LOW SERUM VITAMIN E LEVELS POSITIVELY CORRELATE WITH THE SEVERITY OF ACNE VULGARIS

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ABSTRACT

Acne vulgaris (AV) is a common disorder of the pilosebaceous, especially prevalent in adolescents. Acne vulgaris ranks among the top ten most prevalent diseases globally. Although AV may resolve spontaneously, sequelae such as scar formation can persist, causing aesthetic and psychological disturbances. There is an antioxidant to counteract acne-causing oxidative stress, vitamin E, which is an important antioxidant in the human body. Therefore, vitamin E in the skin can reduce the formation of squalene peroxide and prevent the occurrence of AV. This is an analytical observational study using a cross-sectional design. The investigation was conducted at the Dermatology and Venereology Clinic of Prof. Dr. I.G.N.G. Ngoerah Denpasar Hospital and the laboratory of the Faculty of Medicine, Udayana University, from February 2024 until the sample size was fulfilled. The sample consisted of patients aged 12-45 years with acne vulgaris who visited the clinic and were then selected through consecutive sampling according to the inclusion and exclusion criteria. In the non-AV group, the mean serum vitamin E level was 19.3 ± 0.99 µg/ml, whereas in the AV group, it was 4.49 ± 19.1 µg/ml, indicating a significant variance. There was a positive correlation between low vitamin E levels and the severity of AV. The linearity graph shows the direction of the relationship between serum vitamin E levels and the severity of AV, which leads to the lower right, indicating that the higher the severity of AV, the lower the serum vitamin E levels. The mean levels differed significantly between the non-AV and AV groups. A favorable association was found between low vitamin E levels and the severity of AV.

Keywords: Acne Vulgaris, Severity, Serum Vitamin E, Reactive Oxygen Species (ROS)

INTRODUCTION

Acne vulgaris (AV) is a frequent condition of the pilosebaceous unit that primarily affects adolescents. It ranks among the top ten most prevalent diseases globally. While AV can resolve spontaneously, it may leave long-lasting sequelae such as scar formation causing significant aesthetic and psychological distress (Sibero, 2019).

The estimated prevalence of AV among individuals aged 12 to 24 is 85%. In some studies, comedonal AV reaches up to 100% in both sexes during adolescence. Acne vulgaris affects 73.3% of the population over

20 years old (Alsulaimani et al., 2020). In Indonesia, research conducted by Matthew found that 65% of female medical students in Jakarta suffer from acne (Matthew et al., 2021). Although acne is not life-threatening, it does cause significant morbidity, such as unhappiness, anxiety, and psychological stress. It is also a major cause of psychosocial and psychological problems in adolescents causing anxiety and mood disorders and reducing self-esteem. It is ranked third among chronic skin disorders that cause disability. Therefore, despite some viewing acne as merely a "cosmetic" issue, but its impact on one's health can be profound (Matthew et al., 2021).

The etiology of acne vulgaris remains unclear, shaping ongoing management approaches. Key reasons include increased sebum production, follicular hyperkeratinization, colonization by Propionibacterium acnes bacteria and inflammation which are frequently induced by food, cosmetics and psychological stress (Masterson, 2018). This process starts with the skin being exposed to oxidative stress which is induced by reactive oxygen species (ROS) from both internal and external sources. ROS react with biological components causing inflammation, pore blockages and acne development (Marrot, 2018; Marrot & Nouveau, 2022; Wong et al., 2016).

Skin defends against ROS through enzymatic and non-enzymatic antioxidants like α-tocopherol (vitamin E) which crucial for interrupting lipid peroxidation and reducing acne-causing sebum oxidation. In acne-prone skin, vitamin E reduces inflammation caused by bacteria and excess sebum production thereby reducing swelling and redness. In addition, vitamin E accelerates the healing of acne-prone skin by repairing damaged skin tissue and promoting cell regeneration, resulting in healthier skin and faster recovery from acne lesions.

Studies suggest topical vitamin E can mitigate squalene peroxide formation thereby preventing acne (Datolla, 2020; (Ozuguz et al., 2014). However, to date there is no research confirming a positive correlation between low serum vitamin E levels and the severity of acne vulgaris in Bali.

Based on this background, the formulation of this research question is: What is the relationship between serum vitamin E levels and acne vulgaris severity? What is the mechanism by which low vitamin E levels contribute to increased acne vulgaris severity?

The objectives of this study are to identify and analyze the correlation between low serum vitamin E levels and acne vulgaris severity as well as explain the biological mechanism behind the contribution of low vitamin E levels to acne severity. This study aims to provide a deeper understanding of how vitamin E deficiency can aggravate acne conditions and whether increasing serum vitamin E levels can be an effective strategy to reduce the severity of acne vulgaris.

LITERATURE REVIEW

Vitamin E

Vitamin E refers to a collection of fat-soluble chemicals including tocopherols and tocotrienols, both of which have antioxidant properties (Syukri, 2022). Vitamin E can be found naturally in a variety of foods such as nuts, seeds and green leafy vegetables as well as being available in supplement form. Vitamin E has important benefits for skin health

including anti-inflammatory properties that help reduce inflammation and irritation of the skin (Dattola et al., 2020). Furthermore, its antioxidant qualities protect skin cells against free radical damage, reduce the aging process and improve wound healing. Vitamin E is also a vital component in many skincare products since it helps maintain skin hydration (Saras, 2023).

Studies (Baek & Lee, 2016; Dattola et al., 2020; de Oliveira Pinto et al., 2021; Saras, 2023) on the use of vitamin E in acne treatment show that vitamin E can play an important role in reducing inflammation and accelerating skin healing. The mechanism of action of vitamin E in reducing acne involves its anti-inflammatory and antioxidant properties that reduce cell damage due to free radicals, reduce inflammation in acne-affected skin and repair damaged skin tissue. Research (Ozuguz et al., 2014); (Chello et al., 2021) has shown that vitamin E supplementation can decrease acne severity with studies involving acne vulgaris patients reporting a significant reduction in the number of acne lesions after vitamin E use. In addition, the combination of vitamin E with vitamin C has also been reported to provide synergistic effects in improving skin health and reducing acne (Farris, 2014; Pullar et al., 2017).

Maintaining healthy skin requires enough serum levels of vitamin E where optimal levels help protect the skin from oxidative damage and inflammation. Research (Ozuguz et al., 2014) suggests that vitamin E deficiency may be associated with various skin problems including acne. Low serum levels of vitamin E can increase the skin's susceptibility to oxidative stress which can exacerbate inflammation and slow down the wound healing process. Studies have also revealed that persons with acne tend to have lower serum vitamin E levels than individuals without acne which implying a positive association between vitamin E insufficiency and increased acne severity.

Acne Vulgaris

Acne vulgaris is a common skin disorder that occurs when hair follicles become blocked with oil and dead skin cells, sometimes accompanied by the bacteria Propionibacterium acnes which causes inflammation (Hafsari et al., 2015). Factors that cause acne vulgaris include hormonal changes, excess oil production, bacteria, dead skin cell build-up as well as genetic and environmental factors such as stress and diet. Acne vulgaris can be classified by severity: mild (white and blackheads with few papules and pustules), moderate (more numerous and widespread papules and pustules, possibly with some nodules), and severe (the presence of many nodules and cysts which often leave scars). Treatment of acne vulgaris varies depending on the severity and involves topical and oral treatments as well as lifestyle changes.

The pathophysiology of acne vulgaris begins with increased sebum production by the sebaceous glands triggered by hormonal changes especially androgens. Excess sebum along with dead skin cells clog the hair follicles which in turn forming blackheads (whiteheads and blackheads). Skin-dwelling Propionibacterium acnes bacteria then multiply in this clogged environment which then triggers an immune response that causes inflammation. These bacteria produce enzymes and fatty acids that damage the follicular wall leading to follicular rupture and the

spread of follicular contents into the dermis triggering a further inflammatory response. The result is the formation of papules, pustules, nodules and cysts that are characteristic of inflammatory acne. These mechanisms demonstrate the complexity of acne vulgaris where interactions between hormones, sebum, bacteria and inflammatory responses have a part in the development and severity of this disorder (Sifatullah & Zulkarnain, 2021).

METHODS

The research design is a cross-sectional analytic design to investigate the correlation between serum vitamin E levels and acne vulgaris severity. It was conducted at the Dermatology Clinic of Prof. Dr. I.G.N.G. Ngoerah Denpasar General Hospital with blood samples analyzed at the Faculty of Medicine Laboratory, Udayana University. The study duration spanned from October 2023 until the required sample size was achieved. The target population included Indonesian patients aged 12-45 years with acne vulgaris, while the accessible population comprised those seeking treatment during the study period. Patients with mild, moderate, and severe acne vulgaris were sampled using consecutive sampling. Inclusion criteria encompassed Indonesian citizenship, age 12-45 years and no recent intake of vitamin E supplements or acne treatments within one month prior. Exclusion criteria included chronic diseases, pregnancy, lactation, hormonal contraception use and active smoking. Data analysis involves descriptive statistics (mean, standard deviation, median, interquartile range), cross-tabulation, Kolmogorov-Smirnov test for normality, Levene's test for variance homogeneity and tests for linearity between variables. Statistical comparisons include independent samples t-test for AV vs. non-AV groups and One-Way ANOVA for severity levels of AV. SPSS version 25.0 software is used for all analyses.

RESULTS

Based on the research findings from 67 subjects, it was found that 20 subjects (29.9%) did not experience acne issues, while 47 subjects (70.14%) had acne vulgaris (AV), with 8 subjects (17.1%) categorized as mild, 19 subjects (40.4%) as moderate, and 20 subjects (42.5%) as severe. The non-AV group consisted of 20 participants, with an average age of 29.5 years and a standard deviation of 4.1. Three patients (9.4%) were under the age of 25, and 17 patients (48.5%) were beyond the age of 25. In terms of gender, 5 non-AV patients (26.3%) were male, whereas 15 patients (31.3%) were female.

The AV patient group consisted of 47 participants, with an average age of 24.57 years and a standard deviation of 9.1. Within this group, 29 patients (90.6%) were 25 years or younger, whereas 18 patients (51.5%) were beyond the age of 25. In terms of gender distribution, 14 AV patients (73.7%) were men, whereas 33 patients (68.7%) were women. The AV patient group had a larger proportion of females than the non-AV group (**Table 1**).

Table 1. Characteristics of Research Subjects by Group

Characteristics	Non-AV		AV	
	N = 20	%	N = 47	%
Age	29.5 ± 4.1		24.57 ± 9.11	
(Mean ± SD)	3	9.4	29	90.6
≤ 25 years	17	48.5	18	51.5
25 years				
Gender	5	26.3	14	73.7
Male	15	31.3	33	68.7
Female				
Severity of AV	-	-	8	17.1
Mild	-	-	19	40.4
Moderate	-	-	20	42.5

The independent samples t-test revealed a significant difference in serum vitamin E levels between AV patients (19.3 ± 0.99 µg/ml) and non-AV patients (4.49 ± 19.1 µg/ml; p=0.000). There was a significant difference in serum vitamin E levels between patients older than 25 years (21.45 µg/ml) and those aged 25 years or younger (7.25 µg/ml) with p-value of 0.001. Serum vitamin E levels did not differ significantly across genders with males at 11.77 µg/ml and females at 15.82 µg/ml (p-value = 0.391) (**Table 2**).

Table 2. Differences in Mean Serum Vitamin E Levels Based on Subject Characteristics

Characteristics	Vitamin E Serum Levels (µg/ml)	p
Non-AV	19.3 ± 0.99	0.000
AV	4.49 ± 19.1	
Age		0.001
≤ 25 years	7.25	
25 years	21.45	
Gender		0.391
Male	11.77	
Female	15.82	

Based on the Kolmogorov-Smirnov test for normality, serum vitamin E levels (µg/ml) were normally distributed (p>0.05) across all severity levels except for moderate severity (**Table 3**). The Levene's test for homogeneity indicated significant homogeneity (p>0.05) in age, gender and serum vitamin E levels (**Table 4**).

Table 3. Data Normality Test

Normality Test		Kolmogorov-Smirnov
		P
Vitamin E Serum Levels	Mild AV	0.094
	Moderate AV	0.018
	Severe AV	0.087

Table 4. Data Homogeneity Test

Homogenity Test	Levene Test
	P
Serum vitamin E levels (µg/ml) by severity of AV	0.642

The study analyzed the severity of AV in 67 participants using serum vitamin E levels measured in µg/ml as an indicator (**Table 5**). The mild AV group had an average blood vitamin E level of 25.5 µg/mL. Serum vitamin E levels were substantially lower for moderate severity acne at 5.25 µg/ml on average. In the severe AV group, the average serum vitamin E level was 3.68 µg/ml. A one-way ANOVA study revealed a significant correlation (p=0.01) between mean serum vitamin E levels in µg/ml and severity of AV.

According to the linearity graph below, the trend line illustrating the link between serum vitamin E levels and the severity of AV slopes downhill to the right (**Figure 1**).

Table 5. Distribution of AV Severity and Serum Vitamin E Levels

AV Severity	Sample Size	Mean Serum Vitamin E Level (µg/ml)	P
Mild	8	25.5	
Moderate	19	5.25	0.01
Severe	20	3.68	

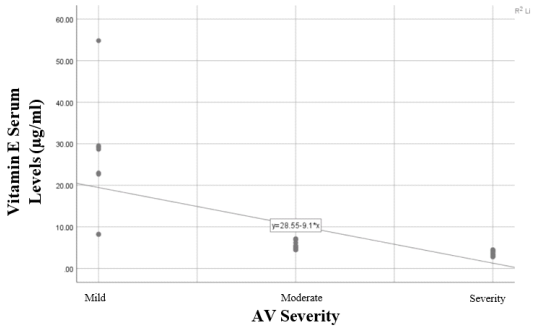

Figure 1. Linearity Test of Serum Vitamin E Level (µg/ml)

DISCUSSION

Acne vulgaris (AV) is a widespread condition of the pilosebaceous unit, generally self-resolving and primarily found in teenagers (Sibero, 2019). The estimated prevalence of AV between the ages of 12 to 25 years is 85%. In several studies, comedonal AV reaches up to 100% in both sexes during adolescence. Acne vulgaris occurs in 73.3% of the population older than 20 years (Alsulaimani et al., 2020).

Based on this study, the group of patients with AV had a mean age of 24.57 ± 9.11 years. While in the non-AV group, the mean age was 29.5 ± 4.1 years. In the age group of 25 years or younger, there were 29 (90.6%) AV patients and 3 (9.4%) non-AV patients. In the age group over 25 years, there were 18 (51.5%) AV patients and 17 (48.5%) non-AV

patients. These findings align with the study conducted on AV patients by Zarfani in Jambi in 2022 which showed that out of 180 AV cases, the highest incidence was reported in the 12-25 age range (77.2%), female gender (77.2%), and among students (65.6%) (Zarfani, 2023). Research indicates that acne onset is more common during puberty due to increased sebum production. This excessive sebum production stimulates the growth of Propionibacterium acnes (Heng et al., 2021).

Female patients accounted for 33 (68.7%) AV cases and 15 (31.3%) non-AV cases. Male patients accounted for 14 (73.7%) in the AV group and 5 (26.3%) in the non-AV group. The proportion of females in the AV patient group is higher in this study, similar to research at the Faculty of Medicine, Tarumanagara University, which stated that out of a total of 280 respondents of various ages, 25.7% were male and 74.3% were female (Amimah & Charissa, 2023). According to research by Goh et al., females often use various cosmetic products to beautify or conceal acne and some cosmetic ingredients are comedogenic which can cause or exacerbate AV (Goh et al., 2016). Some studies suggest that females are more susceptible to emotional stress and have higher demands for facial appearance, which can trigger or exacerbate AV (Lynn et al., 2016).

Based on the findings of this study, severe AV was most commonly found in 20 subjects (42.5%) followed by moderate AV in 19 subjects (40.4%) and mild AV in 8 subjects (17.1%). In Zarfani's study in Jambi, the most prevalent type of acne vulgaris discovered was papulopustular (51.7%), while the most frequent severity of AV was moderate severity (38.3%) (Zarfani, 2023). In Alsulaimani's study in Arab in 2020, out of 54 subjects, mild severity of AV was most frequent (64.8%) (Alsulaimani et al., 2020). Variations in the severity of AV in various studies are caused by multifactorial AV factors geographically such as climate differences, consumed foods, skin types and so forth (Heng et al., 2021).

Vitamin E serves as an antioxidant which protecting the skin from free radicals produced by ROS. Free radicals are chemicals that can cause harm to skin cells and tissues as well as premature aging indications. ROS production in AV can be caused by factors such as stress, exposure to ultraviolet rays, pollution, and unhealthy lifestyles thereby triggering inflammation and worsening pre-existing skin conditions. Vitamin E can capture and neutralize ROS and prevent damage to body cells and tissues thus helping to reduce the risk of AV and playing a role in its healing (Bivona III et al., 2017).

In this study, the analysis of AV severity in 67 participants using serum vitamin E levels as an indicator showed an interesting pattern. In the group without acne, a higher mean serum vitamin E level was found compared to the AV group. The mean serum vitamin E level decreased significantly with increasing AV severity ($p=0.01$). The same results were found when mapping with a linearity graph, which shows that the relationship line between serum vitamin E levels and AV severity points downward to the right, which indicates that higher AV severity correlates with lower serum vitamin E levels. Liu's systematic review and meta-analysis revealed that serum vitamin E levels in acne sufferers were recorded in three trials, totaling 284 cases and 186 controls ($p = 0.240$, $I2 = 83.9\%$). Acne sufferers exhibited

significantly lower serum vitamin E levels than the control group (SMD: -0.67, 95%). CI: -1.05--0.30) (Liu, 2021).

Ozuguz's study found that the severity of acne is negatively correlated with vitamin E and zinc levels. They propose that the indirect association between low vitamin E levels and acne occurs owing to antioxidant depletion caused by oxygen radicals during the inflammatory phase (Ozuguz et al., 2014).

The low vitamin E levels found in patients with severe AV in this study are consistent with previous research showing that low vitamin E levels can cause oxidative stress on the pilosebaceous unit, creating an ideal microaerophilic environment that promotes Propionibacterium acnes colonization and proliferation. Propionibacterium acnes contribute significantly to the AV inflammatory process by generating chemotactic factors for neutrophils. Neutrophils generate free radicals, which damage cells and exacerbate the inflammation process. Inadequate antioxidant protection and increased ROS generation cause oxidative stress, which contributes to the development of inflammatory skin disorders. Vitamin E is a fat-soluble antioxidant that is needed for healthy skin. Low vitamin E levels also increase ROS generation, which promotes oxidative stress and inflammation, all of which contribute to AV pathogenesis (Liu et al., 2021).

There was a significant difference in serum vitamin E levels in patients over 25 years old, with higher serum vitamin E levels (21.45 µg/ml) compared to patients aged 25 years or younger (7.25 µg/ml), with a p-value of 0.001. The age-based difference in vitamin E levels in this study is likely influenced by the distribution of patients, where patients under 25 years old experience more acne than patients over 25 years old, resulting in higher vitamin E levels in patients over 25 years old.

There was no significant difference in serum vitamin E levels based on gender, both in males (11.77 µg/ml) and females (15.82 µg/ml), with a p-value of 0.391. This is similar to the study by Bi, where no significant difference in serum vitamin E levels was found between males and females (Bi, 2019).

This study has several strengths, including significant clinical implications that can assist doctors in planning more effective treatment strategies for patients with AV. If this research is based on rigorous research methods, such as prospective cohort designs or randomized controlled trials, confidence in the results would be higher.

This study has several limitations, including being a cross-sectional study where the correlation between two variables does not always indicate a clear cause-and-effect relationship. For example, in this case, it is difficult to determine whether low serum vitamin E levels trigger increased acne severity or vice versa. Additionally, the study highlights challenges in measuring the variables under study. This study faces difficulties in controlling habitual and environmental factors that can affect both variables, such as diet patterns or sun exposure. Moreover, the use of over-the-counter skincare products can affect clinical assessments of acne vulgaris. The small sample size in this study is also a limitation, which can affect the reliability and generalization of research results. Finally, there may be other factors not considered in this study that could lead to biased

or distorted results, such as confounding variables.

CONCLUSION

Based on the findings of the study, several conclusions can be drawn. Firstly, there is a notable difference in average serum vitamin E levels between the non-AV and AV groups. In the non-AV group, the mean serum vitamin E level was 19.3 ± 0.99 µg/ml, whereas in the AV group, it was 4.49 ± 19.1 µg/ml, indicating a significant variance. Secondly, the research identified a positive correlation between lower levels of vitamin E and the severity of AV. This correlation was depicted in a linear graph showing a downward trend, suggesting that as the severity of AV increases, serum vitamin E levels tend to decrease.

Suggestions

Looking ahead, future studies are recommended to explore causal relationships through case-control research designs. These studies could delve into various potential risk factors such as diet, environmental influences, cosmetic ingredients, stress, hormonal factors, and genetic predispositions associated with AV. Furthermore, clinical trials could investigate the efficacy of different vitamin E supplementation dosages (e.g., 100 IU, 200 IU, and 400 IU) using a before-and-after comparison method among AV patients. Such trials would provide insights into determining the optimal dosage that significantly improves clinical outcomes. Additionally, comparative studies could evaluate whether supplementing standard therapies with vitamin E yields added benefits in managing acne. This comprehensive approach aims to deepen our understanding of how vitamin E impacts acne treatment effectiveness.

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