Vitamin D in Thai Acne Patients: A Cross-Sectional Study

Tin Ruikchuchit* and Premjit Juntongjin

Division of Dermatology, Chulabhorn International College of Medicine, Thammasat University, Pathum Thani, Thailand
*Corresponding author, E-mail: tineeo@gmail.com

Abstract

Acne is a skin inflammatory disorder that affects a large number of people. Vitamin D has been linked to a variety of dermatological conditions, including psoriasis, atopic dermatitis, and acne vulgaris, according to recent research. Vitamin D is involved in immune system modulation as well as the proliferation and differentiation of sebocytes and keratinocytes. Previous studies in Asia revealed vitamin D deficiency was more frequent in acne subjects compared to healthy subjects. However, there is no available data on the vitamin D level among Thai acne patients. This study aims to determine 25-hydroxyvitamin D (25(OH)D) levels in acne-diagnosed participants. The study was conducted at Benchakiti Park hospital, Thailand in June 2021. Twenty patients with a diagnosis of acne were examined for acne severity using the global acne grading system (GAGS) and classified the acne severity into four groups: mild, moderate, severe, and very severe. Serum 25(OH)D levels were measured. Our results demonstrated that none of the acne patients reached a sufficient level of vitamin D. The mean 25(OH)D level was 16.85 ± 4.38 ng/mL. There was no significant correlation between 25-hydroxyvitamin D levels and acne severity. This finding showed that low vitamin D level is very common among acne patients. The study's limitations include a limited number of individuals and a lack of patients with severe and very severe acne.

***Keywords*:** *Acne, Vitamin D, Deficiency*

1. Introduction

Vitamin D is a fat-soluble vitamin that helps the body absorb calcium and phosphorus. When there is insufficient sunlight, vitamin D can be obtained through diet or supplements. Food sources of vitamin D3 include fish, egg yolks, and fortified milk (Lamberg-Allardt & biology, 2006). When exposed to sunlight, ultraviolet B radiation converts 7-dehydrocholesterol to pre-vitamin D3. Vitamin D from the skin and diet is metabolized in the liver to 25-hydroxyvitamin D, which is used to assess a patient's vitamin D status; 25(OH)D is then metabolized in the kidney by the 25(OH)D—hydroxylase enzyme to become an active form of vitamin D. Sufficient vitamin D levels are required to maintain good health. Vitamin D receptors were found in cells and tissue throughout the body. It is involved in bone, muscle, and other non-skeletal systems. Deficiency could cause osteoporosis, bone fracture, muscle weakness, and poor immunological performances (Holick et al.,2011).

Vitamin D deficiency has been identified as a serious public health concern affecting people of all ages. Even in nations with low latitudes, where it was expected that year-round sun exposure supplied enough UVB radiation that can prevent hypovitaminosis D. Women in the Middle East had a high prevalence of low vitamin D levels. Vitamin D deficiency has been linked to a variety of conditions, including non-Hispanic African-American race, smoking, obesity, and diabetes (Parva et al., 2018). Low levels of 25-hydroxyvitamin D have long been linked to osteoporosis, osteomalacia, and increased fracture risk. Additionally, vitamin D takes part in the pathophysiology of chronic liver disease from its anti-fibrotic effect. Other disorders where vitamin D may play a role include non-alcoholic fatty liver disease (NAFLD), chronic kidney disease, and multiple sclerosis (Wang et al., 2017). Vitamin D was found to be associated with skin physiology, particularly in acne pathogenesis. A study of vitamin D effect on cultured sebocytes showed that vitamin D can induce antimicrobial peptides such as LL-37(Lee et al., 2012). Vitamin D also modulates immune systems and regulates sebocytes and keratinocytes proliferation and differentiation (Yildizgören & Togral, 2014).

Psoriasis, atopic dermatitis, vitiligo, systemic lupus erythematosus, polymorphous light eruption, alopecia areata, and acne have all been linked to a lack of vitamin D (Navarro-Triviño et al., 2019). Acne is an inflammatory disease of the pilosebaceous gland (Kurokawa et al., 2009). It has high prevalence mostly in adolescents and young adults. The undesirable physical consequences of acne can be from dyspigmentation to permanent scarring which leads to disfigurement. Depression, social isolation are common psychosocial effects that can also happen to any acne patients (Gieler et al., 2015). Pathogenesis of acne is involved by multiple factors such as increased sebum production, alteration of the quality of sebums lipids, inflammation, changes in hormone and microenvironment, neuropeptides interaction, follicular hyperkeratinization and increased number of *Cutibacterium acnes* (*C. acnes*) (Makrantonaki et al., 2011). Retention hyperkeratosis was found to attribute keratinocyte differentiation in comedonal and popular acne lesions. C. acne promotes the release of cytokines such as interleukin (IL)-6 and IL-8, which cause inflammation (Kurokawa et al., 2009).

Lim et al. (2016) from Korea found no difference in mean 25-hydroxyvitamin D levels between acne patients and healthy controls. The prevalence of vitamin D deficiency, on the other hand, was found to be higher in the acne group (Lim et al., 2016). Another study that supports the link between vitamin D deficiency and acne was conducted in Saudi Arabia. The results indicated that 25-hydroxyvitamin D levels were significantly higher in healthy controls compared to acne patients. However, there was no statistically significant relationship between acne severity and 25-hydroxyvitimin D levels (Alhetheli et al., 2020).

Among the general population, the overall vitamin D levels varied across the nation. In Southeast Asia, vitamin D insufficiency was shown to be less widespread (Lips, 2007). Thailand has the lowest frequency of vitamin D deficiency among these Southeast Asian countries, which might be attributed to the country's proximity to the equator (Chailurkit et al., 2011). Studies of vitamin D status in Thai population showed 45.2% of vitamin D insufficiency, 5.7% of vitamin D deficiency. Low 25(OH)D levels were found to be more frequent among women, younger age, and urban residence (Siwamogsatham et al., 2015).

Even though Thailand has year-round sunshine, which may contribute to a low frequency of vitamin D deficiency in the general population, patients with acne may have concealed low vitamin D status due to its role in disease pathogenesis. For the best of our knowledge, there has never been a study of vitamin D status conducted among acne diagnosed patients in Southeast Asian countries. Therefore, we would like to evaluate 25-hydroxyvitamin D levels among Thai patients and if we could predict the disease severity.

2. Objectives

The purpose of this study is to assess vitamin D status in Thai acne patients and the potential correlation between 25-hydroxyvitamin D and acne severity using the GAGS score.

3. Materials and Methods

Study design

This cross-sectional investigation was carried out in June 2021 at dermatology clinic, Benchakiti Park hospital, Bangkok, Thailand. Thammasat University's Human Research Ethics Committee accepted the study, which followed the Declaration of Helsinki, The Belmont Report, CIOMS Guidelines, and International Practice (ICH-GCP).

Subjects

Twenty participants aged between 20 and 45 years with diagnosis of acne vulgaris by dermatologist were recruited. Participants who were pregnant, lactating, had history of chronic renal disease, polycystic ovary syndrome, or receiving vitamin D supplements were excluded.

Clinical assessment

Physical examination was performed by primary investigator. The global acne grading system (GAGS) score was used to grade the severity of acne. This system categorizes the face, chest, and back into six areas. Each type of lesion is assigned a number: no lesions = 0, comedones = 1, papules = 2, pustules = 3,

and nodules = 4. The factor x Grade (0-4) is used to calculate the score for each area. The sum of the scores in each category location will be graded. Mild is a score of 1-18; moderate is a score of 19-30; severe is a score of 31-38; and very severe is a score of >39 (Doshi et al., 1997).

Table 1 Area factor value in GAGS

Area	Factor
Forehead	2
Right cheek	2
Left cheek	2
Nose	1
Chin	1
Chest and back	3

Serum vitamin D analysis

Serum 25(OH)D was used to determine vitamin D levels. Clotted blood 3 mL were stored at 2-8°C for Vitamin D 25(OH) total analysis using the electrochemiluminescence immunoassay (ECLIA) method, a competitive protein binding immunoassay with electrochemiluminescence detection, on the Roche Cobas e801 analyzer. Specimens were analyzed within 24 hours of being collected. According to endocrine society clinical practice guidelines, vitamin D levels were classified as sufficiency (30 ng/mL or higher), insufficiency (21-29 ng/mL), or deficiency (20 ng/mL or less).(Holick et al.,2011)

Statistical analysis

Stata 14.0 was used to perform statistical analyses. The mean difference was examined using the t-test. To compare categorical data, the chi-square test was used. Spearman's rank-order correlation analysis was used to determine the relationship between serum vitamin D level and GAGS score. Statistical significance was defined as a level of significance with a p-value <0.05.

4. Results and Discussion

4.1 Results

Patient characteristic

Twenty acne participants were enrolled in the experiment. All patients were Thai. The demographic data of acne patients are displayed in Table 2. Patients' age ranged from 20 to 45 years, mean age of 28.4; 65% were female, and 35% were male. Around two-third of the participants had mild severity while one-third had moderate severity. There was no severe or very severe acne subject in this study. Mean of the disease duration was around 12.5 years.

Table 2 Basic characteristics of acne patients

Characteristics	**Acne (n = 20)**
Age (year)	28.4 ± 5.73
Sex (M/F), n (%)	7/13 (35/65)
Acne severity, n (%)	
Mild	13 (65)
Moderate	7 (35)
Severe	0 (0)
Very severe	0 (0)
Duration of acne (year)	12.5 ± 7.45

All values are presented as mean ± SD unless otherwise stated.

Results of 25(OH)D levels by severity group

Total 25-hydroxyvitamin D levels ranged from 11.1 to 25.1 ng/mL. The mean (SD) level of 25(OH)D was 16.85 ± 4.38 ng/mL. There were only mild and moderate severity patients included in this study. Among mild and moderate acne participants, vitamin D levels in both severities were not significantly different (p-value = 0.966) and average serum 25(OH)D levels were 16.88 ± 4.80 ng/ and 16.80 ± 3.85 ng/mL, respectively. (Table 3) The prevalence of vitamin D deficiency showed no significant difference in mild acne group compared to moderate acne group (69.2% vs. 71.4%, p-value = 0.919) as shown in Figure 1 and Table 4.

Table 3 Results of Vitamin D levels according to severity of acne.

Vitamin D levels	Severity of acne		p-value[a]
	Mild (n = 13)	Moderate (n = 7)	
	Mean ± SD	Mean ± SD	
25-hydroxyvitamin D, 25(OH)D (ng/mL)	16.88 ± 4.80	16.80 ± 3.85	0.966

[a]Independent sample t-test

Table 4 Results of vitamin D deficiency according to severity of acne.

Vitamin D levels	Severity of acne				p-value[a]
	Mild (n = 13)		Moderate (n = 7)		
	n	(%)	n	(%)	
Insufficiency	4	(30.8)	2	(28.6)	0.919
Deficiency	9	(69.2)	5	(71.4)	

[a]Chi-square test

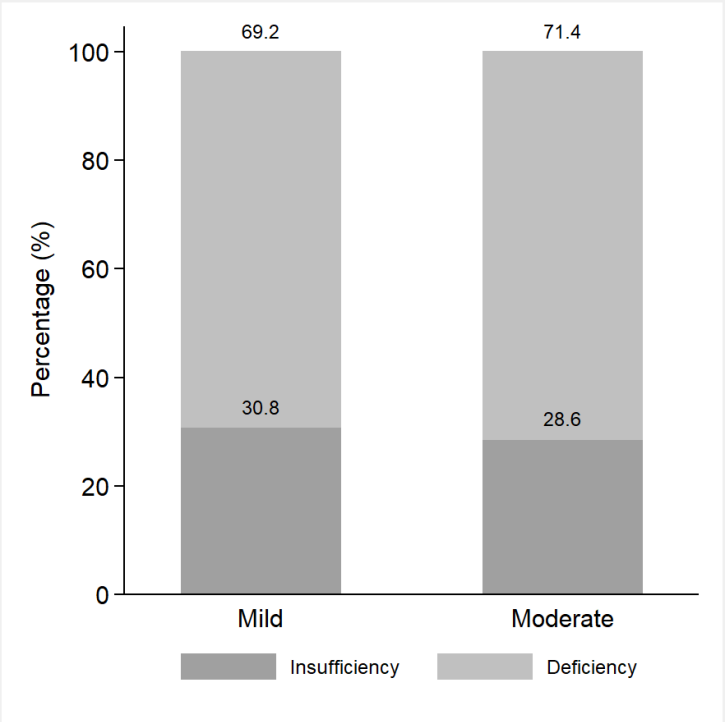

Fig 1 Patient percentages with different vitamin D status

Relationship between 25-hydroxyvitamin D levels and severity of acne

We determined whether 25-hydroxyvitamin D levels was influenced by acne severity evaluated by the GAGS score by using correlation coefficient. Figure 2 showed no significant relationship between 25-hydroxyvitamin D levels and GAGS score. There was only a low inverse correlation. (r = -0.199, 95%CI: 0.589 to 0.267, p-value = 0.401). This might reflect patients with more acne severity score would probably have lower 25(OH)D levels.

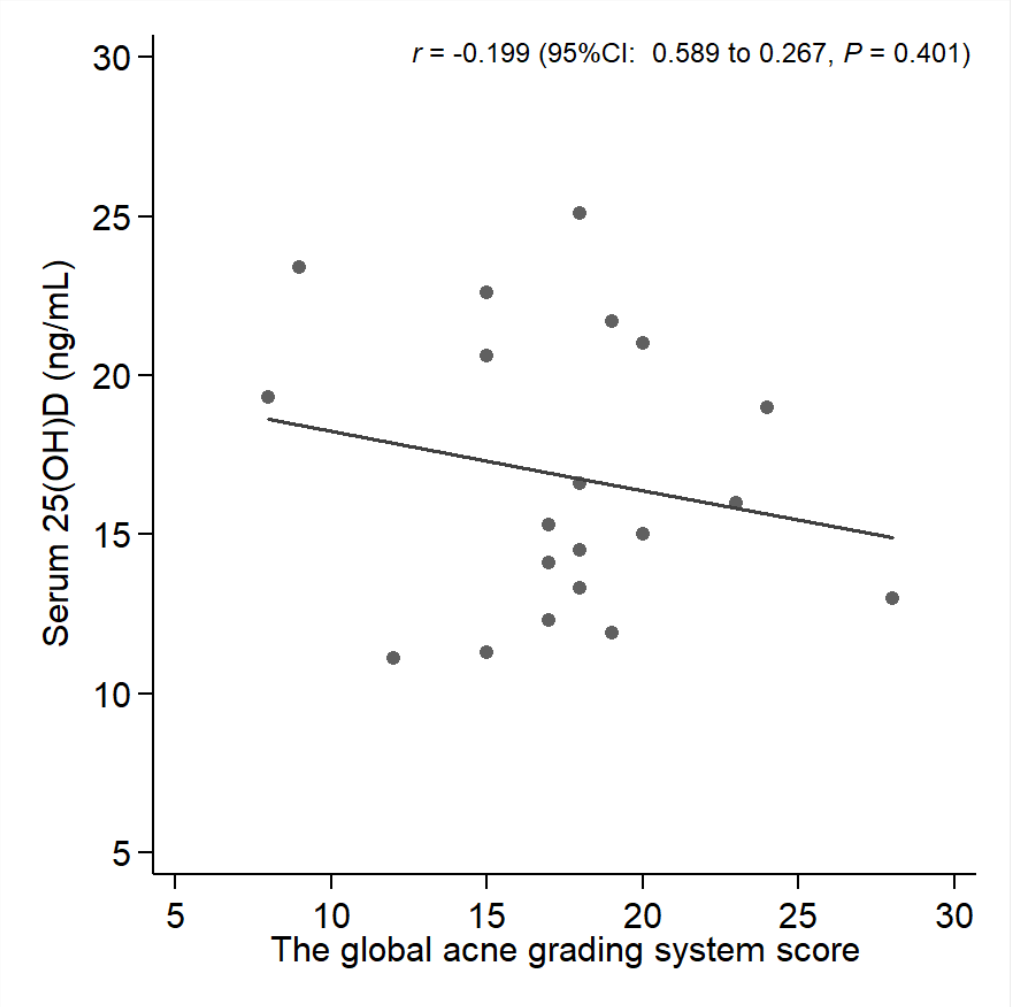

Fig 2 Correlation vitamin D levels and GAGS score

4.2 Discussion

In our study, we assessed twenty acne patients aged between 20-45 years. For clinical assessment, grading of severity was done by using GAGS score, and vitamin D status was tested by blood sampling to analyse serum 25(OH)D level. Results showed low mean serum 25(OH)D level. All of our acne participants were identified as having either insufficient or deficient vitamin D status. No sufficient vitamin D level was found among our subjects. A high prevalence of vitamin D deficiency was found in both mild and moderate acne, with no statistical difference. Moreover, 25(OH)D levels were not associated with acne severity.

Table 5 Summary of the studies for the comparison of serum 25(OH)D levels between acne patiens and healthy controls (HCs)

Study	Study design	Country	Acne (ng/mL), (n)	HCs (ng/mL), (n)	p-value
Toosi 2015	Cross-sectional	Iran	8.4(5–14.1)*, (39)	10.4 (6.58–20.25)*, (40)	0.14
Lim 2016	Case-control	Korea	13.1 ± 9.8, (80)	15.2 ± 7.2, (80)	0.112
Ahmed Mohamed 2020	Case-control	Egypt	21.48 ± 5.46, (100)	31.48 ± 15.04, (100)	0.001
Alhetheli 2020	Case-control	Saudi Arabia	28.8 ± 7.9, (68)	40 ± 11.7, (50)	0.003
Our study 2021	Cross-sectional	Thailand	16.85 ± 4.38, (20)	N/A	

*Values are median (Interquartile range)
All values are presented as mean ± SD unless otherwise stated.

The first study of vitamin D status in acne patients was conducted in Iran, with 39 acne vulgaris patients and 40 healthy controls participating. When acne patients and healthy controls were compared, the median 25(OH)D concentration was quite low (8.4 ng/mL vs 10.4 ng/mL), with no statistically significant difference (Toossi et al., 2015) as shown in Table 5.

The only study conducted in Asia, Korea, included 80 acne patients and 80 healthy controls. The levels of 25-hydroxyvitamin D in the blood were determined. Mean 25(OH)D levels were 13.1 ± 9.8 ng/mL vs 15.2 ± 7.2 ng/mL. Deficiency was found in 48.8% of acne patients and 22.5 % of healthy controls.
The level of 25(OH)D was found to be negatively correlated with the number of inflammatory lesions. Moreover, they found that mean serum vitamin D was also inversely correlate with severity of acne. (Lim et al., 2016).

A later study conducted in Egypt on 100 acne patients and 100 healthy individuals discovered a significant difference in mean 25(OH)D between two groups (21.48 ± 5.46 ng/mL vs 31.48 ± 15.04 ng/mL, p-value = 0.001). They also discovered that vitamin D deficiency was linked to disease severity (Ahmed Mohamed et al., 2020). Another case-control study conducted in Saudi Arabia comparing 68 acne patients with 50 healthy individuals also reported a significant difference in mean serum vitamin D between two groups (Alhetheli et al., 2020).

The relationship between acne and low vitamin D seemed to be inconclusive. In 2021, a meta-analysis, which included 13 articles and a total of 1,362 acne patients and 1,081 healthy controls, was conducted and reported that acne patients had significantly low vitamin D levels. There was also an inverse relationship between vitamin D levels and the severity of acne vulgaris (Hasamoh et al., 2021).

Our study aimed to evaluate vitamin D status among Thai acne patients and the association between 25-hydroxyvitamin D levels and acne severity. Therefore, healthy controls were not included into this study. Although this study might not be able to directly compare to previous studies due to lack of control group, we found some corresponding that deficient of vitamin D was quite prevalent in acne patients. Low inverse correlation of GAGS scores and 25-hydroxyvitamin D levels supported a possible relationship between vitamin D and acne pathogenesis.

Not only the possible relation of vitamin D deficiency status and acne. We also considered the general vitamin D status of healthy Thai population. The study was conducted in 2008-2009, 2,641 adults aged between 15 and 98 years were randomly selected from the Thai National health examination survey cohort. The levels of 25(OH) D in the blood were determined. Bangkok residents had lower vitamin D levels than the rest of the country, according to the findings. (Bangkok, the central, northern, northeastern, and southern provinces) In Bangkok, the overall prevalence of vitamin D deficiency was 64.6%. The level of 25(OH)D was 64.8 ± 0.7 nmol/L (25.92 ± 0.28 ng/mL) (Chailurkit et al., 2011).

Previous studies of vitamin D in dermatologic conditions reported insufficient levels of vitamin D, such as a study on the clinical effect of vitamin D supplementation in mild psoriatic patients with a Psoriatic Area and Severity Index (PASI) score less than 10, age between 18-70 years. Average 25(OH)D levels at baseline were 24.77 ng/mL and 24.13 ng/mL in intervention vs placebo group, which was categorized in the

insufficient level of vitamin D. After a three-month follow-up, the mean PASI score in the vitamin D group had decreased (Disphanurat et al., 2019).

Vitamin D has been linked to a variety of organ systems in the body, including the skin. The association between vitamin D level and acne severity has yet to be determined. The goal of this study is to analyze vitamin D levels in Thai acne patients and the association between 25-hydroxyvitamin D levels and acne severity. Vitamin D deficiency was shown to be quite common among acne patients, according to our findings. None of the subjects had adequate vitamin D levels. This suggested that vitamin D deficiency may play a role in acne etiology. However, there was a very weak inverse connection between 25(OH)D levels and acne severity score. As a result, we may not be able to conclude that serum 25(OH)D levels were actually linked to the severity of acne.

Several factors can explain the high prevalence of vitamin D deficiency and the low level of serum 25-hydroxyvitamin D, such as the insufficiency levels of vitamin D in the overall Thai population, especially those who live in Bangkok (Chailurkit et al., 2011). Air pollution in an urban area is likely to absorb ultraviolet radiation which alters the cutaneous production of vitamin D (Holick, 1995). Another factor for vitamin D deficiency is severe acne patients may tend to avoid spending outdoor periods due to psychological stress (Lim et al., 2016). Lastly, the consequences of the lock-down period from Corona virus outbreak in Thailand led to avoidance of subjects to leave their residence and eventually resulted in the decreased duration of sun exposure during daytime. Our study was conducted in June 2021 at Benchakiti Park Hospital, Bangkok, Thailand, which represented an example of the current vitamin D status in acne patients residing in Bangkok. The limitation included that we only evaluated vitamin D status among acne patients, which had only mild and moderate severity patients participated. A larger investigation should be carried out to confirm the actual vitamin D level of acne patients and to compare them to healthy people.

5. Conclusion

None of the acne patients has sufficient vitamin D level. Vitamin D levels showed a trend of low inversely correlated with disease severity score. Despite the fact that we may not be able to determine that a vitamin D deficiency is linked to acne severity. The high prevalence of vitamin D deficiency among acne patients in this study, on the other hand, may signify the need for vitamin D status evaluation or supplemental recommendation in the future.

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