

Vitamin D As Predictive Biomarker In The Severity of Acne Vulgaris: A Systematic Review

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Abstract:

This systematic review aims to evaluate differences in serum vitamin D levels between individuals with acne vulgaris and healthy individuals and to assess whether vitamin D levels can serve as a predictive biomarker for the severity of acne vulgaris. A systematic search was conducted using Publish or Perish, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, in Scopus, PubMed, Semantic Scholar, and SINTA databases. Eligible studies involved participants aged 12–59 years from Asia and Africa. Nine studies met the criteria, including 1,212 participants (655 with acne vulgaris and 557 healthy controls). The methodological quality of each included study was assessed using the Newcastle-Ottawa Scale (NOS), covering selection, comparability, and outcome domains. Most studies reported lower serum vitamin D levels in acne patients than in controls. Six studies showed a significant inverse correlation with acne severity, while three found no significant correlation, possibly due to influencing factors such as sun exposure, diet, supplements, and lifestyle. Although most studies indicate a significant inverse relationship between serum vitamin D levels and acne severity, the absence of predictive models and statistical validation prevents vitamin D from being established as a clinical predictive biomarker. Further prospective research employing validated predictive tools is required to confirm its role in acne management.

Keywords: *Acne vulgaris; biomarker; inflammation; severity; vitamin D*

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INTRODUCTION

Acne vulgaris affects more than 90% of individuals at some point in their lives, making it one of the most common dermatological conditions worldwide. Acne has long-term effects, including scarring that can cause psychosocial distress (Eichenfield et al., 2021; Matthew et al., 2021; Nasri et al., 2015). Facial scars can alter a person's perception of their body image and negatively affect their overall quality of life, potentially leading to depression and feelings of inferiority. Research by Damayanti et al. (2022) showed a correlation between *acne vulgaris* and quality of life. However, it found no significant correlation between the severity of *acne vulgaris* and quality of life. In contrast, Ayu et al. (2023) and Ghossanidewi et al. (2023) demonstrated that the severity of *acne vulgaris* correlated with quality of life.

Matthew et al. (2021) showed a significant association between psychosocial burden and medical treatment-seeking behavior. *Acne vulgaris* is characterized as a chronic inflammatory disorder of the pilosebaceous unit, which includes the hair follicle and sebaceous gland, primarily triggered by increased sebum production, hyperkeratinization of follicles, bacterial colonization, and subsequent inflammation. *Acne vulgaris* is classified as mild, moderate, or severe based on the count of present inflammatory and non-inflammatory lesions. Earlier

research has highlighted the essential role of the immune system in every stage of acne pathogenesis. Specifically, members of the IL-1 cytokine family play a key role in initiating acne lesions and the associated inflammatory response.

In vitro studies have shown that sebocytes and keratinocytes serve as target cells for vitamin D, modulating their differentiation and proliferation. Vitamin D, a lipophilic steroid hormone often called the "sunshine vitamin," supports optimal human health. The body obtains it through ultraviolet exposure, dietary sources, or supplementation. Vitamin D reduces both the initiation and persistence of inflammation in *acne vulgaris*, inhibits excessive cell proliferation, and regulates keratinocyte apoptosis.

Furthermore, vitamin D helps manage sebocyte hyperplasia, regulates their lipid composition, and controls the release of pro-inflammatory cytokines, including IL-6 and IL-8. Researchers have identified sebocytes expressing vitamin D receptors (VDRs) on their membranes. Serum vitamin D levels may significantly influence *acne* pathogenesis due to its antioxidant and anti-comedogenic properties. Vitamin D insufficiency can exacerbate these mechanisms, as lower serum levels impair skin cell growth and differentiation.

The complex role of vitamin D in immune regulation and inflammatory processes in *acne vulgaris* pathogenesis raises the question of whether it could serve as a predictive biomarker for disease severity. In clinical research, predictive biomarkers estimate the likelihood of outcomes based on therapy, aiding informed decision-making. Beyond indicating disease associations, biomarkers support interventions. Given vitamin D's influence on inflammatory pathways, it holds potential as a predictive biomarker in *acne vulgaris*.

Alhetheli et al. (2020) demonstrated that serum vitamin D levels in control subjects were significantly higher than in those with *acne vulgaris* ($P = 0.003$), but found no significant association between vitamin D deficiency and clinical severity. Conversely, Kazeminejad et al. (2024) reported a higher prevalence of abnormal zinc and vitamin D levels in acne patients ($p = 0.002$ and $p = 0.001$, respectively) and a correlation between disease severity and vitamin D levels. Previous studies have shown inconsistencies in serum vitamin D levels between *acne vulgaris* patients and controls, as well as in the correlation between vitamin D deficiency and severity.

To address these discrepancies, the authors conducted a systematic review evaluating vitamin D's potential as a predictive biomarker for *acne vulgaris* severity. They hope this review provides robust evidence to guide innovative preventive and therapeutic strategies involving vitamin D, helping patients avoid disease exacerbation while improving overall health.

METHOD

The researchers conducted this systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines with the following research questions: What is the difference in vitamin D levels between individuals with acne vulgaris and individuals with healthy skin, and can vitamin D levels serve as a predictive biomarker for the severity of acne vulgaris.

We searched for published articles from the Scopus, PubMed, and Semantic Scholar databases through Publish or Perish and SINTA (Science and Technology Index) from

inception to February 2025. The keywords we used were "(" vitamin D "OR '25-hydroxyvitamin D' OR 'cholecalciferol') AND (" acne vulgaris "OR 'acne severity' OR 'inflammatory acne') AND (" adolescent*"OR 'teenager*' OR 'teenager*') OR (" young adult*"OR 'adult*' OR 'adult')."

This study used the population, intervention, comparison, and outcome (PICO) strategy to include studies that met the following criteria. Population: Individuals with acne vulgaris compared to healthy skin who did not have acne vulgaris. Intervention: Measurement and observation of vitamin D levels in samples. Comparison: Vitamin D levels in acne vulgaris patients versus healthy-skinned individuals. Results: Assess vitamin D levels' correlation and potential role as a biomarker in predicting acne vulgaris severity.

Eligibility criteria included the following: (1) human participants aged 12-59 years, (2) studies conducted in Asia & Africa, and (3) complete studies in English or Bahasa Indonesia. Exclusion criteria were (1) human participants diagnosed with other than acne vulgaris, (2) animal studies, (3) studies that did not delineate vitamin D levels by acne severity, (4) unrelated topics, and (5) studies that were systematic reviews, meta-analyses, case reports, theses, dissertations, and non-original research.

Three reviewers screen each search engine independently and decide whether the study should be included or excluded. Other reviewers can see the decisions (not blinded), and Rayyan Systems Inc. aggregates them. All reviewers discuss differences between decisions. They assess selected journals to extract the following information: author data, study title, study time and location, study design, inclusion and exclusion criteria, number of participants, variables analyzed (mainly serum 25(OH)D levels and acne severity), and results based on P value and correlation coefficient (r).

Study quality was evaluated using the Newcastle-Ottawa Scale (NOS), which covers three domains. The Selection domain (4 points) evaluates how participants were selected, whether case participants represent the actual population, have a precise diagnosis, controls were drawn from the same source, and are free from the condition being studied. The Comparability domain (2 points) assesses whether the study accounted for confounding factors, such as age, gender, BMI, or sun exposure. The Outcomes domain (3 points) evaluates the validity of the acne severity assessment tools used, the adequacy of follow-up, and the methods of outcome assessment. All studies scored seven or higher, indicating high methodological quality.

RESULTS AND DISCUSSION

Study Selection & Characteristics of Included Studies

The flow diagram [Figure 1] shows that 169 studies reviewers searched from all databases. We manually excluded 64 duplicates using Rayyan software. The reviewers then screened the remaining 105 studies based on titles, abstracts, outcomes, and language. They excluded 52 studies for having unrelated themes, 15 for being the wrong publication type, 12 for having bad outcomes, and 1 for being in a foreign language.

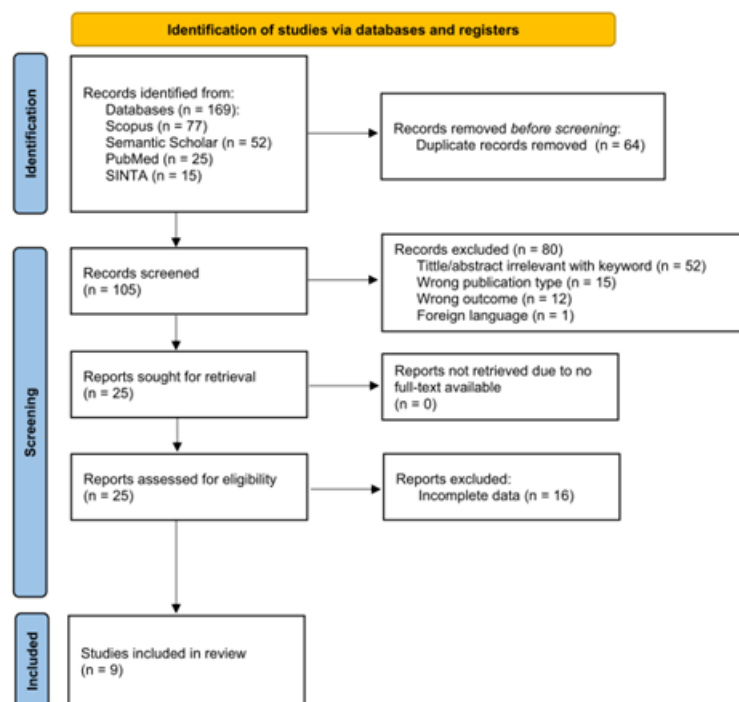


Figure 1. PRISMA flow diagram

Reviewers did a full-text review of the remaining 25 studies and identified nine that meet the inclusion criteria for this review. Nine studies met the inclusion criteria, with 1.212 participants (655 acne patients and 557 control) included. The study sample size ranged from 30 to 134. The studies were conducted in Iran (Goodarzi et al., 2020; Kazeminejad et al., 2024), Turkey (Kemeriz et al., 2020), Saudi Arabia (Alhetheli et al., 2020), Egypt (Elkamshoushi et al., 2021; Sharaf et al., 2022), India (Singh, Dorjay, et al., 2021; Singh, Khurana, et al., 2021), and Pakistan (Naheed et al., 2023) [Table 1]. Moreover, six were case-control studies (Alhetheli et al., 2020; Elkamshoushi et al., 2021; Goodarzi et al., 2020; Kazeminejad et al., 2024; Naheed et al., 2023; Sharaf et al., 2022), two cross-sectional studies (Singh, Dorjay, et al., 2021; Singh, Khurana, et al., 2021), and one prospective case-control study (Kemeriz et al., 2020). Seven studies used GAGS for acne severity grading (Alhetheli et al., 2020; Elkamshoushi et al., 2021; Kemeriz et al., 2020; Naheed et al., 2023; Sharaf et al., 2022; Singh, Dorjay, et al., 2021; Singh, Khurana, et al., 2021), one study used IAEM (Goodarzi et al., 2020), one study used Tutakne (Kazeminejad et al., 2024). Three studies used ELISA methods to measure serum vitamin D levels (Goodarzi et al., 2020; Kazeminejad et al., 2024; Sharaf et al., 2022), another three studies used ECLIA methods (Alhetheli et al., 2020; Kemeriz et al., 2020; Naheed et al., 2023), two studies used CLIA methods (Singh, Dorjay, et al., 2021; Singh, Khurana, et al., 2021), and one study used ELFA methods (Elkamshoushi et al., 2021) [Table 2].

Main Findings

Some studies stated vitamin D status is deficiency, insufficiency, or sufficiency. Reviewers found that vitamin D status in cases and controls varied. In five studies, vitamin deficiency was significantly higher in cases. We identified six studies showing that the more severe the acne,

the lower the serum vitamin D levels, indicating a statistically significant negative correlation. Two of the six studies showed that serum vitamin D levels were significantly lower in patients with acne vulgaris compared to the control group and demonstrated a significant negative correlation between serum vitamin D levels and the severity of acne vulgaris, with all two studies having a P-value < 0.001 (Kazeminejad et al., 2024; Kemeriz et al., 2020).

Two of the six studies showed no statistically significant difference between the control group and patients with acne vulgaris and demonstrated a significant negative correlation between serum vitamin D levels and the severity of acne vulgaris, with all two studies having a P-value < 0.001 (Singh, Dorjay, et al., 2021; Singh, Khurana, et al., 2021). One of the six studies showed that serum vitamin D levels were significantly lower in patients with acne vulgaris compared to control group and demonstrated a significant correlation between serum vitamin D levels and the severity of acne vulgaris, with a P-value of 0.047 (Naheed et al., 2023). Another study showed that serum vitamin D levels were significantly lower in the control group compared to patients with acne vulgaris and demonstrated a significant negative correlation between serum vitamin D levels and the severity of acne vulgaris, with a P-value of 0.03 (Elkamshoushi et al., 2021).

In addition to the six studies mentioned above, we also found three studies showing that serum vitamin D levels have no statistically significant association with the severity of acne vulgaris. Two of the three studies showed that serum vitamin D levels were significantly lower in patients with acne vulgaris compared to the control group (Alhetheli et al., 2020; Sharaf et al., 2022). One of the three studies showed that serum vitamin D levels were significantly lower in the control group compared to patients with acne vulgaris (Goodarzi et al., 2020). The three studies above showed differences in serum vitamin D levels between patients with acne vulgaris and the control group. Two studies conducted by Alhetheli *et al.* (2020) and Sharaf et al. (2022) showed that serum vitamin D levels were significantly lower in patients with acne vulgaris compared to the control group (Alhetheli et al., 2020; Sharaf et al., 2022) [Table 2].

Study Quality Assessment

The methodological quality of all included studies was evaluated using the Newcastle-Ottawa Scale (NOS). The evaluation was based on three NOS domains: selection, adherence, and outcomes. All studies reviewed in this article demonstrated high methodological quality. Specifically, four studies achieved the maximum score of 9 (Alhetheli et al., 2020; Elkamshoushi et al., 2021; Kazeminejad et al., 2024; Sharaf et al., 2022), one study scored 8 (Goodarzi et al., 2020), and the remaining four studies scored 7 out of 9 (Kemeriz et al., 2020; Naheed et al., 2023; Singh, Dorjay, et al., 2021; Singh, Khurana, et al., 2021). These results suggest that the included studies provide a solid foundation for synthesizing evidence on the relationship between serum vitamin D levels and the severity of acne [Table 3].

This systematic review aims to determine the differences in vitamin D levels between individuals with acne vulgaris and individuals with healthy skin and whether vitamin D levels can serve as a predictive biomarker for the severity of acne vulgaris. Researchers must understand the serum vitamin D level thresholds commonly used in studies and clinical practice when interpreting the results. They categorize serum vitamin D levels below 20 ng/mL as deficient, 20–29 ng/mL as insufficient, and ≥ 30 ng/mL as sufficient (El Mongy & Hilal, 2023).

Overall, the findings of this systematic review indicate a significant negative correlation between serum vitamin D levels and the severity of acne vulgaris, although there were some differences in results between the studies reviewed.

Six of the nine studies analyzed found that the lower the serum vitamin D level, the more severe the acne vulgaris, with P values indicating statistical significance ($P < 0.05$). The six studies indicate that vitamin D is associated with the severity of acne vulgaris, as vitamin D exerts anti-inflammatory effects through various biological mechanisms. These mechanisms provide evidence of the immune regulatory role of vitamin D and its anti-inflammatory effects in individuals with acne. Vitamin D suppresses the differentiation of TH17 cells induced by *Cutibacterium acnes* (Samanta, 2021). Vitamin D deficiency leads to increased levels of interleukin 17 (IL-17), a pro-inflammatory cytokine, in individuals with acne, as demonstrated in studies by Elkamshoushi *et al.* (2021) and Singh *et al.* (2021) (Elkamshoushi *et al.*, 2021; Singh, Khurana, *et al.*, 2021).

Another mechanism involves inducing antimicrobial effects by stimulating the production of antimicrobial peptides such as cathelicidin in human sebocytes. Researchers have found that in cultured sebocytes, vitamin D reduces the production of inflammatory cytokines, including interleukin IL-6, IL-8, and matrix metalloproteinase-9 (Kazeminejad *et al.*, 2024). Vitamin D deficiency can lead to increased acne formation, as this vitamin regulates the proliferation and differentiation of sebocytes and keratinocytes and has anti-comedogenic properties. Vitamin D deficiency increases lipogenesis in sebaceous glands, leading to an increase in inflammatory lesions in acne (Iqbal *et al.*, 2023).

The six studies above differed in serum vitamin D levels. A study conducted by Elkamshoushi *et al.* (2021) found that serum vitamin D levels were lower in the control group compared to patients with acne vulgaris. The researchers noted that several factors, such as BMI and sunscreen use, influenced this difference. Additionally, most acne vulgaris patients in the study had a history of moderate to good dairy product intake. Furthermore, the researchers administered vitamin D supplementation to acne vulgaris patients for three months. The results showed a statistically significant increase in serum vitamin D levels from 22.8 ± 5.7 to 35.1 ± 4.5 ng/ml ($P < 0.0001$).

Regarding clinical improvement, there was a statistically significant decrease in disease severity ($P = 0.001$) after supplementation, with the average GAGS score decreasing from 33 (32–37) to 30 (29–30), accompanied by a noticeable reduction in inflammatory lesions compared to non-inflammatory acne lesions (comedones), which remained present (Elkamshoushi *et al.*, 2021). Two other studies conducted by Singh *et al.* (2021) showed that there were no significant differences between the control group and patients with acne vulgaris. However, the researchers did not explain what factors might have caused this to happen.

However, three other studies found no significant association, even though vitamin D levels were lower in the acne vulgaris patient group than in the control group. The researchers mentioned that several factors caused this, such as psychological stress leading individuals to avoid spending long periods outdoors. In severe cases of acne vulgaris, psychological stress itself may be the underlying cause (Alhetheli *et al.*, 2020). Other factors influencing vitamin D levels, such as dietary habits, lifestyle, occupation, and sunscreen use, may be involved (Sharaf

et al., 2022). A study conducted by Goodarzi *et al.* (2020) showed that serum vitamin D levels were significantly lower in the control group compared to patients with acne vulgaris.

According to the researchers, this is due to higher sun exposure or vitamin D intake in patients with acne vulgaris, which aligns with the reason why serum vitamin D levels are not significantly associated with the severity of acne vulgaris (Goodarzi et al., 2020). Although most studies show a statistically significant association between serum vitamin D levels and the severity of acne vulgaris, there is currently insufficient evidence to establish vitamin D as a clinical biomarker for acne vulgaris or as routine therapy. Further research is needed to evaluate whether vitamin D supplementation can improve the severity of acne in patients with vitamin D deficiency, as vitamin D-based therapy may be beneficial for patients with acne vulgaris who have low serum vitamin D levels.

Table 1. Characteristic Studies

| Author, Year | Country | Study Design | Participants (mean age in years) | Adjusted cofounding variables |
|--|--------------|--------------------------|--|--|
| Goodarzi <i>et al.</i> , 2020(Goodarzi et al., 2020) | Iran | Case control | Case : 72 (25.5±7.9) Control : 72 (26.4±8.8) | Age and sex |
| Kemeriz <i>et al.</i> , 2020(Kemeriz et al., 2020) | Turkey | Prospective case-control | Case : 134 (20.11±2.92) Control :129 (20.27±3.17) | Age, sex, and BMI |
| Alhetheli <i>et al.</i> , 2020(Alhetheli et al., 2020) | Saudi Arabia | Case control | Case : 68 (NA) Control : 50 (NA) | Sex, sun exposure, family history, onset and duration |
| Elkamshoushi <i>et al.</i> , 2021(Elkamshoushi et al., 2021) | Egypt | Case control | Case : 30 (17.4±2.7) Control : 15 (17.7±2.3) | Age, BMI, smoking habit, sunscreen use, sun exposure, and dairy intake |
| Singh <i>et al.</i> , 2021(Singh, Dorjay, et al., 2021) | India | Cross-sectional | Case : 50 (22.44±3.073) Control : 30 (24±4.152) | Age, sex, and BMI |
| Singh <i>et al.</i> , 2021(Singh, Khurana, et al., 2021) | India | Cross-sectional | Case : 50 (22.44±3.073) Control : 30 (24±4.152) | Age, sex, and BMI |
| Sharaf <i>et al.</i> , 2021(Sharaf et al., 2022) | Egypt | Case control | Case : 80 (21.66±4.11) Control : 40 (23.15±3.88) | Age, sex, occupation, and BMI |
| Naheed <i>et al.</i> , 2023(Naheed et al., 2023) | Pakistan | Case control | Case : 71 (19.23±7.42) Control : 91 (21.4±6.97) | Age and sunscreen use |
| Kazeminejad <i>et al.</i> , 2024(Kazeminejad et al., 2024) | Iran | Case control | Case : 100 (25.5±6.3) Control : 100 (25.3±5.6) | Age, sex, BMI, occupation, alcohol consumption, and tobacco smoking |

Table 2. Main Outcome of The Studies Included in This Systematic Review of The Correlation Between Serum 25-Hydroxy Vitamin D and Acne Vulgaris

| Author, Year | Mean Serum 25-hydroxy Vitamin D | | P value (serum vitamin D level & acne severity) | Outcome - Result |
|--|---------------------------------|---|---|---|
| | Control | Case | | |
| Goodarzi <i>et al.</i> , 2020(Goodarzi et al., 2020) | 20.39±14.89 | 29.30±16.21 Acne severity (IAEM) Moderate-severe: 26.67±15.83 Very severe: 32.97±16.27 | >0.05 | Vitamin D status – NA Serum vitamin D level (ELISA) – Significantly higher in cases Vitamin D level and acne severity – No significant correlation |
| Kemeriz <i>et al.</i> , 2020(Kemeriz et al., 2020) | 20.27±3.17 | 14.17±7.42 Acne severity (GAGS) | < 0.001 | Vitamin D status – Deficiency is significantly higher in cases Serum vitamin D level (ECLIA) – Significantly lower in cases Vitamin D level and acne severity – Significant negative correlation |
| Alhetheli <i>et al.</i> , 2020(Alhetheli et al., 2020) | 40±11.7 | 28.8±7.9 Acne severity (GAGS) Mild : 26±9.4 Moderate : 31.4±6.9 Severe : 28.4±6.7 | 0.067 | Vitamin D status – NA Serum vitamin D level (ECLIA) – Significantly lower in cases Vitamin D level and acne severity – No significant correlation |
| Elkamshoushi <i>et al.</i> , 2021(Elkamshoushi et al., 2021) | 16.4±7.5 | 25.0±6.5 Acne severity (GAGS) Severe : 25.7±6.5 Very severe : 20±6 | 0.03 | Vitamin D status – Deficiency is significantly higher in control Serum vitamin D level (ELFA) – Significantly higher in cases Vitamin D level and acne severity – Significant inverse correlation |
| Singh <i>et al.</i> , 2021(Singh, Dorjay, et al., 2021) | 20.904±11.66 | 16.652±8.63 Acne severity (GAGS) Mild : 28.06 Moderate : 21.63 | < 0.001 | Vitamin D status – Deficiency is significantly higher in cases |

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| Author, Year | Mean Serum 25-hydroxy Vitamin D | | P value (serum vitamin D level & acne severity) | Outcome - Result |
|--|---------------------------------|--|---|--|
| | Control | Case | | |
| | | Severe : 13.34 Very severe : 9.47 | | Serum vitamin D level (CLIA) – Lower in cases Vitamin D level and acne severity – Significant inverse correlation |
| Singh <i>et al.</i> , 2021(Singh, Khurana, et al., 2021) | 20.904±11.66 | 16.652±8.63 Acne severity (GAGS) Mild : 28.06±9.66 Moderate : 21.63±4.84 Severe : 13.34±4.26 Very severe : 9.47±1.5 | <0.001 | Vitamin D status – Deficiency is significantly higher in cases Serum vitamin D level (CLIA) – Lower in cases Vitamin D level and acne severity – Significant negative correlation |
| Sharaf <i>et al.</i> , 2021(Sharaf et al., 2022) | 114.67±42.36 | 75.51±22.7 Acne severity (GAGS) Mild to very severe : 25.73±10.61 | 0.927 | Vitamin D status – NA Serum vitamin D level (ELISA) – Significantly lower in cases Vitamin D level and acne severity – No significant correlation |
| Naheed <i>et al.</i> , 2023(Naheed et al., 2023) | 52.63±31.244 | 43.14±17.954 Acne severity (GAGS) | 0.047 | Vitamin D status – Deficiency evident in cases Serum vitamin D level (ECLIA) – Significantly lower in cases Vitamin D level and acne severity – Significant correlation |
| Kazeminejad <i>et al.</i> , 2024(Kazeminejad et al., 2024) | 27.7±12.5 | 16.9±6.0 Acne severity (Tutakne) Grade 1 : 22.9±3.9 Grade 2 : 18.3±5.7 Grade 3 : 14.8±3.5 Grade 4 : 10.3±2.9 | < 0.001 | Vitamin D status – Abnormal vitamin D levels significantly higher in cases Serum vitamin D level (ELISA) – Significantly lower in cases Vitamin D level and acne severity – Significant negative correlation |

Notes : GAGS=Global Acne Grading System; IAEM=Indonesian Acne Expert Meeting; ELISA=Enzyme-Linked Immunosorbent Assay; ECLIA=Electrochemiluminescence Immunoassay; ELFA=Enzyme-Linked Fluorescent Assay; CLIA=Chemiluminescence Immunoassay

Table 3. Newcastle-Ottawa Scale (NOS) Assessment of Study Quality

| Author | Title | Newcastle-Ottawa Scale (NOS) | | | Total |
|--|---|------------------------------|-------------------|-------------|------------|
| | | Selection (4) | Comparability (2) | Outcome (3) | |
| Goodarzi <i>et al.</i> , 2020(Goodarzi et al., 2020) | Comparison of serum levels of calcium, vitamin-D, phosphorous and C-reactive protein in acne patients versus healthy subjects | 4 | 1 | 3 | 8/9 |
| Kemeriz <i>et al.</i> , 2020(Kemeriz et al., 2020) | Evaluation of 25-hydroxy vitamin D levels and disease severity in patients with acne vulgaris | 2 | 2 | 3 | 7/9 |
| Alhetheli <i>et al.</i> , 2020(Alhetheli et al., 2020) | Vitamin D Levels in Patients with and without Acne and Its Relation to Acne Severity: A Case-Control Study | 4 | 2 | 3 | 9/9 |
| Elkamshoushi <i>et al.</i> , 2021(Elkamshoushi et al., 2021) | Serum levels of 25 hydroxyvitamin D and IL17A and their association with acne severity in patients with severe and very severe acne vulgaris | 4 | 2 | 3 | 9/9 |
| Singh <i>et al.</i> , 2021(Singh, Dorjay, et al., 2021) | The interplay of vitamin D and body mass index in acne patients vs. controls | 3 | 2 | 2 | 7/9 |
| Singh <i>et al.</i> , 2021(Singh, Khurana, et al., 2021) | Correlation of Serum 25 Hydroxy Vitamin D and Interleukin-17 Levels with Disease Severity in Acne Vulgaris | 3 | 2 | 2 | 7/9 |
| Sharaf <i>et al.</i> , 2021(Sharaf et al., 2022) | Serum 25-Hydroxy Vitamin D: A Possible Role in Acne Vulgaris | 4 | 2 | 3 | 9/9 |
| Naheed <i>et al.</i> , 2023(Naheed et al., 2023) | Correlation between the severity and type of acne vulgaris lesions with serum vitamin D levels: A cases control study of HIT Hospital, Taxila | 3 | 1 | 3 | 7/9 |
| Kazeminejad <i>et al.</i> , 2024(Kazeminejad et al., 2024) | Serum zinc, selenium, and vitamin D levels in patients with acne vulgaris: A case-control study | 4 | 2 | 3 | 9/9 |

CONCLUSION

This systematic review revealed that individuals with acne vulgaris typically exhibit lower serum vitamin D levels than those with healthy skin, with six of nine studies demonstrating a statistically significant inverse correlation between vitamin D levels and acne severity—suggesting more severe cases in those with deficiency—while the remaining three found no significant association, possibly due to confounding factors like psychological stress, sun exposure, diet, lifestyle, occupation, and sunscreen use. These findings bolster vitamin D's potential as a predictive biomarker for acne severity. However, no reviewed studies employed predictive models or statistical validation to confirm its clinical utility. For future research, prospective studies using validated predictive tools, such as machine learning models or longitudinal cohort designs, are recommended to rigorously establish serum vitamin D as a biomarker, enabling its use in preventing acne progression and guiding personalized treatments.

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