

LETTER TO THE EDITORS

Research Letter

Dear Editor,

Vitamin D deficiency in patients with acne vulgaris: A systematic review and meta-analysis

Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous unit characterised by increased sebum production and inflammatory cytokines released from the sebaceous glands.¹ Recent studies have found that vitamin D affects these important aspects of acne pathogenesis.^{2,5} Hydroxyvitamin D [25(OH)D] is considered the most appropriate index for the accurate reflection of the vitamin D levels.⁴ Serum levels and deficiency of 25(OH)D have been investigated in acne vulgaris by multiple studies with inconsistent results.^{5,6} We conducted this systematic review and meta-analysis to explore the association between vitamin D and acne vulgaris.

We performed a systematic search in PubMed, Scopus, CINAHL and Cochrane databases for all published peer-reviewed English language literature until 20 April 2019 following PRISMA guidelines. The search terms used were 'vitamin D' or '25-hydroxyvitamin D' or '25-hydroxycholecalciferol' combined with 'acne.' All case-control studies that compared the prevalence of vitamin D deficiency or serum vitamin D levels in acne vulgaris and healthy controls were included. Two authors independently assessed the studies, and discrepancies were resolved by consensus. Studies with insufficient data, case reports and reviews were excluded. Quality of the studies was assessed by the Newcastle-Ottawa scale. Standardised mean difference (SMD) for continuous data and odds ratio (OR) for dichotomous data was calculated. Considering the baseline heterogeneity among included subjects, we used the random-effects model.⁷ The I^2 statistic was used to assess the heterogeneity. The analysis was performed using Comprehensive Meta-Analysis version 3 software (Biostat, Englewood, NJ, USA).

In total 11 studies, which included 1099 acne vulgaris patients and 842 healthy controls, were finally selected (Table 1). PRISMA flow diagram showing the study selection process is shown in Fig. S1. Nine studies provided data on the serum vitamin D levels and six studies provided data on the prevalence of vitamin D deficiency. Meta-analysis revealed significantly lower serum vitamin D level in acne vulgaris patients compared to the healthy controls

(SMD = -1.4 [95% CI -2.26 to -0.55], I^2 = 97%; Fig. 1). Subgroup analysis and meta-regression were not performed due to limited data. In the sensitivity analysis performed by excluding a single study at a time, the vitamin D level remained significantly lower in the acne vulgaris group. Analysis of six studies showed that vitamin D deficiency was three times more likely to be prevalent in the acne vulgaris patients (OR = 2.97 [95% CI 1.35 to 6.52], I^2 = 74%) compared to the healthy controls (Fig. 2). Funnel plot examination revealed that the studies included for the analysis of serum vitamin D level (Egger's test, P = 0.28) and vitamin D deficiency (Egger's test, P = 0.52) did not exhibit publication bias.

Vitamin D plays an important role during the regulation of the immune system and the proliferation and differentiation of keratinocytes and sebocytes. It has been implicated in the pathogenesis and treatment of multiple dermatological disorders such as psoriasis, atopic dermatitis, vitiligo, acne vulgaris and alopecia areata.⁸ A recent study found that vitamin D exerts a regulatory function on human sebocytes *in vitro* including sebaceous lipogenesis.² The study also reported that reduced serum vitamin D levels may contribute to the increased sebaceous gland volume and seborrhoea in acne patients.² Inflammatory cytokines from the sebaceous glands play an important role in acne pathogenesis and treatment with vitamin D has been shown to decrease expression of cytokines like interleukin (IL)-6, IL-8, IL-17 and metalloproteinase-9.^{5,9} A clinical study showed an improvement of inflammatory acne lesions with vitamin D supplementation; however, it was limited by a small sample size.⁵

Our review showed lower serum levels of vitamin D and higher prevalence of vitamin D deficiency in acne vulgaris patients. However, most of the included studies did not adjust for confounders like sun exposure, geographical location and dietary factors which can independently influence the vitamin D status in acne patients. Patients are advised against sun exposure due to the use of photosensitive drugs for the treatment of acne.¹⁰ In addition, acne patients tend to avoid dairy products which are one of the important dietary sources of vitamin D in their fortified form. In our study, significant heterogeneity was present in both analyses due to the variability in effect estimates of the included studies, which could be due to the baseline differences among included subjects. Due to these limitations, the results of this study should be interpreted with caution.

In conclusion, this meta-analysis found preliminary evidence of vitamin D deficiency in acne vulgaris patients. However, studies with larger sample sizes controlling for factors like sun exposure, geographical location and dietary habits are needed to confirm these primary results.

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Conflicts of Interest: None declared.

Table 1 Characteristics of included studies

Study, Year	Country	Cases (M/F, mean age in years)	Controls (M/F, mean age in years)	Adjusted confounding variables	Outcome - Result	NOS
Leachman and colleagues, <i>Arch Dermatol.</i> 1999; 135: 961–5	USA	18 (18/0, 19.7)	14 (14/0, 25)	Age, sex, weight, height	Serum vitamin D level – No significant difference between cases and controls	7
Toossi and colleagues, <i>Clin. Cases Miner. Bone Metab.</i> 2015; 12: 238–42	Iran	39 (11/28, 24.2)	40 (12/28, 27.2)	Age, sex, BMI	Serum vitamin D level – No significant difference between cases and controls [†] Vitamin D deficiency – No significant difference between cases and controls Additional comments: No significant difference of serum vitamin D levels between cases and controls in subgroup analysis stratified by sun exposure time	7
Yildizgören and colleagues, <i>Dermatoendocrinol.</i> 2014; 6: e983687	Turkey	43 (16/27, 25.1)	46 (19/27, 25.2)	Age, sex, weight, height, BMI, phototype Additional comments: Subjects using sunscreen regularly were excluded	Serum vitamin D level – Significantly lower in cases Vitamin D deficiency – Significantly more prevalent in cases	7
El-Ramly and colleagues, <i>J. Egypt Womens Dermatol. Soc.</i> 2016; 13: 99–105	Egypt	60 (12/48, 20)	60 (12/48, 24.6)	Age Additional comments: No significant difference between cases and controls regarding sun exposure	Serum vitamin D level – No significant difference between cases and controls Vitamin D deficiency – No significant difference between cases and controls	6
Lim and colleagues, <i>PLoS One</i> 2016; 11: e01611162	Egypt	80 (35/47, 20.9)	80 (39/41, 21)	Age, sex, BMI Additional comments: No significant difference between cases and controls regarding sunscreen use	Serum vitamin D level – No significant difference between cases and controls Vitamin D deficiency – More prevalent in cases	8
Abd-Elhamed and colleagues, <i>J. Cosmet. Dermatol.</i> 2019; 18: 671–6	Egypt	135 (81/54, 21)	150 (72/78, 23.1)	Age, sex, BMI	Serum vitamin D level – Significantly lower in cases	7
Amon and colleagues, <i>Dermatoendocrinol.</i> 2018; 10: e1442159	Germany, UK and USA	86 (31/55, 21.2)	71 (17/54, 49.2)	None	Serum vitamin D level – Significantly lower in cases Vitamin D deficiency – Significantly more prevalent in cases	6
El-Hamd and colleagues, <i>J. Cosmet. Dermatol.</i> 2018; 20: 1–5	Egypt	90 (42/48, 20.7)	60 (27/33, 23.8)	Age, sex and BMI	Serum vitamin D level – Significantly lower in cases	7
Stewart and colleagues, <i>Dermatoendocrinol.</i> 2018; 10: e1442160	Australia	453 (205/248, 22.8)	250 (101/149, 23.1)	Age and sex	Vitamin D deficiency – Significantly more prevalent in cases	6
Swelam and colleagues, <i>J. Cosmet. Dermatol.</i> 2018; 00: 1–8	Egypt	50 (15/15, 25.7)	50 (16/14, 24.6)	Age and sex	Serum vitamin D level – Significantly lower in cases	7
Karabay and colleagues, <i>Türkiye Klinikleri J. Dermatol.</i> 2019; 29: 1–6	Turkey	65 (NA, NA)	41 (NA, NA)	Age and sex Additional comments: Subjects using sunscreen regularly were excluded	Serum vitamin D level – No significant difference between cases and controls	6

[†]Mean and standard deviation not available for analysis. BMI, body mass index; M/F, male/female; NOS, Newcastle–Ottawa scale.

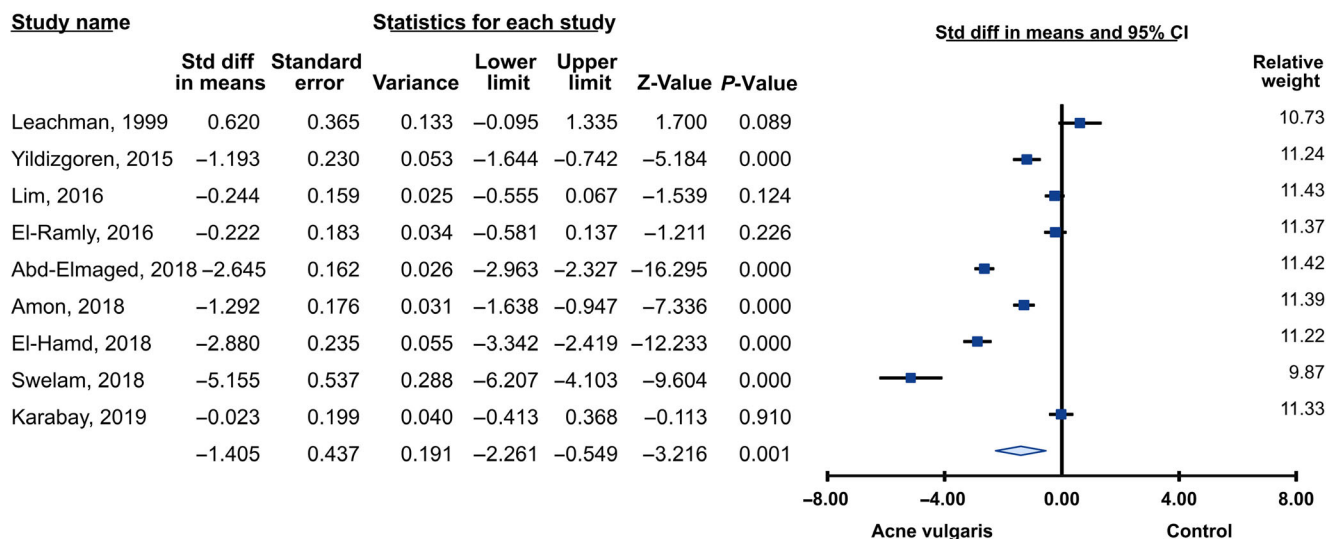


Figure 1 Forest plots showing the comparison of serum vitamin D levels between patients with acne vulgaris and healthy controls.

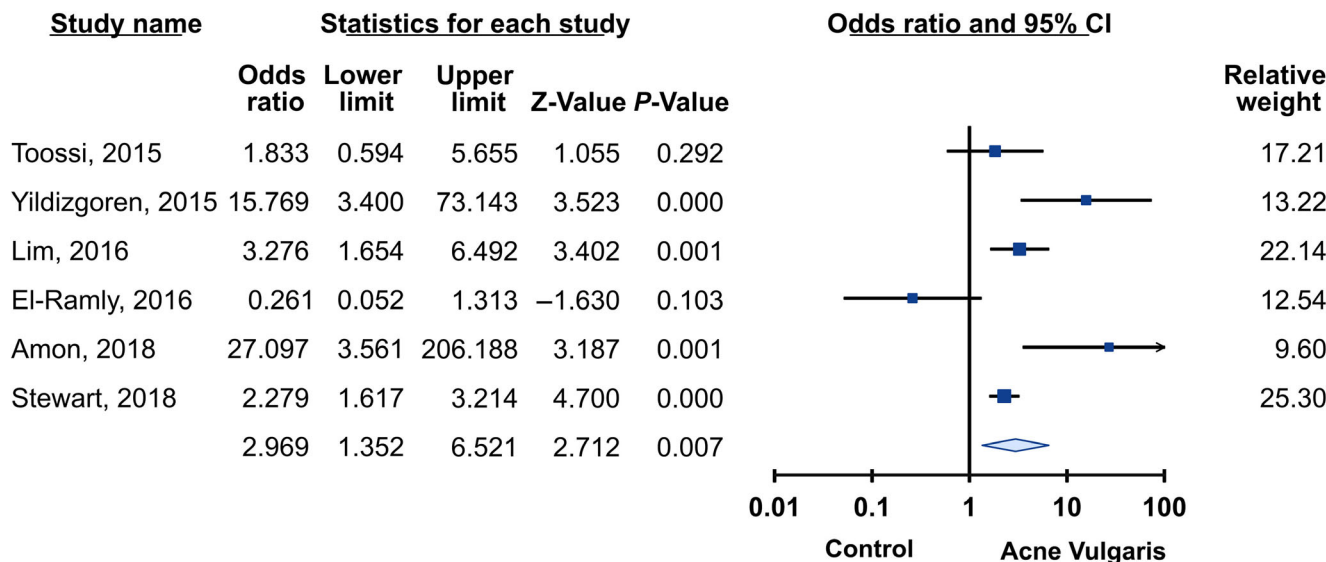


Figure 2 Forest plots showing the comparison of the prevalence of vitamin D deficiency between patients with acne vulgaris and healthy controls.

Moreover, studies evaluating the efficacy of vitamin D supplementation in acne vulgaris may be rewarding.

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Prakash Acharya | Mahesh Mathur
 Department of Dermatology, College of Medical Sciences,
 Bharatpur, Nepal

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Figure S1. Search strategy and study selection process using PRISMA flow diagram.