Correlation between Serum 25-Hydroxyvitamin D Level with Acne Vulgaris Severity

Fitri Puspita[*], Rointan Simanungkalit[**], AriyatiYosi[**]

[*]Post Graduate of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia
[**]Departement of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, Medan, Indonesia

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***Abstract*- Introduction:** Acne vulgaris (AV) is a chronic inflammatory disease of the pilosebacceous unit characterized by the formation of open and closed comedones, papules, pustules, nodules and cysts. Vitamin D has an antiinflammation and anticomedogenic effects. Correlation between vitamin D and AV is presumed to exists only in patients with AV inflammatory lesions.

Objective: To determine the correlation between serum 25-hydroxyvitamin D (25(OH)D) level and AV severity.

Methods: This is is a cross-sectional analytic study, involving 30 subject AV patients. The Saphiro Wilk test is used to determine the normality of data distribution and the Spearman correlation test is used to determine the correlation between serum 25(OH)D level and AV severity. The severity of AV of each participant was classified into mild, moderate and severe based on Indonesian Acne Expert Meeting 2015 (Lehmann, 2002 modification).

Results: The highest propotion was women (80%), age group 17 – 25 years (83,33%), and AV with family history (80%). The lowest serum 25(OH)D level was men 16,68 (13,01 – 70,3) ng/mL, age group 17 -25 years 16,7 (3,61 – 98,3) ng/ mL, AV with family history 12,74 (3,61 – 27,2) ng/mL, and severe AV 5,63(3,61 – 17,20) ng/mL, there was astrong negative correlation between serum 25(OH)D level with AV severity (r= -0,792, p<0,05).

Conclusion: Lower level of serum 25(OH), the severity of acne vulgaris became an increasingly heavy.

***Index Terms*-** acne vulgaris, 25-hydroxyvitamin D, severity, Indonesian Acne Expert Meeting

I. Introduction

Acne vulgaris (AV) is a disease of pilosebaceous unit characterized by the formation of non-inflammation lesions (open and closed comedones) and inflammation lesions (papules, pustules, nodules and cysts).[1-2] The term acne is derived from Greek word “acme” which is used in the sense of skin eruption and vulgaris indicate the meaning “common”.[3] AV affects the skin regions with the densest sebaceous follicles populations which include face, nupper part of chst and the back.[4,5]

The grading of AV based on the type of lesions, affected surface area and their severity that can help in deciding which therapies are needed in each individual. However, no grading system has been accepted universally.[3,6] Indonesian Acne Expert Meeting (2015), modification Lehmann (2002) is a quantitative scoring system to assess the severity of AV. According to this score AV was graded as mild, moderate, and severe.[7]

The pathogenesis of AV is multifactorial, but there is four main pathogenesis: epidermal follicular hyperkeratinization, increased sebum production, *Propionibacterium acnes* (*P. acnes*) within the follicle, and inflammation.[8,9]

Vitamin D is a fat-soluble steroid hormone, which plays an important role in calcium homeostasis, immune system regulations, and cell growth and differentiation.[10] Main source of vitamin D is de novo synthesis in the skin by ultraviolet B rays of sunlight (290-315 nm) and small proportion is obtained from dietary source. A few in vitro studies have published data that support the theory that vitamin D has a functional role in AV development. Vitamin D regulates the proliferation and differeniation of keratinocytes and sebocytes.[11,12]

Study in Korea (2016) reported 48,8% of patients with AV had deficiency in serum 25(OH)D level, but only 22,5% of the healthy control. In subsequent trial, improvement in inflammatory lessions was notes after supplementation with vitamin D in 39 AV patients with 25(OH) deficiency.[13] Study in Egypt (2016) also reported serum 25(OH) level in patients with AV lower than healthy control. While study in Kuwait (2018) reported there is no significant correlation between serum 25(OH) level with AV severity.[14]

Nowaday, studies about correlation between serum 25(OH)D level and AV severity are still controversial, so we interested to assess about the correlation between serum 25(OH)D and AV severity.

II. METHOD

This research was conducted from September 2019 until December 2019. It was an observational analytic study with a cross-sectional design involving 30 patients with AV who came to Departement of Dermatology and Venereology H. Adam Malik General Hospital Medan. Each participant will sign an informed consent and will undergo anamnesis, dermatological examination and blood test for serum 25(OH)D levels. The patients were then be categorized into 3 groups according AV severity by Indonesian Acne Expert Meeting (2015), Lehmann (2002) modification.

Patients with polycystic ovaries, pregnant, thyroid, parayhyroid, renal, cardiovascular, cancer, tuberculosis, diabetes mellitus, psoriasis, sistemic lupus erythematous, scleroderma disorders and also patients receiving drugs vitamin D supplement

and AV therapy (oral and topical) in last 1 months were exluded from the study.

The Saphiro Wilk test is used to determine the normality of data distribution and Spearman correlation test is used to determine the correlation between serum 25(OH)D level and AV severity

This research was carried out after obtaining permission from the Research Ethics Commission of the Faculty of Medicine, Universitas Sumatera Utara and a research permit from the Directorate of Human Resources and Education of the Research and Development Installation of H. Adam Malik General Hospital Medan.

III. RESULTS

Patient's characteristics

This study included 30 subjects of AV, 24 patients (80%) were female and 6 patients (20%) were male. Most of patients were predominantly age group 17-25 years (83,33%) and the lowest was age group 36-45 years (6,67%). From all the subjects, majority had family history of AV as much as 18 people (60%) and among 30 AV patients, 10 patients (33,3%) with mild severity, 10 patients (33,3%) with moderate severity, and 10 patients (33,33%) with severe severity. The characteristics of AV in the study population are shown in Table 1.

Table 1. Patients characteristics

Variables	Number of cases (%)
Sex :	
Male	6 (20)
Female	24 (80)
Age group (years) :	
17-25	25 (83,33)
26-35	3 (10)
36-45	2 (6,67)
Family history :	
Yes	18 (60)
None	12 (40)
AV severity :	
mild	10 (33,33)
moderate	10 (33,33)
severe	10 (33,33)

Serum 25-Hydroxyvitamin D Level

Serum 25(OH)D levels in women 18,5 (3,61-98,3) ng/mL was higher than men 16,68 (13,01-70,30) ng/mL. The highest serum 25(OH)D level were age group 36-45 years 26,37 (25,84-26,9) ng/mL, followed by age group 26-35 years 19,89 (12,48-70,3) ng/mL, and age group 17-25 years 16,7 (3,61-98,3) ng/mL. Based on family history, serum 25(OH)D levels was higher in AV without family history 25,34 (14,02-98,3) ng/mL than AV with family history 12,74 (3,61-27,2) ng/mL, the highest serum 25(OHD) levels are at mild AV which is 26,37 (14,02-98,3) ng/mL and the lowest level at severe AV is 5,63 (3,61-17,2) ng/mL, shown in Table 2.

Table 2. Serum 25(OH)D levels

Variables	25(OH)D levels Median (Min-Max) ng/mL
Sex :	
Male	16,68(13,01-70,30)
Female	18,5 (3,61-98,3)
Age group (years) :	
17-25	16,7 (3,61-98,3)3 (10)
26-35	19,89 (12,48-70,3)
36-45	26,37 (25,84-26,9)
Family history :	
Yes	12,74 (3,61-27,2)
None	25,34 (14,02-98,3)
AV severity :	
mild	26,37 (14,02-98,3)
moderate	18,34 (12,48-27,2)
severe	5,63 (3,61-17,2)

Correlation between Serum 25(OH)D Level with Acne Vulgaris Severity

There was a significant strong negative correlation between serum 25(OH)D serum with AV severity ($p = <0.05$, $r = –0.719$), shown in Table 3.

Table 3. Correlation between Serum 25(OH)D levels with acne vulgaris severity

Variable	p	r
25(OH)D with AV severity	<0.05	–0.719

IV. DISCUSSION

AV is a chronic inflammatory disease of pilosebaceous follicles, characterized mainly by comedones and inflammatory lessions such as pustules, papules, nodules, cysts, andd scars.[1-3] From a total of 30 patients AV in our study, the proportion of female (80%) was higher than male (20%). It was consistent with the study in Egypt (2017) reported that more proportion of female (60%) than male (40%).[15] Otherwise, study in South India reported that the proportion of male (55,7%) was higher than female (44,3%).[16] This discrepancy between these studies may be due to the difference in the number of samples. AV often heralds the onset of puberty. In girls, the occurrence of AV may precede menarche by more than a year.[1]

AV can occur at any age. The highest distribution was age group 17-25 years (83,33%) and the lowest was age group 36-45 years (6,67%). This results were consistent with the Global Burden Disease reported that the most psoriasis patients were age group 12-25 years.[1,17] Study in Malysia (2018) also reported that that the most AV patients were age group 14-20 years (87,7%).[18] AV prevalence hits its peak during the middle-to-late teenage period, with more than 85% of adolescents affected, and then steadily decreases. However, AV may persist through the third

decade or even later, particularly in women. It has been shown that females with high DHEAS levels are predictors of severe or long-standing AV.[1,2]

AV paients with family history (60%) was higher than AV without family history (40%). It was consistent with the study in China (2013) reported that 78% AV patients had father and mother with AV.[19] AV usually occurs early and more severe in AV patients who had family history.[1,20]

According to the gender, serum 25(OH) level in female 18,5 (3,61 -98,3) ng/mL was higher than male 16,68 (13,01-70,30) ng/mL. It was consistent with study in Denmark (2009) reported that serum 25(OH)D level in female was higher than men. Vitamin D Binding Protein (VDBP) in female was significant higher than men, and it had positive correlation with total 25(OH)D.[21]

The highest serum 25 (OH)D level was age grup 36-45 years 26,37 (25,84-26,9) ng/mL and the lowest was ag group 17-25 years 16,7 (3,61-98,3) ng/mL. It was consistent with study in Denmark (2009), study of the global serum 25(OH)D status in the general population, it was found that the lowest serum 25(OH)D level was at an age group of ≤ 15, and the highest was at the age group of 66-75 years, but there was no significant relationship between the level 25(OH)D with age.[21]

In this study, serum 25(OH)D level in AV patients with family history 12,74 (3,61-27,2) ng/mLwas lower that AV patients without family history 25,34 (14,02-98,3) ng/mL. It was inconsistent with study in Turkey (2018) reported that serum 25(OH)D level in AV patients with family history (14,21±0,5) ng/mL was higher than AV patients without family history (9,99±1,4) ng/mL.[14]

The lowest serum 25(OH)D levels was severe AV 5,63 (3,61-17,20) ng/mL and the highest serum 25(OH)D levels was mild AV 26,37 (14,02-98,3) ng/mL. It was consistent with the study in Egypt (2018) reported that the lowest serum 25(OH) levels was severe AV (11,32 ± 6,45) ng/mL.[15] Vitamin D has an antiinflammation and anticomedogenic effects. The presence of *P. acnes* in AV lesion leads to secretion of various inflammatory cytokines, including Interleukin (IL)-8 and IL-12 in addition to the recruiment of activated T helper 1 (Th1) and Th17 lymphocytes to the site of early AV lesions.[14,15,22] Vitamin D also inhibits T-cell proliferation and suppresses the production of B- cell opsonizing antibodies, and reduces Th17.[22] The association between vitamin D and AV is pesumed only in between vitamin D level and AV severity in patients with inflammatory lesions.[14]

According to this study there was a significant strong negative correlation between serum 25(OH)D serum with AV severity (p = <0.05, r = –0.719). Study in Korea (2016) reported there was a significant strong negative correlation between serum 25(OH)D serum with AV severity (p = <0.001, r = –0.512).[13] Study in Iran (2015) showed there was no significant correlation between serum 25(OH)D and AV severity (p = 0,45, r = 0.12).[23] The difference in the correlation between serum 25(OH)D levels with severity of AV can be influenced by genetic factors, dietary intake or vitamin D supplementation, and the length of exposure to sunlight that varies in each individual.

V. CONCLUSIONS

The correlation between 25(OH)D serum level with AV severity has significant negative correlation. Lower level of serum 25(OH)D, the severity of AV became an increasingly heavy. These results may indicate that vitamin D play a potential role in AV. Further studies are needed to determine the benefits of vitamin D derivatives administration to AV patients, as a basis for consideration of additional therapy in the management of AV in health services.

VI. SUGGESTION

This research can be done with a larger sample size.

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AUTHORS

First Author – Fitri Puspita, Post graduate of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara, fitripuspita1588@gmail.com

Second Author – Rointan Simanungkalit, Departement of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara.

Third Author – Ariyati Yosi, Departement of Dermatology and Venereology, Faculty of Medicine, Universitas Sumatera Utara