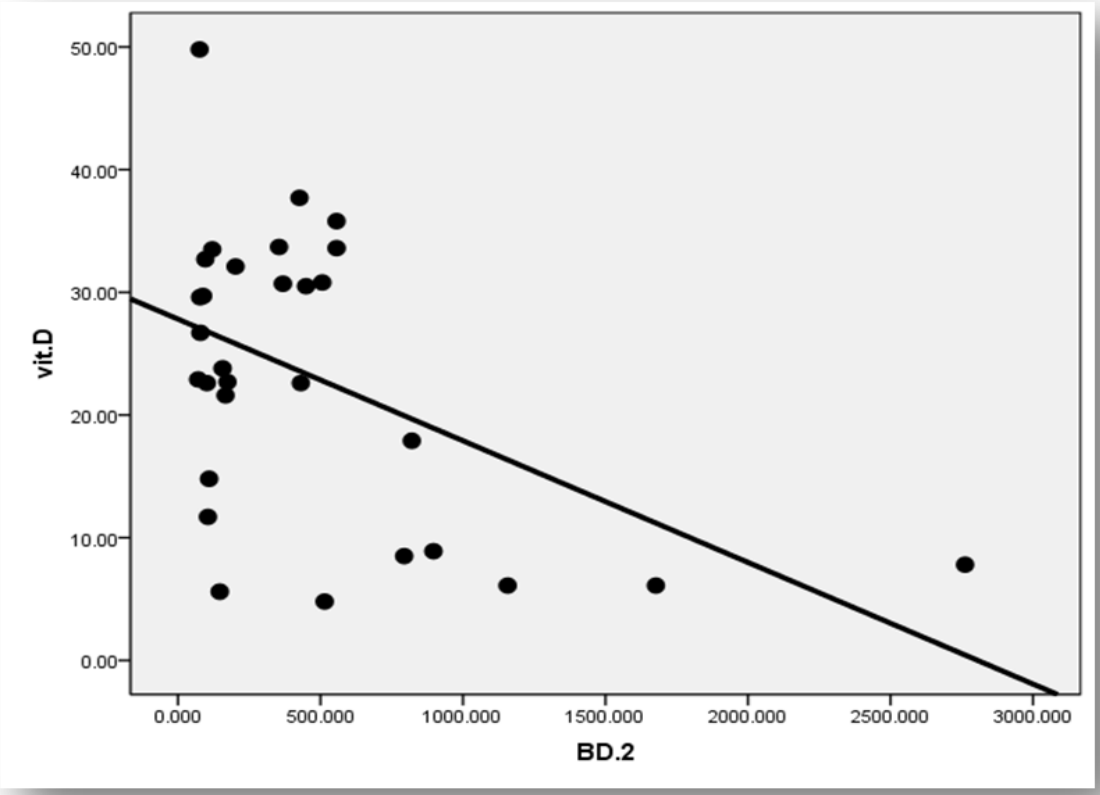

Figure 2: