



Prevalence of Depression in Mexican Patients with Pemphigus Vulgaris: An Observational Study

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Summary

Introduction: Pemphigus vulgaris is an autoimmune bullous disease mediated mainly by IgG autoantibodies directed to desmosome proteins. The mental health of these patients has not been extensively described in previous studies.

Objective: To identify the prevalence of depression in Mexican patients with pemphigus vulgaris.

Material and methods: A descriptive, observational study with Mexican patients diagnosed with pemphigus vulgaris was performed. Disease severity was classified according to body surface affected. Data were analyzed descriptively through central tendency and dispersion measures and comparatively with chi square test and Mann-Whitney rank test. Logistic regression was performed to determine the association between variables.

Results: 60 patients were evaluated; 45% presented depression (27/60; 18 women and 9 men); the average age was 32 years (21-58) in patients with depression versus 47 years (27-61) in those without depression ($P = 0.001$). Habitual residence, time of disease progression and duration of immunosuppressant (systemic corticosteroids) showed no significant differences between groups. Low socioeconomic level presented statistical differences ($P = 0.022$). The affected body surface was not related to depression. Oral disease severity was unrelated to depression.

Conclusions: The prevalence of depression in Mexican patients with pemphigus vulgaris is higher than that reported in general population.

Keywords

Depression, Mexican patients, Pemphigus vulgaris, Prevalence

Introduction

Severe and chronic dermatological diseases are frequently associated with psychiatric comorbidity between 10.1-17.2% of patients [1], with personality traits, psychological stress, sexual and psychosocial anguish, and deterioration of quality of life [2]. Most studies on psychiatric comorbidity in dermatological disorders derived from Western countries, focusing on conditions such as psoriasis, vitiligo, lupus erythematosus, dermatomyositis and leprosy [2,3].

Pemphigus vulgaris is a chronic, autoimmune, blistering disease with mucocutaneous involvement and mediated by anti-IgG antibodies directed to the intercellular substance (desmogleins in the desmosoma) [4]. Prevalence of psychiatric disorders in dermatological diseases is reported between 12.2-47.6% [5,6], and 30-

33% in medical-surgical patients [2]. Depression is one of the most frequent manifestations in patients with autoimmune diseases, especially in those with systemic lupus erythematosus. However, in patients with pemphigus, a prevalence of depression of 26% has been reported [2]; similarly, in a study of Barrimi, et al. [7] a prevalence of depression of 27% was reported. A chronic disease

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such as pemphigus vulgaris is a condition that requires a complicated and active process of adaptation to the disease, a complex action of biomedical, evolutionary, behavioral and psychosocial processes is usually observed on these patients. The aim of the study was to identify the prevalence and characteristics of depression in Mexican patients with pemphigus vulgaris.

Material and Methods

A cross-sectional and comparative study was carried out between January of 2015 and January of 2016 in our consultation. The presence and degree of depression, age, gender, family history of depression and the patient's marital status, as well as disease characteristics, such as the affected body surface area, severity of oral mucosa and immunosuppressive treatment were evaluated.

Selection criteria

Patients with a diagnosis of pemphigus vulgaris per clinical (flaccid blisters with exulcerations, mucositis and a positive Nikolsky sign - a positive traction of apparently healthy skin-), histological (suprabasal blister with acantholysis) and immunological criteria (IgG deposits between suprabasal keratinocytes), aged between 18 and 60 years were included. Patients with a previous diagnosis of a psychiatric disorder other than depression, those with some other physical or neuropsychiatric condition that made the study difficult, and those who decided not to participate in the study were excluded.

Sample size calculation

The total population of the consultation was included in the established period and they agreed to participate; sample size calculation was not performed.

Evaluation Tool

For the diagnosis of depressive state, the Hamilton Depression Scale instrument was applied in its reduced version; [8] the scale was validated in Spanish, includes 17 common statements of depression. Each question has between three and five possible answers, with a score of 0-2 or 0-4 respectively. The total score ranges from 0 to 52; (0-7), mild/minor depression (8-13), moderate depression (14-18), severe depression (19-22), and very severe depression (> 23). It is self-administered or it can also be read to the patient by the health professional.

The affected body surface was reported in percentage, considering as 1% the patient's palm without including the fingers. The severity of the oral mucosa was categorized arbitrarily as mild, moderate and severe.

Procedures

Patients selected from the afore mentioned consul-

tation, previous explanation of the purpose of the study and the instructions of filling the form was stated; and once the patient agreed to participate in the study, the Hamilton's depression scale was applied to the patient by the same researcher (ATS). Demographic variants (age, sex, marital status at the time of the study, School degree, place of residence) were recorded, as well as the information obtained from the files on the intervening variables of interest (disease evolution, mucocutaneous condition and Immunosuppressive treatment at the time of the study).

Statistical Analysis

The qualitative variables were analyzed by percentages, and the quantitative ones, with means, standard deviations and ranges (minimum and maximum). The proportions comparison was performed with chi square and the numerical variables with U-Mann-Whitney test. A bivariate analysis was performed to compare the characteristics of each of the variables to be studied between patients with and without depression, and the association with odds ratio was determined. A logistic regression model was used. The dependent variable was the presence or absence of depression and, as an independent variable, the affected body surface was adjusted according to age, sex, disease duration (pemphigus vulgaris), mucocutaneous condition and immunosuppressive treatment at the time of study, marital status at the time of study, School degree and place of residence. For the analysis of the information the statistical program SPSS version 27.0 was used. The 95% Confidence Intervals (CI) were calculated and a statistical significance of $P < 0.05$ was considered.

Ethical Considerations

The study was developed in accordance with ethical standards, the Regulation of the General Law on Health in the Field of Research for Health, as stipulated in good clinical practice and as agreed in the Declaration of Helsinki. The patient's written consent was requested for the application of the questionnaire. The study was classified without risk and the strict confidentiality and anonymity of the patients were maintained. Patients with depression were referred for follow-up to the Psychiatry service. The protocol was approved by the Hospital's Local Research and Ethics Committee, under registration number DI/03/113/15.

Results

Demographics

A total of 60 patients with a diagnosis of pemphigus vulgaris were included in our study, of whom 53% (36/60) were women and 47% (28/60) were men. [Table 1](#)

Table 1: Clinical characteristics of patients with pemphigus vulgaris in relation to the presence or absence of depression.

Variable	PV with depression (n = 27)	PV without depression (n = 33)	P value
Age (mean ± SD) years	37.56 ± 13.55	48.35 ± 16.32	0.001
Gender (Female) %	18 (66.6)	12 (36.4)	0.001
Educational level	Elementary (21 patients, 77%)	Elementary (26 patients, 78%)	NS
Marital status	Divorced (12 patients, 44.4%)	Divorced (15 patients, 45.4%)	NS
Place of residency	CDMX (18 patients, 66.6%)	CDMX (22 patients, 66.6%)	NS
Disease duration (months)	7.5	7.9	NS
Duration of immunosuppressants (months)	3.4	3.6	NS
Body surface area affected (%)	28.43	32.33	NS
Severity of mucositis	Mild = 7 patients; moderate = 18; severe = 2 patients	Mild = 10 patients; moderate = 21 patients; severe = 2 patients	NS

PV = Pemphigus Vulgaris; SD = Standard Deviation; CDMX = Mexico City; NS = Not Significant.

Table 2: Risk factors for depression in patients with pemphigus vulgaris.

Variable	OR	CI 95%	P value
Age (≤ 40 years)	4.6	1.43-6.98	0.052
Gender (Female)	2.1	0.98-2.44	0.05
Marital status (divorced)	3.1	1.26-7.38	0.001
Residency (CDMX)	0.97	0.25-2.39	NS
BSA (≥ 10%)	1.3	0.23-4.27	NS
Severity of mucositis (moderate to severe)	1.6	.55-8.34	NS
Steroids pulse (present)	1.33	0.78-4.12	NS
Systemic steroids use 1 mg/kg/day (≥ 3 months)	2.65	0.88-9.21	NS

OR = Odds Ratio; CI 95% = 95% Confidence Interval; BSA = Body Surface Area Affected; NS = Not Significant; CDMX = Mexico City.

shows the main sociodemographic characteristics of the patients included in the study and their association with depression. The mean age was 37.56 years (range 28-59 years). The mean duration of disease was 7.5 months (range 1-13 months). Mucocutaneous variant of pemphigus vulgaris was the most common clinical variant (49/60 patients), eleven patients had mucosal variant of the disease.

Presence of depression

The prevalence of depression was 45% of patients (27 patients: 18 women (30%) and 9 men (15%)). Depression severity was classified as mild (score of 8-13) in 7 cases and as moderate (score of 8%) in 18 patients. A score of 14-18 (severe depression) was reported in two patients; very severe depression status, according to the results of the Hamilton scale, was not found in the sample studied. A female predominance was observed in patients under 40-years-old, divorced and living in Mexico City, with similar frequencies compared to patients without depression.

Depression versus disease severity

Table 1 shows the time of evolution of pemphigus vulgaris (months) in patients with and without depressive disorder regardless of its severity, without significant difference (P = 0.261). Logistic regression was performed, with the presence or absence of depression as dependent variable and an adjustment was made for each of the in-

tervening variables of interest (age, sex, marital status, body surface affected at the time of study, severity of mucositis and immunosuppressive treatment). The results are shown in Table 2. In this table we observe that age, gender, and marital status, influence the development of depression in the patient with the disease. The severity of the disease and immunosuppressive treatment may influence the risk of depression, although in our study this risk was not significant in both aspects.

Discussion

Mental disorders are considered a global health problem. It is estimated that in 2020, depression will occupy the second place as a disabling condition, and the first in developed countries. On average, depression affects 15% of the general population [9].

Pemphigus vulgaris is a chronic and severe autoimmune disease that may be associated with psychiatric comorbidity [3]. As there were no studies in our population that determine the presence of psychiatric alterations in patients with pemphigus vulgaris, this study considered as a working hypothesis that showed that at least 20% of these patients have depression.

In our study, using the Hamilton Depression Scale in patients with pemphigus vulgaris, a prevalence of depressive disorder of 45% was reported, a picture that is higher than the observed in general population and comparable to that reported in other studies of both pem-

phigus and other autoimmune diseases such as systemic lupus erythematosus (44%).

Similar to the literature consulted [3], we observed a predominance of the female gender in 30% of cases. We did not find significant differences between the groups of patients with depression and without depression with respect to the time of evolution of the disease and the duration of the immunosuppressive treatment. The latter in relation to previous studies establishing the dubious association between the use of corticosteroids and psychiatric symptoms; this association (systemic steroids-psychiatric disorders) has been treated in different studies with controversial results [10-14].

With regard to the affected body surface and the severity of mucositis, in the logistic regression model, there is an odds ratio of 1.3 and 1.6 respectively, which means that patients who develop a greater mucocutaneous condition are 30 to 60% more likely to present depression; however, there is no statistically significant difference and the confidence intervals are wide. Marital status (divorced) has an odds ratio = 3.1; i.e. divorced pemphigus vulgaris patients are two times more likely to have depression than non-divorced pemphigus vulgaris patients, with a statistically significant difference.

Our study showed some degree of depression in 45% of the cases; two studies have evaluated the presence of depression in patients with pemphigus, Tabolli, et al. [15] reporting a prevalence higher than 50%; other study presented by Layegh, et al. [16] reported a prevalence of depression of 27.2% in these group of patients; the first coincides with our study, although in both studies there were no reports of severe or very severe depression.

In the patients of our study, the presence of depression was not related to the treatment ($P = 0.305$) and disease severity ($P = 0.344$); similar to the observed with the rest of the variables. This coincides with the study by Layegh, et al. [16] which did not demonstrate an association between depression with sex, age or duration of the disease, as well as the treatment used (immunosuppressive therapy).

In general, the prevalence of depression in patients with autoimmune diseases reaches significant levels, and the incidence of mental illnesses, such as depression, has been shown to be unrelated to age, gender, duration of illness or even the dose of glucocorticoids or cytotoxic drugs, as with comorbidities such as atherosclerosis and myocardial infarction. In this sense, depression plays a significant role in the health status of patients with pemphigus vulgaris. The mechanism by which depression occurs in pemphigus vulgaris is controversial, although some situations such as negative events, the underlying disease itself and treatment side effects (mainly on sys-

temic immunosuppressant) may contribute to the development of depression [3,16]. Moreover, in few cases, depression may precede the disease manifestations [17-19]; on the other hand, it can be related to poor treatment adherence [9], and thus leading to worse prognosis.

More studies are needed in other populations to compare with the results presented in our study.

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