**Original Research Paper**

**Biomedical Science**

# VITAMIN D LEVELS AS PREDICTORS OF ACNE SEVERITY

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**ABSTRACT** **Background:** Acne is the most common skin disease of adolescents and young adults. It is a complex skin disorder that distresses many patients because of its chronicity. Acne vulgaris is a common inflammatory disorder of the pilosebaceous unit. Vitamin D regulates the immune system and the proliferation and differentiation of keratinocytes and sebocytes. Vitamin D deficiency may facilitate the pathogenesis of acne **Methods:** This research is an observational study with cross-sectional data collection methods to determine Vitamin D levels as a predictor of acne severity in patients. The study was conducted in a laboratory at the Royal Prima Medan General Hospital, starting in July 2022. Sampling was carried out consecutively for all affordable populations who met the study criteria, namely 30 patients suffering from acne. **Results and Discussion:** The cut Point value of 23.57 pg/mL for vitamin D levels to predict the severity of acne vulgaris, a sensitivity value of 87.5%, a specificity of 78.6%, a positive predictive value of 87.5% and a negative predictive value are obtained. of 84.6%, the accuracy of vitamin D levels to predict the severity of acne vulgaris was 83.3%. **Conclusions and suggestions:** Our study shows that vitamin D levels can be used to predict the severity of acne vulgaris. The more severe the severity of the acne, the lower the Vitamin D in the blood.

**KEYWORDS :** Acne, Vitamin D.

## I. INTRODUCTION

Acne is the most common skin disease of adolescents and young adults. It is a complex skin disorder that distresses many patients because of its chronicity. Although multiple factors contribute to acne development, chronic inflammation is an important mechanism. Several inflammatory mediators such as cytokines and neuropeptides have been identified in acne lesions. There are many factors which regulate sebaceous glands function including androgen stimulation, Vitamin D, and insulin-like growth factor one. Sebaceous follicles that have micro-comedones provide an anerobic and lipid-rich environment which is ideal for Propionibacterium acnes activity.[1,2]

Acne vulgaris is localized in areas with the highest density of pilosebaceous units, including mainly the face, back, chest, and shoulders. Classification is essential and guides in the decision of treatment options.[4] Acne is categorized according to severity into mild, moderate, and severe. Typical lesions of mild acne are characterized by the presence of closed and open comedones with few inflammatory lesions limited to the face. Whereas, in moderate acne, there is an increase in inflammation with papules and pustules on the face. The trunk area could also be affected by mild lesions. Finally, the presence of nodules and cysts are a hallmark of severe acne. Here, widespread lesions of trunk area together with facial lesions are characteristic.[3,4]

Vitamin D has a number of functions. It is associated with systemic inflammatory diseases such as rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease. In dermatological diseases, Vitamin D plays an important role as an immune modulator in atopic dermatitis, psoriasis, and alopecia. Vitamin D regulates the immune system and the proliferation and differentiation of keratinocytes and sebocytes. Moreover, it has anticomedogenic and antioxidant effect. Hence, a Vitamin D deficiency may facilitate the pathogenesis of acne. In vitro studies identified Vitamin D receptors in human sebocytes. Vitamin D has been found to modulate lipid and cytokine production which suggest its possible role in acne pathophysiology. Our study aims to determine whether Vitamin D levels can be used as a predictor of severity in patients with acne.[5]

## II. METHODS

This research is an observational study with cross-sectional data collection methods to determine Vitamin D levels as a predictor of acne severity in patients. The study was conducted in a laboratory at the Royal Prima Medan General Hospital, starting in July 2022. Sampling was carried out consecutively for all affordable populations who met the study criteria, namely 30 patients suffering from acne. Inclusion criteria included acne patients and willing to participate in the study. Exclusion criteria included patients who had received therapy, pregnant patients, female patients using contraception, patients taking vitamin D and patients using corticosteroids. Each sample was examined for vitamin D. Examination of vitamin D was examined using an automatic device. Architect with the principle of Chemiluminescence

## III. Statistic Analysis

Data analysis was performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) for Windows. The description of the characteristics of the research subjects is presented in the form of tables and descriptions. Differences in Vitamin D levels in patients who have acne and patients without acne use the Unpaired T test if the data is not normally distributed, then Mann Whitney is used. All statistical tests with p < 0.05 were considered significant.

## IV. RESULT

Most of the subjects were female, amounting to 26 people (86.7%). The mean age of the subjects was 29.7 years with the youngest being 22 years old and the oldest being 39 years old. Based on the examination of the degree of severity of acne,

there were 16 people with severe degrees followed by patients with moderate degrees totaling 10 people (86.7%) and mild degrees totaling 4 people (53.3%).

**Table 1. Demographic Characteristics of Research Subjects**

| Demographic Characteristics | n = 30 |
|---|---|
| Sex, n (%) | |
| Male | 4 (13,3) |
| Female | 26 (86,7) |
| Age, Years | |
| Mean (SD) | 29,7 (5,21) |
| Median (Min – Max) | 29 (22 – 39) |
| Severity of Acne, n (%) | |
| Mild | 4 (13,3) |
| Moderate | 10 (33,3) |
| Severity | 16 (53,3) |

Table 2 displays the vitamin D levels of all research subjects. The average vitamin D level was 22.35 pg/mL with the lowest level being 9.28 pg/mL and the highest level being 49.86 pg/mL
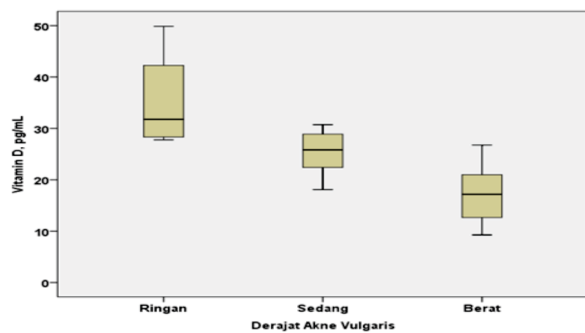
**Table 2. Vitamin D Levels**

| Vitamin D, pg/mL | n = 30 |
|---|---|
| Mean (SD) | 22,35 (8,42) |
| Median (Min – Max) | 22,41 (9,28 – 49,86) |

Table 3 displays the vitamin D levels of all study subjects based on the severity of acne vulgaris. The highest mean levels of vitamin D were found in patients with mild degrees of acne with an average of 35.29 pg/m. The lowest level of vitamin D was seen in patients with severe acne with an average of 17.31 pg/mL. Using the Oneway Anova test showed that there were differences in vitamin D levels based on the degree of acne vulgaris (p<0.001).

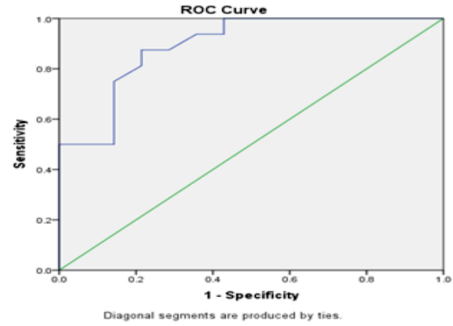**Table 3. Vitamin D levels based on the severity of acne**

| The severity of acne | Mean (SD) | Median (Min–Max) | p |
|---|---|---|---|
| Mild | 35,29 (10,17) | 31,76 (27,77 – 49,86) | <0,001* |
| Moderate | 25,23 (4,28) | 25,83 (8,09 – 30,72) | |
| Severe | 17,31 (5,31) | 17,18 (9,28 – 26,75) | |

*Oneway Anova



**Figure 1. Scatterplot Graph of Vitamin D Levels based on Degree of Severity of Acne vulgaris**

The results of the follow-up test (Posthoc) shown in table 4, it shows that there are significant differences in vitamin D levels between mild and moderate acne sufferers (p=0.019), between mild and severe degrees (0<0.001) and between moderate and severe degrees (p=0.006). The results of the analysis using the ROC curve (figure 2) showed that the AUC area of vitamin D levels in predicting the severity of acne vulgaris was 89.3% with a p value <0.001 and 95% CI 77.9% - 100%. This shows that vitamin D levels can be used to predict the severity of acne vulgaris with a moderate level of ability (AUC > 70% - 80%).



**Figure 2. ROC Curve of Vitamin D Levels in Predicting the Severity of Acne Vulgaris**

**Table 4. Vitamin D Levels in Predicting the Severity of Acne Vulgaris**

| Vitamin D | Severity of acne vulgaris | | Sensitivity | Spesitivity | NDP | NDN |
|---|---|---|---|---|---|---|
| | Severe | Mild/Moderate | | | | |
| ≤23,57 | 14 | 3 | 87,5% | 78,6% | 82,4% | 84,6% |
| >23,57 | 2 | 11 | | | | |

The cut Point value of 23.57 pg/mL for vitamin D levels to predict the severity of acne vulgaris, a sensitivity value of 87.5%, a specificity of 78.6%, a positive predictive value of 87.5% and a negative predictive value are obtained. of 84.6%, the accuracy of vitamin D levels to predict the severity of acne vulgaris was 83.3%.

**V. DISCUSSION**

This study was followed by 30 patients with acne vulgaris. Most of the subjects were female, amounting to 26 people (86.7%). The mean age of the subjects was 29.7 years with the youngest being 22 years old and the oldest being 39 years old. Similar with the study conducted by Daye et al, 2022. They conducted a study of 76 patients who experienced acne. The results of their study showed that most of the subjects were female, totaling 49 people and the rest were female. The mean age of the subjects was 20.78 ± 5.62 years, with the youngest being 16 years old and the oldest being 35 years old.[6]

Different from the study conducted by Armughan et al, 2022. The results of their study showed that the majority of subjects were male, totaling 30 people and 26 female. The mean age of the subjects was 22.7 years with the youngest being 16 years old and the oldest being 49 years old.[7]

Acne is a chronic inflammatory skin disease that primarily affects the face, chest and back, with a prevalence of nearly 95 percent in adolescents. Several large studies have reported the prevalence of juvenile acne ranging from 81 to 95 percent in young men and 79 to 82 percent in young women. Acne in men usually appears between the ages of 14 and 17 and in women between the ages of 16 and 19. However, there are cases where teenage acne can occur.[8]

Acne clinically affects adult women more frequently than men. The clinical lesions of adult acne are usually considered to be different from juvenile acne. Furthermore, young men are affected more frequently than young women and generally present the most severe form of the disease, because skin type also influences acne differences in the sexes. Skin tissue in men is relatively thicker, so the damage or scarring caused can be more severe than in women.[8]

Adult acne mainly affects women with seborrhea, comedones and inflammatory lesions. Morphologically, the classic picture of adult acne consists of a papulopustular inflammatory lesion on the lower face. Acne usually appears gradually and is mild to moderate in severity, in contrast to the

juvenile form. The literature describes differences in the clinical profile of adult and adolescent acne.[9]

Generally the clinical appearance of juvenile acne shows hyperseborrhea and non-inflammatory lesions spreading over all areas of the face with many small open or closed comedones. This is due to the fact that during adolescence, androgen levels increase and cause glands (sebaceous glands) to be stimulated and oil (sebum). During this period, the ducts of the glands (sebaceous ducts) are often blocked, causing the release of fat (sebum) to flow unevenly over the surface of the skin.[9]

In addition, these glands are frequently infected with bacteria (Propionibacterium acnes), while the clinical course of adult acne consists of predominantly, long-lasting inflammatory lesions. nodules, and cysts on the lower third of the face, neck, and jaw.[9]

Genetic factors also play a strong role. Smoking has also been associated with abnormal follicular keratinization and inflammation through lipid peroxidation of sebum in comedones by causing oxidative stress. In some studies say, the severity of acne is similar between the sexes but the quality of life is more impaired in women than men. Moreover the duration of acne appears to be an important factor responsible for the poorer perception of the disease by women. Adult acne in women has been linked to depression, anxiety, psychological stress, and suicidal ideation.[9]

Based on the examination of the degree of severity of acne, there were 16 people with severe degrees followed by patients with moderate degrees totaling 10 people (86.7%) and mild degrees totaling 4 people (53.3%).

The results of our study are different from the study conducted by Tossi et al, 2015. They conducted a study of 1048 research subjects, where the majority of their research subjects were teenagers and the rest were adults. Where the age range of their research subjects was 20.26 years. The results of their study showed that overall, 1048 research subjects obtained 448 people (43%) mild acne, 434 people (41%) moderate acne and 166 people (16%) severe acne.[10]

Similar study conducted by Roengritthidet et al, 2021. This study investigated the relationship between acne severity and diet/lifestyle factors in 2,467 Thai adolescents and adults. The results of their study showed that the prevalence of mild acne was 52%, moderate acne was 22%, and severe acne was 8%. No acne was found in 18% of participants.[11]

Acne is a multifactorial inflammatory condition of the polysebaceous follicle. Acne classification based on mild, moderate and severe severity. Acne is a chronic inflammatory disease of the sebaceous follicles. Pathophysiology of acne severity is triggered by the formation of acne lesions: hyperseborrhoea, abnormal follicular keratinization, and Propionibacterium acnes proliferation in the pilosebaceous glands. The risk of acne severity is said to increase if there are family members with a history of acne. Increased age at puberty, seborrhea, premenstrual phase, mental stress, and sweet and oily foods are recognized as risk factors for moderate to severe acne. Conversely, gender, spicy food, and smoking were not related to acne severity. Certain skin quality and nutritional habits can influence the severity of acne.[12]

Our study, we displayed vitamin D levels of all research subjects based on the severity of acne vulgaris. The highest mean levels of vitamin D were found in patients with mild degrees of acne with an average of 35.29 pg/m. The lowest level of vitamin D was seen in patients with severe acne with an average of 17.31 pg/mL. Using the Oneway Anova test

showed that there were differences in vitamin D levels based on the degree of acne vulgaris (p<0.001).

Based on a study by Lim et al, 2016. This study involved 80 patients with acne and 80 healthy controls. Serum 25-hydroxyvitamin D (25(OH)D) levels were measured, and demographic data were collected. 25(OH)D deficiency was detected in 48.8% of patients with acne, but only in 22.5% of healthy controls. 25(OH)D levels were inversely related to acne severity, and there was a significant negative correlation between 25(OH)D levels and acne severity (mild, moderate and severe 6 (22.2) vs 18 (51.4) vs 15 (83.3). ( p = 0.002).[13]

Study conducted by Alhetheli et al, 2020. They conducted a cross-sectional study involving 68 patients with acne vulgaris and 50 matched healthy controls. Serum 25-hydroxyvitamin D (25(OH)D) levels were measured for healthy patients and controls. This study resulted in lower serum levels of 25-hydroxyvitamin D in patients with acne vulgaris compared to healthy controls. This is statistically significant with a value of P = 0.003. Regarding age, sex, and sun exposure, there was no significant variation in serum 25-hydroxyvitamin D levels. But the results of their study showed no significant difference between the severity of acne (mild, moderate, severe degrees) on serum 25-hydroxyvitamin D levels.[14]

Acne is a chronic inflammatory disease, occurs due to several factors, abnormal desquamation of the follicular epithelium, insulin-like growth factor 1 (IGF-1) and androgen-stimulated increase in sebum production, colonization of P. acnes in the follicle and inflammation triggers hyperkeratinization and obstruction. pilosebaceous follicles that cause acne lesions. Inflammation is a key component in the pathogenesis of acne. IL-1, a proinflammatory cytokine, is thought to trigger the activation of proliferating keratinocytes. In acne lesions with increased proinflammatory cytokines including TNF- , IL-1 , IL-8 and IL-10, matrix metalloproteinases, defensin 4, and granulysin have been reported. Increased production of chemokines, IL-8 and activator protein (AP)-1, provides migration of circulating inflammatory cells to the tissues. Proin inflammatory cytokine expression.[15]

Among these cytokines IL 1 is a trigger in remodeling of the pilosebaceous unit and initiation of comedogenesis, while IL-8 is a molecule that attracts neutrophils to the pilosebaceous unit and IL-12 induces the expression of antimicrobial peptides. In addition, microbial ligands (such as P. acnes) can activate several pathways that can lead to the release of inflammatory cytokines (IL-1, IL-6, IL-8, IL-10, IL 12 and TNF-α). TLR activation also causes the release of antimicrobial peptides, (human defensin 1 and human defensin 2) which play an important role in the innate immune response. receptor ligands expressed in sebocytes; such as androgens and estrogens, Peroxisome proliferator-activated receptor ligands (PPAR), neuropeptides (NP), liver-X receptor ligands, histamine, retinoids, and vitamin D are some of the factors that influence sebocyte function.[15]

25-hydroxyvitamin D (25(OH)D) plays a role in the functioning of the immune system through its effects on T and B lymphocytes, dendritic cells and macrophages. In addition, it has antioxidant and anti-comedogenic properties. Vitamin D also influences the proliferation and differentiation of keratinocytes and sebocytes. Vitamin D plays a role in the proliferation and differentiation of keratinocytes and sebocytes and there are studies showing the effects of vitamin D in acne patients. Vitamin D has been shown to reduce the expression of inflammatory biomarkers, such as IL-6, IL-8, and matrix metalloproteinases.[16]

In acne P. acnes induces Th17, which stimulates the expression of IL-17, an inflammatory cytokine that is increased in acne

patients, is also inhibited by vitamin D. Furthermore, vitamin D exhibits antimicrobial effects by inducing antimicrobial peptides, such as: LL-37, in human sebocytes . The active vitamin D metabolite affects human sebocytes and keratinocytes via the nuclear vitamin D receptor (VDR). 1,25 dihydroxyvitamin-D3 (1,25 (OH) 2D3) has been shown to inhibit proliferation and stimulate keratinocyte differentiation which can lead to comedo formation, perhaps the first step in acne.[17]

The results of the analysis using the ROC curve showed that the AUC area of vitamin D levels in predicting the severity of acne vulgaris was 89.3% with a p value <0.001 and 95% CI 77.9% - 100%. This shows that vitamin D levels can be used to predict the severity of acne vulgaris with a moderate level of ability (AUC > 70% - 80%). Using the cut point value for vitamin D levels of 23.57 pg/mL to predict the severity of acne vulgaris, a sensitivity value of 87.5% was obtained, a specificity of 78.6%,

The results of our analysis are not much different from the study of Hassan et al, 2022. They conducted a study of 300 acne patients. Based on the severity of acne, patients are divided into mild, moderate and severe degrees. All patients were examined for vitamin D. The results of their study obtained an AUC area of 0.92, and the accuracy of vitamin D levels in predicting the severity of acne vulgaris was 97%. This shows that vitamin D levels can be used to predict the severity of acne vulgaris with a moderate level of ability (AUC > 70% - 80%). Using the cutoff point for vitamin D levels of 10.1 ng/mL to predict the severity of acne vulgaris, a sensitivity value of 95% and a specificity of 98.8% was obtained.[18]

And now evidence has described the comedic effects of vitamin D and its role as a modulator of the immune system, a regulator of fat cell and keratinocyte proliferation and differentiation, and as an antioxidant. Identification of vitamin D receptors on human fat cells and modulation of lipid and cytokine production by vitamin D suggests a possible link between vitamin D and acne. The study concluded that vitamin D deficiency was more common in acne patients and 25(OH)D levels were inversely associated with acne severity, especially in patients with inflammatory lesions. This points to the role of vitamin D deficiency in causing acne.[18]

## VI. CONCLUSION
Our study shows that vitamin D levels can be used to predict the severity of acne vulgaris. The more severe the severity of the acne, the lower the Vitamin D in the blood.

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