ORIGINAL ARTICLE

Depression in patients with pemphigus: Is it a major concern?

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ABSTRACT

It is suggested that some dermatological diseases due to their chronicity, impact on the body image, unlikelihood of complete recovery and frequent recurrences are one of the major predisposing factors towards depression. Therefore, we aimed to evaluate the rate and level of depression among pemphigus vulgaris and pemphigus foliaceus patients, two of the most common causes of hospitalization in dermatology units. This research was conducted on 55 patients with active pemphigus vulgaris and pemphigus foliaceus referring to pemphigus clinics or admitted as inpatients to the dermatology ward of Qaem and Imam Reza hospitals, Mashhad, Iran, from April 2008 to September 2009. The research tool was the Beck Depression Inventory. Collected data was analyzed by χ^2-test Student's *t*-test. Twenty-six (47.3%) patients were female and 29 (52.7%) were male. The mean age was 42.34 $\pm$ 18.98 years. The prevalence rate of clinical depression was 28% in pemphigus vulgaris and 20% in pemphigus foliaceus cases. Depression prevalence showed no significant difference between these two groups (*P* = 0.873). In conclusion, pemphigus patients are at risk for mild depression.

Key words: Beck Depression Inventory, depression, pemphigus foliaceus, pemphigus vulgaris.

INTRODUCTION

Chronic skin diseases with their great impact on the perception of an individual about his/her appearance, besides having multiple recurrences, can be a major underlying cause for depression. Such diseases mainly include autoimmune bullous skin disease of which one the most common presentations is pemphigus diseases. Although this affects all races, pemphigus diseases mostly occur in India, Malaysia, China and the Middle East, in comparison to Western countries.[1,2] To note, this disease is one of the major causes of hospitalization in dermatology units of Iran.

The term "pemphigus" refers to a group of autoimmune blistering diseases of the skin and mucous membranes resulting from an immune response against intercellular adhesion molecules and desmosomes. When circulating immunoglobulin G antibodies attack desmogleins (desmosomal cadherin involved in epidermal intercellular adhesions) the cells become separated from each other and the epidermis becomes "unglued", a phenomenon called acantholysis that leads to bullae formation.[1] The two major subtypes, vulgaris and foliaceus, are distinguished by the depth of the cleavage plane in the epidermis.

It seems that the negative effect caused by multiple blisters and erosions on the patient's appearance, including avoiding people, believing that a total cure is impossible and finally the morbidity resulting from different treatment techniques, provide the initial bases leading towards depression in such cases. As the studies conducted in this field are very rare and none have been performed in Iran, we aimed to evaluate the rate and level of depression among pemphigus vulgaris and pemphigus foliaceus patients, two of the most common causes of hospitalization in dermatology units.

METHODS

This is a descriptive cross-sectional study performed on active pemphigus vulgaris and pemphigus foliaceus patients either hospitalized in the dermatology unit or referred to the pemphigus clinic of Qaem and Imam Reza educational hospitals, Mashhad, Iran, from March 2008 through September 2009.

Seventy-two patients with a confirmed diagnosis of pemphigus vulgaris and pemphigus foliaceus based on the histopathology of skin lesion biopsy specimens stained with hematoxylin–eosin, and also direct immunofluorescence examination entered the study. The sampling method was non-

randomized and target-based. All patients who had either been hospitalized or referred to the pemphigus clinics of Qaem and Imam Reza hospitals during the study period with no history of hospitalization in a psychiatry unit or receiving such interventions, no history of psychosis, drug dependency or other major psychiatry disorders, cognitive or organic brain disorders and also epilepsy, were enrolled in the study. The study protocol was fully described and an informed consent was provided by each patient. All cases who did not wish to cooperate or were not educated enough to fully understand the questionnaires were excluded. Thus, the questionnaire was finally completed by 55 cases. The data was collected in two categories. The first category consisted of patient's age, sex, type of underlying disease, prescribed steroid dose (based on disease severity from 0.5–2 mg/kg per day that for ease of statistical tests we classified as 0.5–1 mg/kg per day as <40 mg for mild disease, 1–1.5 mg/kg per day as 40–80 mg for moderate disease and 1.5–2 mg/kg per day as >80 mg per day for severe ones), disease duration, type of treatment regimen classified as steroid alone or in combination with an adjuvant (mostly azathioprine 2–3 mg/kg per day); and extent of skin and mucosal involvement graded on Kumar *et al.*'s criteria,[3] a simple arbitrary scoring system which was used at the time of sampling, consisting of oral (0, no mucosal involvement; 1, minimal disease [only buccal mucosa, labiogingival, lingual, palatal or pharyngeal involvement]; 2, moderate disease [buccal and labiogingival, lingual, palatal or pharyngeal involvement]; and 3, severe disease [extensive oral erosions, i.e. >3 mucosal sites affected]) and skin scores (0, quiescent disease; 1, minimal disease [≤10% body surface area [BSA] involved]; 2, moderate disease [11–30% BSA involved]; 3, severe disease [>30% BSA involved]).

In the second category, the Beck Depression Inventory Second Edition (BDI-II) was completed by each patient on their discharge day in order to evaluate the main variables leading to depression. The BDI-II is a questionnaire consisting of 21 tests, each scored 0–3. This test is a widely used instrument for measuring the existence and severity of depression that was originally published in 1961 and later revised as the BDI-1A in 1978. In this version, the questionnaire is designed for adults, and includes items relating to symptoms of depression such as hopelessness and irritability, cognitions such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss and decreased libido. Higher total scores show more severe depressive symptoms. After completing the Persian version of the BDI-II questionnaire (cut-offs: 0–15, minimal or no clinical depression; 16–30, mild; 31–46, moderate; 47–63, severe depression),[4,5] the collected data was analyzed using SPSS software ver. 11.5 and then compared by χ^2-test and Student's *t*-test. In this study, the BDI-II results were studied from all aspects in the abovementioned first category. To note, on an ethical basis, all patients with a score above 19 line were referred to a psychiatrist for further evaluation. $P < 0.05$ was considered statistically significant.

The study protocol was approved by the Research Council's Ethical Committee of Mashhad University of Medical Sciences.

RESULTS

Among the 55 studied cases, 50 (90.9%) were afflicted with pemphigus vulgaris and five (9.1%) with pemphigus foliaceus. Twenty-nine (52.7%) were male and 26 (47.3%) female. According to the χ^2-test, no significant difference was found between the two sexes ($P = 0.55$). Mean ($\pm$ standard deviation) age of the studied patients was 42.34 $\pm$ 14.98 years. Ages ranged 17–79 years. When distributing the patients into age groups by decade, 40–49-year-old patients were of the highest number with 13 (23.6%) cases. The mean duration of disease chronicity was 18.36 $\pm$ 18.88 months. Table 1 shows the disease type and demographic parameters of the studied patients.

The BDI score ranged 0–34 with a mean score of 11.9 $\pm$ 8.52. The distribution of depression among the studied cases is shown in Table 2. Clinical depression was detected in 27.2% of cases including 24% of the mild and 4% of the moderate type in the pemphigus vulgaris group whereas in total, only 20% of cases were affected with mild depression in the pemphigus foliaceus group and none with the moderate form. Severe depression was not diagnosed in any of the studied cases.

When comparing the rate of different forms of depression among the studied cases based on sex, age and disease duration, no significant difference was observed according to the χ^2-test ($P = 0.313$, =0.922 and =0.506, respectively).

Systemic corticosteroids are known to have psychological side-effects and can result in depression; in order to assess the probable interventional role of this factor, the patients were divided into three groups based on the administrated steroid dose (<40 mg, 40–80 mg and >80 mg/day). The correlation between the patients' depression score results and their consumed steroid dose at the time of completing the questionnaire was analyzed. The χ^2-test showed no significant difference regarding the comparison of these two factors ($P = 0.903$).

In addition, the role of treatment regimen (steroid alone or in combination with an adjuvant which was administrated in order

Table 1. Type of disease and demographic characteristics of patients

	PV	PF
Sex		
Male	26	3
Female	24	2
Age range (years)	21–79	17–38
Disease duration (months)	2–72	3–26
Oral disease severity		
None	0	5
Mild	11	0
Moderate	14	0
Severe	25	0
Extent of skin involvement		
Mild	4	0
Moderate	26	3
Severe	20	2

PF, pemphigus foliaceus; PV, pemphigus vulgaris.

Table 2. Frequency and severity of depression based on BDI score results in pemphigus patients

Results of Beck score	Frequency	%
Normal (0–15)	40	72.7
Mild depression (16–30)	13	23.6
Moderate depression (31–46)	2	3.7
Severe depression(47–63)	0.0	0.0
Total	55	100

BDI, Beck Depression Inventory.

to better control the disease and alleviate steroid side-effects) on the rate of depression was studied; comparing the prevalence of different forms of depression with the type of treatment regimen showed no meaningful difference by χ^2-test (P = 0.900; Table 3).

DISCUSSION

Pemphigus is a chronic bullous and often debilitating disease due to its type, severity, extent and location of lesions. It has a negative impact on the patient's appearance, has no easy treatment, a high rate of recurrence, a long hospitalization period and need to receive immunosuppressive drugs.[6] The combination of such factors besides the morbidity caused by existing treatment regimens (mainly systemic corticosteroids, especially at high doses) can lead to major psychological trauma, severe depression or even suicide.[7]

Nevertheless, very few reports have been published on the quality of life of such patients or the possibility of depression evaluated by highly reliable and qualified tools.[8–11]

Namazi has reported a case in which a young lady affected with pemphigus vulgaris hospitalized in the dermatology unit of Tehran's Razi hospital attempted suicide by jumping from her hospital room window. In this study, he emphasized the need for precise evaluation of pemphigus vulgaris patients on the basis of the prescribed medications' psychological side-effects and considering a well-planned therapeutic approach regarding such disorders if necessary.[12]

Terrab *et al.*,[9] having applied the Public Health Questionnaire composed of 36 questions, also Mishuffer *et al.* in Germany,[10] Paradise in Italy[8] and Ghodsi *et al.* in Iran,[11] having implemented the quality of life scoring system in pemphigus patients, witnessed a remarkable decline in their quality of life.

It seems that besides our study, that by Tabolli *et al.*[13] is the only work which has focused on the incidence of depression in pemphigus vulgaris patients. Fifty-eight patients affected with pemphigus, 51 of the vulgaris and seven of the foliaceus type based on a questionnaire filled in by them, were studied from three aspects: (i) public health; (ii) depression; and (iii) anxiety. Eventually, it revealed results similar to psoriasis from the aspect of the effect and load of the disease, and on the other hand showed a dramatic decline in the patients' quality of life in comparison to the general population.[13]

In the above-mentioned study, depression was observed in more than 50% of the cases which is similar to those reported in psoriasis and acne studies. However, in our study clinical depression was only seen in 27.2% of cases; mild and moderate depression in 24% and 4% of pemphigus vulgaris patients, respectively; and only mild depression was seen in a total of 20% of cases with pemphigus foliaceus. Severe depression was not seen in any single case. These differences could be due to cultural backgrounds and the qualifications of the studied cohorts.

Pemphigus foliaceus patients in Tabolli *et al.*'s study[13] achieved a higher score in general and psychosocial health in comparison to pemphigus vulgaris cases, but this difference was not statistically significant which could be due to the small number of foliaceus cases. In our study, although the percentage of mild and moderate depression was higher in the pemphigus vulgaris group, but again due to the small number of foliaceus patients, no significant difference was seen between the rate of depression and type of the skin disease (P = 0.873); this was similar to Tabolli *et al.*'s[13] results in which pemphigus vulgaris patients achieved the highest depression score.

As systemic corticosteroids have their own psychological side-effects which can result in depression,[14–16] in order to investigate the possible interfering role of this factor, the cases were divided into three subgroups based on the administrated

Table 3. Frequency of depression based on BDI score and disease type, treatment regimen and steroid dose

	Normal		Minor depression		Moderate depression		Severe depression		
	F	%	F	%	F	%	F	%	*P*
Disease type									
PV	36	72	12	24	2	4	0	0	0.873
PF	4	80	1	20	0	0	0	0	
Steroid dose									
<40 mg/day	19	76	5	20	1	4	0	0	0.903
40–80 mg/day	12	66.7	5	27.8	1	5.6	0	0	
>80 mg/day	9	75	3	25	0	0	0	0	
Treatment regimen									
CS alone	24	75	7	21.9	1	3.1	0	0	0.900
CS plus adjuvant	16	69.6	6	26.1	1	4.3	0	0	

CS, corticosteroids; F, frequency of depression; PV, pemphigus vulgaris, PF; pemphigus foliaceus.

steroid dose, and the depression score results were analyzed in accordance to these subgroups. No statistically significant difference was observed between the rate of depression and the administrated steroid dose ($P = 0.903$). The correlation between the rate of depression and the treatment regimen was not significant either ($P = 0.900$); as this relevancy was not assayed in Tabolli *et al.*'s study,[13] it is one of the major advantages of the present work.

The biggest limitation of the current study was its sampling method, which due to some problems was done over a short time period (1.5 years). If this research could have been performed over a longer period of time and on a larger population, the studied groups would have been of a more similar status based on the extent and severity of the disease and the administrated drug dose.

Moreover, the research tool in this study was the self-evaluating BDI-II questionnaire, which is only an indicator of the depression syndrome but cannot clearly define the presence and type of depression; besides, some patients were not qualified enough to complete the questionnaire on their own so had to be excluded from the study. Regarding such issues, implementing a diagnostic interview and more accurate tests should be considered in future studies. It also seems apparent that the simultaneous survey of depression and self-image could lead to more precise results.

Finally, considering the high prevalence of autoimmune bullous disease in our region and their major impact on the patients' quality of life, focusing future studies on evaluating the quality of life of patients with bullous disease and particularly pemphigus is strongly suggested.

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