RESEARCH ARTICLE

# Correlation and assessment of vitamin D deficiency with disease severity in patients suffering from pemphigus vulgaris

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## Abstract

**Objective:** To determine correlation between vitamin D deficiency and severity of pemphigus vulgaris.

**Method:** The prospective, cross-sectional study was conducted at the Department of Dermatology, Lady Reading Hospital, Peshawar, Pakistan, from December 2021 to June 2022, and comprised patients of pemphigus vulgaris, confirmed by histopathology and direct immunofluorescence. An expert dermatologist examined the patients at baseline to minimise inter-observer bias, and the Pemphigus Disease Area Index score was calculated for each patient. Blood samples were drawn from the medial-cubital vein, and centrifuged at 3000rpm for 10 min at 40C to check for serum vitamin D levels using the enzyme-linked immunosorbent assay technique. Data was analysed using SPSS 22.

**Results:** Of the 89 patients, 49(55.1%) were females and 40(49.9%) were males. The overall mean age was 38.48±13.365 years. The mean vitamin D level of the patients was 17.4882±14.70505 mg/dl, with 66(74.2%) patients having vitamin D deficiency and 7(7.9%) having vitamin D insufficiency. There was negative but non-significant correlation of vitamin D level with disease severity ($r$=-0.131, $p$=0.22).. Vitamin D deficiency had no significant association with age, gender, area of living, socioeconomic status, duration of disease and educational level of the patients ($p$>0.05).

**Conclusion:** Serum vitamin D level was found to have a negative correlation with severity of pemphigus vulgaris.

**Keywords:** Pemphigus vulgaris, Vitamin D deficiency, Chronic autoimmune bullous. (JPMA 75: 726; 2025)

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## Introduction

Pemphigus vulgaris (PV) is a chronic autoimmune bullous disease that belongs to a group of skin diseases in which intraepidermal acantholysis occurs. It affects 0.76 to 16.1 per million population worldwide.[1] Both T and B cells express vitamin D receptors, which indicates that vitamin D may have an active role in immune modulation and immunity.[2,3] Studies indicate that calcitriol inhibits the production of T cell cytokines, and expands the population of circulating Treg cells.[4] This description suggests that vitamin D metabolism may have an important role in autoimmune disorders, including pemphigus.[5] Though the incidence of pemphigus is low, it varies worldwide, ranging from 0.05 to 2.7 per 100,000 per year, but recent data suggests the incidence is increasing even if the reasons are uncertain.[6]

Vitamin D is a hormone that plays a role in maintaining optimal level of calcium and phosphorus in the body. It is also an important immunomodulator, and the association of several autoimmune diseases has been found with poor vitamin D status. Decreased vitamin D level is commonly seen in many populations worldwide. In Pakistan, a study showed that 58.17% and 26.65% of the general population had vitamin D deficiency and insufficiency, respectively.[7] A case-control study in Iran concluded that PV patients were more vitamin D-deficient compared to healthy controls (75% vs 45%) ($p$=0.053).[8]

In Pakistan, to our knowledge, no data is available regarding Vitamin D deficiency in PV patients. The current study was planned to fill the gap in literature by finding the vitamin D level in PV patients, and PV's correlation with disease severity.

## Patients and Methods

The prospective, cross-sectional study was conducted at the Department of Dermatology, Lady Reading Hospital, Peshawar, Pakistan, from December 2021 to June 2022. After approval from the institutional ethics review board, the sample was raised using consecutive non-probability sampling technique. All diagnosed PV patients, confirmed by histopathology and direct immunofluorescence, aged 18-65 years with blisters formation within a week prior to presentation were included. Patients with any autoimmune diseases other than PV or with parathyroid disorders, renal or liver dysfunction, malabsorption disorders, malignancies, cardiovascular diseases and diabetes mellitus were excluded.

After taking written, informed consent from all the patients, data was collected using a structured questionnaire (Appendix), including gender, age, area of residence,

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**Appendix:** The study proforma.

**Frequency of vitamin d deficiency in patients with pemphigus vulgaris**
**Case No:** _____ MR No: _____
**Consent:** Yes/No
**Histopathology/ DIF report confirmed Pemphigus Vulgaris:** Yes/No
**Name:** _____
**Address:** _____
**Contact No**: _____
**Gender**: Male / Female
**Age**: _____Years
**Residence:** Urban / Rural
**Socioeconomic status**: Low / Middle / High
**Educational Status:** Educated / Uneducated\
**Sun Exposure:** Yes / No
**PDAI Score:**
**Vitamin D level:** _____
**Vitamin D Deficiency:** Yes / No
**Vitamin D Insufficiency:** Yes / No

education, monthly income, socioeconomic status (SES), sun exposure, medical history, administration of drugs and supplements.

An expert dermatologist examined the patients at baseline to minimise inter-observer bias, and the Pemphigus Disease Area Index (PDAI) score was calculated for each patient. Scores of <15, 15-45 and >45 was considered mild, moderate and severe PV, respectively.[9] Blood samples were drawn in 5cc disposable syringes from the medial-cubital vein, and they were centrifuged at 3000rpm for 10 minutes at 40°C to check for serum vitamin D levels using the enzyme-linked immunosorbent assay (ELISA) technique with a 25-0M vitamin D ELISA assay test kit using CLIA method (The machine used was ATELLICA IM, Model number [11068008], manufactured by [Simens Healthcare Diagnostics], [Tarrytown, NY, USA]). Vitamin D levels <20 ng/ml were taken as vitamin D deficiency, while 20-29ng/ml were taken as vitamin D insufficiency.

Data was analysed using SPSS 22. Data was expressed as mean±standard deviation or as frequencies and percentages, as appropriate. Stratification of the patients was done according to their age, gender, SES, education level, area of residence, and PV duration was done, and association with vitamin D deficiency was explored using binary logistic regression. P<0.05 was considered significant.

## Results

Of the 89 patients, 49(55.1%) were females and 40(49.9%) were males. The overall mean age was 38.48±13.365 years, with 59(66.3%) patients aged >30 years and 30(33.7%) aged <30 years. The mean vitamin D level of the patients was 17.4882±14.70505 mg/dl, with 66(74.2%) patients having vitamin D deficiency and 7(7.9%) having vitamin D insufficiency (Tables 1-2). There was negative but non-significant correlation of vitamin D level with disease severity ($r$=-0.131, $p$=0.22)

PV was more severe in patients with low vitamin D level ($r$=-0.173, $p$=0.10) (Figure). No association of vitamin D deficiency was found with age groups, gender, area of residence, SES, duration of disease, and educational level of the patients ($p \leq 0.05$) (Table 3).

**Table-1:** Dry socket and menstrual cycle.

| Numerical Variables | Mean±SD |
|---|---|
| Age (years) | 38.48±13.365 |
| Monthly Income (Rs) | 41000.00 ± 28873.057 |
| Vitamin D Level (mg/dL) | 17.4882 ± 14.70505 |
| Mean duration of disease (in months) | 32.26 ±29.003 |

SD: Standard Deviation

**Table-2:** Demographic variables and vitamin D status of the patients.

| Variable | n (%) |
|---|---|
| **Age** (years) | |
| < 30 | 30 (33.7) |
| > 30 | 59 (66.3) |
| Gender | |
| Male | 40 (44.9) |
| Female | 49 (55.1) |
| **Socioeconomic status** | |
| Low | 13 (14.6) |
| Medium | 46 (51.7) |
| High | 30 (33.7) |
| **Residence** | |
| Urban | 31(34.8) |
| Rural | 58 (65.2) |
| **Educational Status** | |
| Educated | 35 (39.3) |
| Uneducated | 54 (60.7) |
| **Vitamin D Deficiency** | |
| Yes | 66 (74.2) |
| No | 23 (25.8) |
| **Vitamin D Insufficiency** | |
| Yes | 7 (7.9) |
| No | 82 (92.1) |

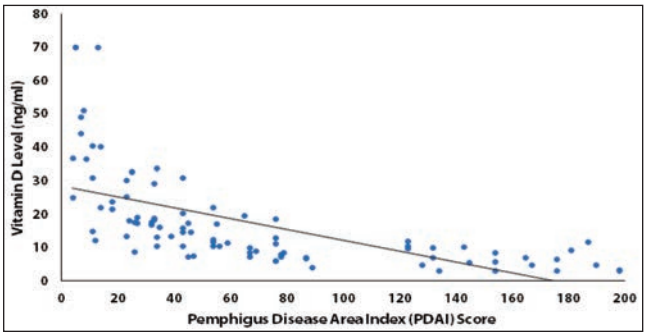


**Figure:** Relationship between vitamin D level and severity of pemphigus vulgaris (Pemphigus Disease Activity Index [PDAI] Score).

**Table-3:** Association of vitamin D status with demographic variables.

| Variable | Univariate Regression | | Multivariate Regression | |
|---|---|---|---|---|
| | Unadjusted OR | *p*-value | Adjusted OR | *p*-value |
| Age Groups | 0.308 (0.09-0.97) | 0.04 | 0.32 (.10-1.05) | 0.06 |
| Gender | 0.429 (0.17-1.03) | 0.05 | 0.45 (0.18-1.1) | 0.08 |
| Socio-Economic Status | 0.64 (0.17-2.4) | 0.75 | - | - |
| Educational Status | 0.99 (0.42-2.3) | 0.98 | - | - |
| Residence | 0.71 (0.3-1.7) | 0.46 | - | - |
| Duration of disease | 1.00 (0.98-1.01) | 0.63 | - | - |

Reference category: age <30 years, gender male

## Discussion

PV is an autoimmune blistering disorder (AIBD) that significantly affects patients' quality of life. Vitamin D is a hormone that plays a key role in calcium and phosphorus homeostasis in the body. It also plays a crucial role in modulating immune responses, with emerging evidence highlighting its impact on autoimmune conditions. A review in 2022 emphasised the immunomodulatory effects of vitamin D and suggested its potential role in the development of autoimmune diseases.[10] A pivotal role in skin health is played by vitamin D precursor that are produced by keratinocytes. It actively participates in immune modulation of AIBDs by B cell apoptosis, and enzyme regulation is required in the process along with T Helper 2 (Th2) cell differentiation, and Treg functions.[11]

The skin's ability to synthesise vitamin D and its responsiveness to this vitamin is crucial for maintaining skin integrity, promoting innate immune responses against infections, and aiding in the processes of wound-healing and tissue repair. Vitamin D's effects on keratinocytes, Toll-like receptor 2 (TLR2) induction, and its role in cellular differentiation collectively contribute to skin health and its capacity to respond to environmental challenges and injury. Therefore, to prevent skin diseases and their exacerbation, an optimal level of vitamin D is required in the body.[8]

Globally, abnormal vitamin D level is commonly seen across populations. A survey in Pakistan found that 58.17 % of the general population had vitamin D deficiency, while 26.65% had insufficient level of vitamin D.[7] These findings are in accordance with the current study where maximum number of the patients were found to have low vitamin D levels. Similarly, the current study showed that the prevalence of hypovitaminosis D was more in the population having poor SES. This was consistent with earlier findings.[12] However, no association of vitamin D deficiency with age groups, gender, area of residence, SES, educational status or duration of the disease was seen in the current study.

The low vitamin D status in PV patients might be due to several reasons, including decreased production of vitamin D by skin cells as in burnt patients, reduced sun exposure for protection of the damaged skin, or production of anti-vitamin D antibodies in autoimmune skin diseases, such as systemic lupus erythematosus (SLE).[13,14] Poor sun exposure and other environmental factors, including dietary habits, may be associated with low vitamin D levels. Though all the participants of the current study gave history of daily sun exposure and outdoor activities, duration and timings of such exposure and dietary habits were not quantified. Similarly, none of the patients had ever had serum vitamin D level checked before to assess possible deficiency.

Marzano et al. emphasised that vitamin D deficiency may have an important role in PV pathophysiology. There is a potential link between vitamin D deficiency and PV severity. Literature shows that patients suffering from AIBDs, both PV and bullous pemphigoid, have an increased prevalence of vitamin D deficiency and vertebral fractures. Vitamin D levels are inversely associated with disease intensity and vertebral fractures occur in spite of normal bone mass density.[15]

A negative correlation between vitamin D level and PV severity was found in the current study. These findings were coherent with literature.[16] A study showed hypovitaminosis D in patients suffering from AIBDs more profound in the active disease phase.[17] Incorporating vitamin D assessment into the management of PV may be crucial for optimising treatment strategies.

Despite the fact that there is a potential relationship between vitamin D and PV, only a few published studies could be found in the literature[10-17] on the subject, and all of them yielded results similar to those in the current study. However, the exact underlying mechanism of this relationship still needs to be explored. Though studies on relationship of vitamin D deficiency and PV severity have been done globally, the current study, to our knowledge, is the first to assess the relationship between vitamin D and PV.

The current study was conducted at the largest referral centre of dermatology in Peshawar, which minimised the potential for selection bias. However, the sample size of the study was small, and that might be the reason that the results were statistically non-significant.

The current study has limitations as all the diagnosed PV patients had already used steroids and immuno-suppressants along with vitamin D and calcium in the past. Such medications could potentially affect vitamin D metabolism, immune responses, or even skin health independently of the disease itself, making it challenging

to attribute the observed differences solely to vitamin D levels.

Future prospective studies with larger sample sizes and rigorous methodologies are warranted. Additionally, exploring the impact of vitamin D supplementation on disease progression could provide further insights into its therapeutic potential for PV patients.

**Limitations:** One of the limitations of this study is lack of formal sample size calculation, as we included all the patients of Pemphigus vulgaris meeting inclusion criteria in the study period. While this enhances study's representativeness, it may compromise the statistical power needed to detect subtle differences or associations. Additionally, the generalisability of our findings to broader population may be constrained, as the sample size was determined by availability rather than a predefined calculation.

## Conclusion

Serum vitamin D level in PV patients had a negative correlation with severity of the disease. Hypovitaminosis D was noted in diagnosed PV cases, but the effect of vitamin D deficiency in PV causation was not seen. Both the incidence and exacerbation of PV could be prevented by keeping an optimal level of serum vitamin D.

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**Author Contribution:**
**MMP:** Concept, statistical analysis, interpretation and final approval.
**AQK:** Statistical analysis, data collection and interpretation of data.
**AS:** Data collection and writing.
**KK & SMN:** Critical analysis and final approval.
**AI:** Literature review and drafting.