



INVESTIGATING THE PREVALENCE AND IMPACT OF VITAMIN D DEFICIENCY AMONG INDIVIDUALS WITH PEMPHIGUS VULGARIS: A COMPREHENSIVE EVALUATION OF PATIENT OUTCOMES

¹Waqar Ali Khan, ²Alia Javed, ³Dr. Nadir Ali, ⁴Dr. Waqar Ahmed, ⁵Dr.Farrah Majeed, ⁶Dr Mashal Khan

¹Rawal Institute of Health Sciences Islamabad, Waqar.khan005@yahoo.com

²Family Hospital And Sultana Foundation Rwp, Aliyajaved82@gmail.com

³Medical Officer CMH Rawalakot, Nadir.awan495@gmail.com

⁴CMO CMH Rawalakot, wikich00@gmail.com

⁵MBBS Graduate from MBBSMcmirpurAJK ,Ex HO DHQ teaching Hospital mirpur.

bilalmajeed713@gmail.com

⁶Medical Officer, mashalsaghirkhan786@gmail.com

Abstract:

Objective: Vitamin D deficiency has been linked to several autoimmune illnesses, which may alter the frequency and severity of these diseases. A lack of vitamin D has been identified as a possible contributor to the onset or worsening of autoimmune disease. This study's main objective was to determine the prevalence of low vitamin D levels among people with pemphigus vulgaris.

Methods: 76 participants with pemphigus vulgaris, aged 20 to 50, of either gender, were included in the research. Participants who had diabetes mellitus, chronic liver disease, acid peptic illness, or chronic kidney failure were excluded. Blood samples from the patients were collected, and the pathology division of the facility received them for vitamin D testing.

Results:The patients in the research had an average age of 34.54 years, with a standard deviation of 6.70 years. 47 patients (61.84%) out of the total number of patients were between the ages of 20 and 35. 39 (51.32%) of the 76 patients were men, and 37 (48.68%) were women, making the male-to-female ratio 1.1 to 1. The patients' illness lasted an average of 6.41 months on average, with a standard deviation of 2.48 months. With a standard variation of 4.57 kg/m², the average body mass index (BMI) was 26.19 kg/m². While 21 patients (27.63%) did not exhibit any vitamin D insufficiency, 55 patients (72.37%) were determined to be deficient in it.

Conclusions:It has been shown in this study that a large proportion of people with pemphigus vulgaris have a considerable vitamin D deficit.

Keywords: vitamin D, pemphigus vulgaris, autoimmunity

DOI Number: 10.48047/nq.2023.21.6.NQ23082

NeuroQuantology2023;21(6): 777-784



Introduction:

Autoantibodies that target desmosomes are a defining feature of the pemphigus category of chronic autoimmune disorders. Desmogleins-1 and Desmoglein-3 are two forms of desmosomes that these autoantibodies selectively target, causing acantholysis, or the lack of cell-to-cell adhesion. Pemphigus comes in two primary forms: pemphigus foliaceus, which targets the 160 kDa Dsg1 antigen and tends to spare mucosal tissues, and pemphigus vulgaris, which targets the 130 kDa Dsg3 antigen and often affects mucosal surfaces. (1) On the oral mucosa, pemphigus vulgaris often begins with the development of superficial, flaccid blisters that swiftly erupt and cause painful erosions. Patients may find it

challenging to eat or drink as a result. Later, when the illness spreads to the skin, flaccid bullae and erosions appear most often on the head, face, upper chest, back, and proximal extremities. (2) The precise underlying causes of pemphigus vulgaris are yet unknown. The development of the illness, however, may also be influenced by several environmental triggers and hereditary variables, according to the available research. (3) The most severe and prevalent form of pemphigus, which makes up around 70% of all cases, is pemphigus vulgaris. According to estimates, there are between 1 and 5 instances per million people per year. Pemphigus vulgaris may affect both men and women, with most occurrences occurring in people between the ages of 40 and 60. (4)



Figure 1: Pemphigus Vulgaris

Recent studies have looked at the role of hypovitaminosis D in autoimmune skin conditions that cause bullous lesions. The prevalence and severity of several autoimmune diseases have been connected to vitamin D insufficiency, which has been identified as a

factor that may promote or exacerbate autoimmunity. (5) Vitamin D is associated with PV development because it controls the immune system by influencing B and T cell proliferation, T helper cell differentiation, and the regulation of regulatory T cells. Vitamin D

may increase the number of regulatory T cells by suppressing the synthesis of IL-17, acting as an immunosuppressive agent. (6) Some studies (7) discovered that PV and BP patients had higher rates of hypovitaminosis D, but others did not. In a research, vitamin D insufficiency was discovered in 73% of pemphigus vulgaris patients. (8)

We have decided to research to more fully comprehend the relationship between vitamin D levels and pemphigus vulgaris in the particular local population. The majority of prior study has been conducted on communities in the West and elsewhere, which may be geographically dissimilar from ours. As a consequence, there is a dearth of information about the local populace. We want to add to the body of knowledge and provide doctors with useful information by measuring vitamin D levels in people with pemphigus vulgaris in our region. Patients with pemphigus vulgaris will benefit from this study's early detection and care of vitamin D insufficiency, which will eventually improve their quality of life.

Methods:

Study Design: The Department of Dermatology at Mayo Hospital in Lahore performed cross-sectional descriptive research from November 9, 2022, to May 8, 2023. The study's goal was to learn more about the skin disorder pemphigus vulgaris in individuals 20 to 50 years old who had been treated for more than a month after getting a clinical and histological diagnosis of the illness. The research excluded participants who had an acid peptic illness, chronic liver disease, diabetes mellitus, chronic renal disease, and those who were hesitant to take part. A computation based on the required confidence level and margin of error yielded a sample size of 76.

Patients were included depending on their availability and compliance with the inclusion criteria after being chosen by non-probability sequential sampling. Before being included in the research, each subject gave their informed permission and the review committee granted their request for ethical approval. To check for

vitamin D insufficiency, a 3 mL blood sample from each patient was taken under very sterile circumstances and forwarded to the hospital's pathology laboratory for analysis. Data on the patient's demographics (age, gender, BMI) and vitamin D levels were gathered using a pre-made questionnaire.

Statistical Analysis: A statistical program that is often used in social science research, SPSS version 22.0, was used to gather and analyze the data for this study. The average (mean) and variability (standard deviation) for numerical parameters such as the age of patients, the length of pemphigus vulgaris, and BMI were reported by the researchers.

The researchers provided the frequency and percentage of each category for categorical factors such as gender, area of residence (rural or urban), employment (field work or office job/others), sun exposure (low, medium, high), and presence/absence of vitamin D insufficiency.

The data were stratified by age, gender, pemphigus vulgaris duration, BMI, location of residence, employment, and sun exposure to explore the connections between the different variables. The chi-square test, a statistical analysis used to establish if there is a significant correlation between categorical variables, was then carried out.

In this study, a significance threshold of less than 0.05 was chosen to determine statistical significance, which means that the researchers consider the association between the variables to be statistically significant if the derived p-value from the chi-square test is less than 0.05.

Results:

The demographics and patient features in this research of 76 people with the chronic autoimmune disease pemphigus vulgaris were examined. Males made up 51.32% (39) of the total patients, while females made up 48.68% (37) for a male-to-female ratio of 1.1:1. The patients ranged in age from 20 to 50, with an average age of 34.54 years with a standard

deviation of 6.70. The bulk of patients (61.84%, or 47) were between the ages of 20 and 35. The average BMI was 26.19 kg/m², and the average illness duration was 6.41 ± 2.48 months.

51.32% (39) of the patients resided in rural regions, while 48.68% (37) of them did so in urban areas. According to the occupational distribution, 14.47% (11) of the patients were employed in other professions, compared to 40.79% (31) office employees and 44.74% (34) field workers. 44.74% (34) of people had little sun exposure, 22.37% (17) had medium sun exposure, and 32.89% (25) had excessive sun exposure.

Patients with pemphigus vulgaris were more likely to be vitamin D deficient than non-patients (72.37% (55) of the patients had vitamin D insufficiency, compared to 27.33% (21) who did not (Figure 2). According to the data analysis, there was no discernible difference in vitamin D insufficiency between men (74.36%) and females (70.27%) (P=0.690). Additionally, it was shown that 68.97% of patients aged 41–60 and 74.47% of patients aged 20–40 had vitamin D deficiencies, respectively.

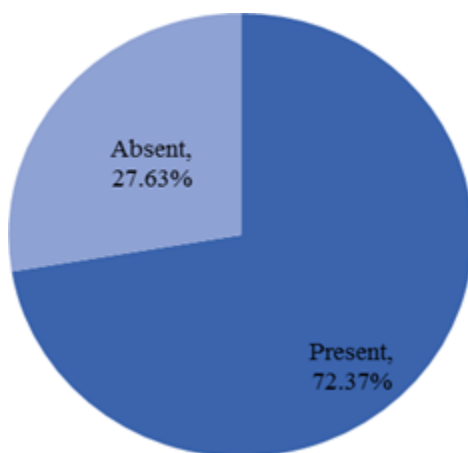


Figure 2: The prevalence of vitamin D deficiency in people with pemphigus vulgaris.

As 74.0% of patients with an illness duration of 6 months and 69.23% of patients with a disease duration >6 months had vitamin D insufficiency, there was no discernible difference in the prevalence of vitamin D deficiency depending on disease duration (p=0.659). Considering BMI, vitamin D insufficiency was discovered in 80% of obese individuals and 69.64% of patients who were not fat. Additionally, there was no discernible difference in the percentage of patients with a vitamin D deficit between those who lived in rural regions (71.79%) and those who did so in urban areas (72.97%) (p=0.909).

Table 1 shows how vitamin D insufficiency is distributed according to the profession, while Table 2 shows how it is stratified according to sun exposure.

Table 1: Classification of vitamin D deficiency according to the profession

Occupation	Vitamin D deficiency				p
	Absent		Present		
	n	%	n	%	
Office	9	29.03	22	70.97	0.058
Field	6	17.65	28	82.35	
Other	6	54.55	5	45.45	

Table 2: Classification of vitamin D deficiency according to sun exposure

Sun exposure	Vitamin D deficiency		p
	Absent	Present	

	n	%	n	%	
Low	12	35.29	22	64.71	0.058
Medium	5	29.41	12	70.59	
High	4	16	21	84	

Discussions:

Autoantibodies against the desmosome Desmogleins (Desmoglein3- and Desmoglein1-specific autoantibodies) cause PV, while autoantibodies against the hemidesmosome antigens BP180 and BP230 cause BP. (9) Until now, immunosuppressive medications, particularly steroid medication, have served as the gold standard of treatment for both conditions. (10)

Through its impact on the immune system, vitamin D has lately been linked to the onset or worsening of autoimmune disease. (11) Hypovitaminosis D has been associated with both the prevalence and severity of several autoimmune diseases. (12) Since some studies found a higher frequency of hypovitaminosis D in PV and BP patients, the topic of hypovitaminosis D in inflammatory bullous skin illnesses has been studied. Others, however, were unable to see these links (13,14) The discrepancies may be explained by the previous study's lower sample size and the prevalence of hypovitaminosis D in otherwise fit persons. (15) This study examined the prevalence of vitamin D insufficiency among people with pemphigus vulgaris. According to earlier studies, 73% of people with pemphigus vulgaris had insufficient levels of vitamin D. These results are consistent with those findings. (16) PV sufferers' low levels of vitamin D may be caused by several different things. A loss in the skin's capacity to synthesize vitamin D, as observed in burn victims, is one likely cause. Furthermore, these people may get less sun exposure to preserve their damaged skin. Numerous investigations have shown anti-vitamin D antibodies in autoimmune skin diseases, such as systemic lupus erythematosus. (17)

Vitamin D could represent an environmental element that generally regulates self-tolerance, as shown by our study's conclusion that it has

been connected to a variety of autoimmune diseases. (18) One group was examined who had autoimmune illnesses, while the other group was not. They found that 14% of individuals without autoimmune illnesses had vitamin D deficiency, compared to 23% of those with autoimmune disorders. The results were in line with our investigation as a consequence. (19)

Another case-control research that was carried out to assess vitamin D levels in recently diagnosed patients found that blood vitamin D levels in PV patients were considerably lower than those in controls. determining that considerably reduced levels of vitamin D may be the reason for the illness deteriorating and that these specific people need to take supplements. (20) Therefore, the outcomes aligned with our research.

There are inconsistent results from earlier research on the frequency of hypovitaminosis D in persons with autoimmune blistering skin illnesses. However, the results of the present extension research and later data5 did not support the prior findings of low 25-OH vitamin D levels in PV and BP patients. (21,22) Given that the control group's average 25-OH vitamin D levels were within the acceptable range of insufficient amount, this disparity may be caused by the prior studies' small numbers of participants and the reality that vitamin D shortage is frequent even in healthy individuals. Different individuals with pemphigus vulgaris from underdeveloped countries exhibited lower blood levels of vitamin D than healthy controls. Studies on the prevalence of vitamin D deficiency throughout the world have also shown that despite Middle Eastern countries receiving abundant sunshine, Asia and the Middle East have greater rates of low vitamin D levels than Europe and the USA (23,24). This mismatch may result from poor vitamin D



consumption and the reduced UV exposure brought on by wearing robes. Previous research revealed inadequate and contradictory evidence about the relationship between medical results and vitamin D levels.

The results of research done on Iranian people (which varied from 27.4% to 55.1%) were considerably different from those of the control group, where hypovitaminosis D was shown to occur with a very high frequency (91%), according to the analysis of previous studies. (25) Additionally, a metanalysis produced inconsistent results. The prevalence of hypovitaminosis D seemed to be higher in healthy individuals than in those with pemphigus vulgaris. The discrepancy may be due to a large BMI difference between healthy volunteers and pemphigus patients.

Our study's main flaw was improper meal intake because of oral erosions and ulcerations, which may have led to low vitamin D levels. Another drawback was that the hospitalized patients received less sun exposure, which resulted in less vitamin D production. To reduce problems and morbidity related to pemphigus vulgaris, we advise early identification and management of this condition in these specific individuals.

Conclusions:

Our investigation has led us to the conclusion that people with pemphigus vulgaris commonly have low vitamin D levels, which is strongly supported by our findings. This suggests that vitamin D deficiency and the autoimmune skin condition are significantly related. It is important to note that vitamin D is essential for several biological processes, including immune system control and skin health. Therefore, the association between vitamin D deficiency and pemphigus vulgaris that we found may have important implications for understanding and treating the illness.

References:

1. Ramani, P., Ravikumar, R., Pandiar, D., Monica, K., Krishnan, R. P., Ramasubramanian, A., & Sukumaran, G.

- (2022). Apoptolysis: a less understood concept in the pathogenesis of Pemphigus Vulgaris. *Apoptosis*, 27(5-6), 322-328.
2. Kianfar, N., Dasdar, S., Mahmoudi, H., & Daneshpazhooh, M. (2022). Burden of pemphigus vulgaris with a particular focus on women: A review. *International journal of women's dermatology*, 8(3), e056.
3. Didona, D., Paolino, G., Di Zenzo, G., Didona, B., Pampena, R., Di Nicola, M. R., & Mercuri, S. R. (2022). Pemphigus vulgaris: present and future therapeutic strategies. *Dermatology Practical & Conceptual*, 12(1).
4. Polakova, A., Kauter, L., Ismagambetova, A., Didona, D., Solimani, F., Ghoreschi, K., ... & Hudemann, C. (2022). Detection of rare autoreactive T cell subsets in patients with pemphigus vulgaris. *Frontiers in Immunology*, 13, 979277.
5. Zou, H., & Daveluy, S. (2022). Pemphigus vulgaris after COVID-19 infection and vaccination. *Journal of the American Academy of Dermatology*, 87(3), 709-710.
6. Martora, F., Fabbrocini, G., Nappa, P., & Megna, M. (2022). Reply to 'Development of severe pemphigus vulgaris following SARS-CoV-2 vaccination with BNT162b2' by Solimani et al. *Journal of the European Academy of Dermatology and Venereology*.
7. Goebeler, M., Bata-Csörgő, Z., De Simone, C., Didona, B., Remenyik, E., Reznichenko, N., ... & ARGX-113-1701 Investigator Study Group. (2022). Treatment of pemphigus vulgaris and foliaceus with efgartigimod, a neonatal Fc receptor inhibitor: a phase II multicentre, open-label feasibility trial. *British Journal of Dermatology*, 186(3), 429-439.
8. Tovanabutra, N., Bax, C. E., Feng, R., Kushner, C. J., & Payne, A. S. (2022).



- Temporal outcomes after rituximab therapy for pemphigus vulgaris. *Journal of Investigative Dermatology*, 142(4), 1058-1064.
9. Miyachi, H., Konishi, T., Hashimoto, Y., Matsui, H., Fushimi, K., Inozume, T., & Yasunaga, H. (2023). Clinical course and outcomes of pemphigus vulgaris and foliaceus: A retrospective study using a nationwide database in Japan. *The Journal of Dermatology*, 50(2), 212-221.
 10. Saffarian, Z., Samii, R., Ghanadan, A., & Vahidnezhad, H. (2022). De novo severe pemphigus vulgaris following SARS-CoV-2 vaccination with BBIBP-CorV. *Dermatologic therapy*, 35(6).
 11. Martinez, N., McDonald, B., & Crowley, A. (2022). A case report of the beneficial effect of oclacitinib in a dog with pemphigus vulgaris. *Veterinary Dermatology*, 33(3), 237-e65.
 12. Akoglu, G. (2022). Pemphigus vulgaris after SARS-CoV-2 vaccination: a case with new-onset and two cases with severe aggravation. *Dermatologic therapy*, 35(5), e15396.
 13. Kaur, B., Kerbrat, J., Kho, J., Kaler, M., Kanatsios, S., & Cirillo, N. (2022). Mechanism-based therapeutic targets of pemphigus vulgaris: A scoping review of pathogenic molecular pathways. *Experimental Dermatology*, 31(2), 154-171.
 14. Matthews, R., & Ali, Z. (2022). Comorbid mental health issues in patients with pemphigus vulgaris and pemphigus foliaceus. *Clinical and Experimental Dermatology*, 47(1), 24-29.
 15. Martora, F., Martora, L., Fabbrocini, G., & Marasca, C. (2022). A case of pemphigus vulgaris and hidradenitis suppurativa: may systemic steroids be considered in the standard management of hidradenitis suppurativa?. *Skin Appendage Disorders*, 8(3), 265-268.
 16. Huda, S., Chau, B., Chen, C., Somal, H., Chowdhury, N., & Cirillo, N. (2022). Caspase Inhibition as a Possible Therapeutic Strategy for Pemphigus Vulgaris: A Systematic Review of Current Evidence. *Biology*, 11(2), 314.
 17. Saleh, M. A., & Saleh, N. A. (2022). Pemphigus vulgaris relapse during the coronavirus disease pandemic. *Dermatologic Therapy*, 35(4), e15354.
 18. Martora, F., Battista, T., Nappa, P., Fabbrocini, G., & Megna, M. (2022). Pemphigus vulgaris and COVID-19 vaccination: Management and treatment. *Journal of Cosmetic Dermatology*.
 19. Chernyavsky, A., Khylynskyi, M. M., Patel, K. G., & Grando, S. A. (2022). Chronic exposure to the anti-M3 muscarinic acetylcholine receptor autoantibody in pemphigus vulgaris contributes to disease pathophysiology. *Journal of Biological Chemistry*, 298(3).
 20. Baker, J., Seiffert-Sinha, K., & Sinha, A. A. (2022). Patient genetics shape the autoimmune response in the blistering skin disease pemphigus vulgaris. *Frontiers in Immunology*, 13.
 21. Rosi-Schumacher, M., Baker, J., Waris, J., Seiffert-Sinha, K., & Sinha, A. A. (2023). Worldwide epidemiologic factors in pemphigus vulgaris and bullous pemphigoid. *Frontiers in Immunology*, 14.
 22. Falcinelli, F., Lamberti, A., Cota, C., Rubegni, P., & Cinotti, E. (2022). Reply to 'development of severe pemphigus vulgaris following SARS-CoV-2 vaccination with BNT162b2' by Solimani F et al. *Journal of the European Academy of Dermatology and Venereology*.
 23. Schmitt, T., Pircher, J., Steinert, L., Meier, K., Ghoreschi, K., Vielmuth, F., ... & Waschke, J. (2022). Dsg1 and Dsg3 composition of desmosomes across

- human epidermis and alterations in pemphigus vulgaris patient skin. *Frontiers in Immunology*, 13, 2124.
24. Calabria, E., Canfora, F., Mascolo, M., Varricchio, S., Mignogna, M. D., & Adamo, D. (2022). Autoimmune mucocutaneous blistering diseases after SARS-CoV-2 vaccination: A Case report of Pemphigus Vulgaris and a literature review. *Pathology-Research and Practice*, 153834.
 25. Brescacin, A., Baig, Z., Bhinder, J., Lin, S., Brar, L., & Cirillo, N. (2022). What protein kinases are crucial for acantholysis and blister formation in pemphigus vulgaris? A systematic review. *Journal of Cellular Physiology*, 237(7), 2825-2837.