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Original Article

Vitamin D deficiency in patients with pemphigus vulgaris: A cross sectional study

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Abstract

Background Several autoimmune disorders have been correlated to vitamin D deficiency, including their incidence and severity, and has been identified as a factor that may cause or worsen autoimmunity.

Objective The main objective was the assessment of vitamin D deficiency in pemphigus vulgaris patients.

Methods A total of 76 patients with pemphigus vulgaris, 20 to 50 years of age of either gender were included. Patients with chronic renal failure or chronic liver disease, acid peptic disease and diabetes mellitus were excluded. Blood samples were collected from patients and forwarded to the institution's pathology department for vitamin D testing.

Results Mean age was 34.54±6.70 years. Majority of the patients i.e. 47 (61.84%) had age between 20 to 35 years. Out of 76, 39 (51.32%) patients were males and 37 (48.68%) were females with male to female ratio of 1.1:1. Mean duration of disease was 6.41±2.48 months. Mean BMI was 26.19±4.57 kg/m^2. Frequency of vitamin D deficiency in pemphigus vulgaris patients was seen in 55 (72.37%) patients while 21 (27.63%) have shown no vitamin D deficiency.

Conclusion This study concluded that there is high frequency of vitamin-D deficiency in pemphigus vulgaris patients.

Key words
Pemphigus vulgaris, autoimmunity, vitamin D deficiency.

Introduction

Pemphigus is a collection of chronic, autoimmune illnesses caused by autoantibodies against desmosomes proteins. It is defined by the destruction of epithelial adhesion molecules, particularly Desmogleins-1 and Desmogleins-3, resulting in cell-to-cell contact loss (acantholysis).[1] Pemphigus has two major variants; pemphigus vulgaris with 130 kDa Dsg3 as target antigen, usually showing mucosal lesions and pemphigus folliaceus with 160 kDa Dsg1 as target antigen, that spares mucosal surfaces.[2] Pemphigus vulgaris initially presents with oral mucosal superficial flaccid blister that rupture rapidly to form painful erosions making oral intake difficult for patient. The disease then progresses to skin with appearance of flaccid bullae and erosions mainly on scalp, face, upper chest, back proximal extremities.[3] PV's basic causes have yet to be identified. However, it appears that hereditary variables are important, and environmental stimulants can have an

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impact on illness occurrence.[1] The most severe and frequent type is Pemphigus vulgaris (PV), comprising up to 70% of all cases of pemphigus with incidence of 1 to 5 cases per million population per year involving both men and women with a mean age between 40 and 60 years.[4]

Hypovitaminosis D's significance in autoimmune bullous skin diseases has lately been investigated. Vitamin D deficiency has been linked to the incidence and severity of various autoimmune illnesses and has been identified as a factor that may cause or worsen autoimmunity.[5] PV development is linked to vitamin D, due to its role in regulation of the immune system through affecting the B and T cells proliferation, T helper cells differentiation, and the regulating the regulatory T cells. By suppression of the production of IL-17, vitamin D may enhance the population of regulatory T cells, thus playing a repressive role in the immune system.[6] Hypovitaminosis D was found to be more common in PV and BP patients in some investigations,[5,7] while others failed to find such associations.[8,9] In a study, vitamin D deficiency was seen in 73% patients of pemphigus vulgaris.[10]

There are some studies conducted on western and populations of other regions to evaluate this association, which are different geographically from our population and to the best of my knowledge there is limited data on our local population. So, it was decided to conduct this study to quantify the vitamin D in people with pemphigus vulgaris in local population so that some inferences can be derived that would add to the literature in our local population and would be helpful for the clinicians to approach the pemphigus vulgaris for early recognition and management of vitamin D deficiency so that the quality of life of these particular patients can be improved.

Material and Methods

In the Department of Dermatology, this cross sectional, descriptive study was executed, at Bahawal Victoria Hospital in Bahawalpur from May 18 to November 17, 2017. Patients of both genders Aged 20-50 years with clinically and histopathologicaly diagnosed pemphigus vulgaris of >1 month duration and having treatment were enrolled in the study. Patients with acid peptic disease, chronic liver disease, diabetes mellitus, and chronic kidney disease and those not willing to participate were excluded from the study. Sample size was 76 as calculated by using formula $n=z^2pq/d^2$ where Z=1.96, p=73.0%, q=100-p, d=10%. The patients were enrolled using a non-probability consecutive sampling procedure.

After approval from the ethical review committee, 76 patients presenting to the outpatient Department of Dermatology, Bahawal Victoria Hospital, Bahawalpur, using the non-probability, consecutive sampling approach, and patients were chosen if they met the inclusion criteria. Each patient provided a signed, informed consent. Following that, each patient's 3 mL blood sample was obtained under stringent aseptic circumstances and sent to the institutional pathology laboratory for testing of vitamin D to determine whether or not they had vitamin D deficiency. The predesigned proforma was used to record all of the data collected from the patients, including demographic information (age, gender, BMI), and their vitamin D levels.

SPSS (Statistical Package for the Social Sciences) version 22.0 was used to record and analyse the data. The mean and standard deviation of numerical factors such as the patients' age, pemphigus vulgaris duration, and BMI were provided. Categorical variables such as gender, place of living (rural or urban), occupation (field work or office work/others),

sun exposure (low/ medium/ high) and vitamin D deficiency (present/ absent) were presented as frequency and percentage. Effect variables such as age, gender, duration of pemphigus vulgaris, BMI, place of residence, occupation, and sun exposure were stratified, and a chi square test was used after stratification. Significant was defined as a P-value of less than 0.05.

Results

Out of 76 patients, 39 (51.32%) were males and 37 (48.68%) were females with male to female ratio of 1.1:1. Age range was from 20 to 50 years with mean age of 34.54±6.70 years with majority of the patients i.e. 47 (61.84%) being between 20 to 35 years of age. Mean duration of disease was 6.41±2.48 months and Mean BMI was 26.19±4.57 kg/m^2. Out of 76 patients 39 (51.32%) were living in rural areas and 37 (48.68%) were living in urban areas. Regarding occupation filed workers, office workers and others were 34 (44.74%), 31 (40.79%) and 11 (14.47%) respectively. Out of 76, 34 (44.74%), 17 (22.37%) and 25 (32.89%) patients have low, medium and high sun exposure respectively.

Vitamin D deficiency in pemphigus vulgaris patients was seen in 55 (72.37%) patients while 21 (27.63%) have shown no vitamin-D deficiency **(Figure 1)**.

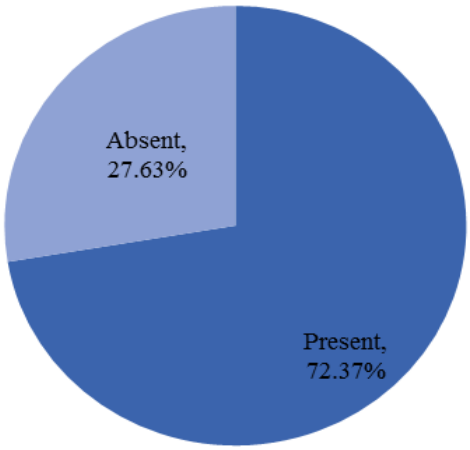

Figure 1 Frequency of vitamin D deficiency in pemphigus vulgaris patients.

Table 1 Stratification of vitamin D deficiency with respect to occupation**.**

Occupation	*Vitamin D deficiency*		*p-value*
	Present	*Absent*	
Field worker	28 (82.35%)	06 (17.65%)	0.058
Office worker	22 (70.97%)	09 (29.03%)	
Others	05 (45.45%)	06 (54.55%)	

Table 2 Stratification of vitamin D deficiency with respect to sun exposure**.**

Sun exposure	*Vitamin D deficiency*		*p-value*
	Present	*Absent*	
Low	22 (64.71%)	12 (35.29%)	0.058
Medium	12 (70.59%)	05 (29.41%)	
High	21 (84.0%)	04 (16.0%)	

Vitamin D deficiency was seen in 74.36% male and 10.27% female population with no statistical significance (P=0.690). Vitamin D deficiency was noted to be 74.47% in patients with 20-40 years of age and 68.97% in patients with 41-60 years of age.

74.0% patients with duration of disease ≤6 months and 69.23% patients with duration of disease >6 months were having vitamin D deficiency with no statistical significance (p=0.659). Regarding distribution of vitamin D deficiency with respect to BMI, it was 69.64% and 80% in non-obese and obese patients respectively. Vitamin D deficiency was present in 71.79% and 72.97% patients living in rural and urban areas respectively having no statistical significance (p=0.909).

Stratification of vitamin D deficiency with respect to occupation and sun exposure is shown in **Table 1 and 2** respectively.

PV is induced by autoantibodies against Desmogleins of desmosomes (Desmoglein3-specific autoantibodies and Desmoglein1-

specific autoantibodies), whereas BP is caused by autoantibodies against two hemidesmosome antigens, BP180 and BP230.[11] Immunosuppressive drugs, notably corticosteroids, have been the standard of care for both disorders to date.[7,12]

Vitamin D has recently been linked to starting or aggravating autoimmunity through influencing the immune system.[13] The occurrence and severity of particular autoimmune ailments have been linked to hypovitaminosis D.[7] The issue of hypovitaminosis D in autoimmune bullous skin disorders has been discussed since certain studies discovered an elevated incidence of hypovitaminosis D in PV and BP patients.[5,8] Others, on the other hand, were unable to identify such connections.[9,14] The smaller sample size of the existing study, as well as the incidence of hypovitaminosis D in otherwise healthy adults, could explain the disparities.[15]

This research was done to see how common vitamin-D deficiency is in pemphigus vulgaris patients. The age range of the participants in our study was 20 to 50 years, with a mean age of 34.54±6.70 years. The majority of the patients, 47 (61.84%), were between the ages of 20 and 35. 39 (51.32%) of the 76 patients were males, while 37 (48.68%) were females, with male to female ratio of 1.1:1. Vitamin D deficit was found in 55 (72.37%) of pemphigus vulgaris patients, while 21 (27.63%) showed no vitamin D deficiency.

This data is consistent with research by Bouaddi *et al.*,[10] which found vitamin D insufficiency in 73% of pemphigus vulgaris patients.[18] Low vitamin D levels in PV patients could be related to a variety of factors. One probable explanation is a reduction in the skin's ability to synthesise vitamin D, as seen in burned individuals. Furthermore, to protect their injured skin, these individuals may have less sun exposure. Anti-vitamin D antibodies have been found in autoimmune skin illnesses including systemic lupus erythematosus in several studies.[16]

As concluded in our study the fact that vitamin D has been linked to a number of autoimmune illnesses shows that it may be an environmental component that generally controls self-tolerance.[17] Pelajo *et al.*[16] studied two groups, one with autoimmune diseases and the other without. They discovered that 23 percent of people with autoimmune disorders were vitamin D deficient, while 14% of those without autoimmune disorders were vitamin D deficient. As a result, the findings were consistent with our research.

Another case control study conducted by Mahnaz *et al.*[18] to evaluate vitamin D levels in newly diagnosed patients revealed that compared to controls, serum vitamin-D was significantly lower in PV patients (-8.90; 95% CI, 2.29-15.51; P=0.009). Concluding that significantly lower levels of vitamin D may be cause of disease worsening and needs to be supplemented in these particular patients. So, the results were consistent with our study.

Previous studies on the prevalence of hypovitaminosis D in people with autoimmune blistering skin disorders have conflicting findings. Indeed, previous findings of low 25-OH Vit. D levels in PV and BP patients[7] were validated by subsequent data[5] and the current extension study's findings, but not by two other studies.[8,9] This discrepancy could be related to the previous studies' small sample sizes and the fact that vitamin D deficiency is common even in healthy people14, as indicated by the control group's mean 25-OH Vit. D levels being within the range of insufficiency.

Despite the difference in mean age of patients between this study (34.5 years) and that of

Marzano *et al.*[7] (66.1 years), PV patients still had low vitamin D levels.[5] Different pemphigus vulgaris patients from developing nations had lower blood vitamin D levels than healthy controls. Studies on the vitamin D status throughout the globe have also shown that the Middle East and Asia have higher rates of hypovitaminosis D than do North America and Europe,[19,20] even though Middle Eastern regions get a plenty of sunlight. This discrepancy could be based on inadequate vitamin D intake and the decreased UV exposure caused by wearing robes. Studies conducted previously showed insufficient and conflicting findings between clinical outcomes and vitamin D levels.

Analysis of other studies revealed that hypovitaminosis D occurred with a very high frequency (91%) in the control group, which is significantly different from the findings of studies conducted on Iranian citizens (which ranged from 27.4% to 55.1%).[21-23] Furthermore, a metanalysis revealed conflicting findings. Hypovitaminosis D rates seemed to be greater in healthy people than in pemphigus vulgaris patients. Between healthy participants and patients with pemphigus, there was a significant BMI difference (25.39±4.30 vs. 27.52±4.65 kg/m^2, p=0.01) may be the cause of the disconcordance.

Limitations

The major limitation of our study was reduced intake of proper diet due to oral ulcerations and erosions that may have contributed to reduced levels of vitamin D. Another limitation was decreased sun exposure of the admitted patients leading to reduced synthesis of vitamin D.

Recommendations

We recommend that there should be early recognition and treatment of this disease in these particular people to minimize complications and morbidity associated with pemphigus vulgaris.

Conclusion

Our study concluded that patients with pemphigus vulgaris often have vitamin D deficiencies.

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