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Clinical and Evolutionary Characteristics of Pemphigus by Gender: Comparative Study of 330 Cases

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Authors' contributions

This work was carried out in collaboration among all authors. Authors AF and MEA designed the study, performed the statistical analysis, wrote the protocol, and wrote the manuscript. Authors MM, NI, LB and KS they revised the manuscript revision. All authors read and approved the final version of the manuscript.

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ABSTRACT

Introduction: Pemphigus is a group rare heterogeneous of intraepidermal autoimmune chronic bullous dermatoses associated with a high risk of morbidity and mortality. Despite its rarity, this condition persists as the most prevalent among bullous dermatoses in the Maghreb, including Morocco. Very few studies have investigated the significant influence of gender on the clinical phenotype, the activity score and the evolution of the disease. Our study objective is to analyze clinical and evolutionary characteristics of pemphigus based on gender differences.

Materials and Methods: A comparative retrospective descriptive study was conducted on 142 male and 188 female pemphigus patients treated at the "Department of Dermatology in Ibn Sina University Hospital, Rabat," between 1990 and 2022. Data from medical records were analyzed,

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focusing on variables such as age at diagnosis, disease duration, medical history, presence of autoimmune conditions, clinical subtypes, extent of cutaneous and mucosal involvement, and disease progression. Data entry and analysis were performed using Excel and the Statistical Package for the Social Sciences.

Results: There were no significant differences in age, and both sexes had the same disease duration prior to diagnosis. The occurrence of pemphigus in women has been more closely associated with autoimmune diseases (25 cases compared to 2 cases in men). Regarding the phenotypes of pemphigus, pemphigus herpetiformis, pemphigus vegetans, and pemphigus vulgaris were more common in women. Isolated mucosal involvement was also more prevalent in women. Women exhibited a more severe Pemphigus Disease Area Index (PDAI) than men. In both male and female patients, the main treatment approach mainly involved oral corticosteroids, followed by an association of corticosteroids and cortisone-sparing agents. Azathioprine was the most frequently administered immunosuppressant (91.6%), with rituximab being used as the initial therapy in 8% of cases.

Regarding disease progression, complete remission was noted in 83 women and 52 of men. No notable variances were observed in terms of bleaching time, relapse rates, or mortality.

Conclusion: Our findings suggest that gender might impact the clinical presentation of pemphigus patients. Specifically, we observed a higher prevalence of pemphigus herpetiformis, pemphigus vegetans, mucosal involvement, severe Pemphigus Disease Area Index (PDAI), and comorbid autoimmune diseases among women. However, our analysis indicates no significant disparities regarding disease progression or prognosis.

Keywords: Pemphigus; gender; bullies dermatosis; autoimmune diseases.

1. INTRODUCTION

Pemphigus encompasses a group of rare acantholytic autoimmune dermatoses affecting mucocutaneous membranes, characterized by the loss of cell-to-cell adhesion leading to the formation of bullae and erosions. Various subtypes of pemphigus have been distinguished based on their unique clinical and hisological manifestations, including pemphigus vulgaris (PV), pemphigus vegetans, pemphigus seborrheic (PS), pemphigus foliaceus (PF), pemphigus herpetiformis (PH), and paraneoplastic pemphigus (PNP) [1].

At the core of pemphigus pathogenesis is the presence of immunoglobulin (Ig) antibodies targeting proteins located on the cell surface of keratinocytes, specifically desmogleins [2,3,4].

Pemphigus occurs worldwide (incidence varies from 0.5 to 34 cases/million inhabitants/year) and impacts individuals of all races and ethnicities [2,5].

Despite its rarity, this condition persists as the most prevalent among bullous dermatoses in the Maghreb, including Morocco [6]. Very few studies have investigated the significant influence of gender on the clinical phenotype, the activity score and the evolution of the disease. Our study objective is to analyze clinical and evolutionary characteristics of pemphigus based on gender differences.

2. MATERIALS AND METHODS

A comparative retrospective descriptive study was conducted on 142 male and 188 female pemphigus patients treated at the “Department of Dermatology in Ibn Sina University Hospital, Rabat,” between 1990 and 2022.

The diagnosis of pemphigus was established based on a combination of clinical, immunological (indirect immunofluorescence with positivity for antibodies anti-intercellular substance, anti-desmoglein 1 and/or 3), and histological criteria.

Data from medical records were analyzed, focusing on variables such as age at diagnosis, disease duration, medical history, presence of autoimmune conditions, clinical subtypes, extent of cutaneous and mucosal involvement, and disease progression. Data entry and analysis were performed using Excel and the Statistical Package for the Social Sciences.

3. RESULTS

There were negligible differences observed in age distribution between females (52.24±14 years) and males (54.05±15 years), with both

sexes experiencing an average disease duration of 13 months before diagnosis. Females exhibited a higher prevalence of autoimmune diseases, including dysthyroidism (9 cases), type 1 diabetes (5 cases), rheumatoid arthritis (5 cases), systemic lupus (2 cases), autoimmune hepatitis (1 case), Gougerot-Sjogren's syndrome (1 case), vitiligo (1 case), and autoimmune sclerosing cholangitis (1 case), in comparison to males, who were associated with type 1 diabetes (2 cases) and vitiligo (1 case).

Regarding clinical phenotypes, pemphigus herpetiformis, pemphigus vegetans, and pemphigus vulgaris were more prevalent in females than in males respectively 11cases in females compared to 2 cases in males, 20 women vs 13 men and 78 women vs 56 men. Superficial forms were distributed as follows: seborrheic pemphigus (53 cases in females vs. 50 cases in males), foliaceous pemphigus (25 cases in females vs. 20 cases in males), with one case of paraneoplastic pemphigus noted in each gender. Isolated mucosal involvement was more frequent in females than in males (15 cases vs. 3 cases, respectively), and the severity of Pemphigus Disease Area Index (PDAI) was higher in females than in males (145 vs 96 cases respectively).

Treatment protocols involved oral corticosteroids in 55% of cases and a combination of corticosteroids with cortisone-sparing agents in 45% of cases for both genders. Azathioprine was the most commonly prescribed immunosuppressant (91.6%), while rituximab was used as first-line therapy in 8% of cases, regardless of gender.

Regarding disease progression, complete remission was achieved in 48% of females (83 cases) and 40% of males (52 cases). No significant variations were detected concerning bleaching time (80 days for females vs. 73 days for males), relapse rates (30% in females vs. 28% in males), or mortality rates (16 cases in females vs. 17 cases in males). Females tended to experience relapses 49 months after complete remission, while males experienced relapses after 52 months, on average.

Table 1. Summarizes the clinical characteristics and progression of pemphigus according to patient gender

		Women	**Men**
Number of cases		**188 cases**	**142 cases**
Average age		52.24 +/- 14 years	54.05 +/- 15 years
Mean duration of disease before diagnosis		13 months	13 months
Association with autoimmune diseases		25 cases (13.3%): 9 cases: dysthyroidism, 5 cases: diabetes type 1 5 cases: rheumatoid arthritis 2 cases: systemic lupus 1 case: autoimmune hepatitis 1 case: Gougerot-Sjogren's 1 case: vitiligo 1case: autoimmune sclerosing cholangitis	2 cases (1.4%): 1 case: diabetes type 1 1case: vitiligo
Type of pempgighus	P herpetiformis	11 cases (5.85%)	2 cases (1.4%)
	P vegetans	20 cases (10.6%)	13 cases (9.1%)
	P vulgaris	78 cases (41.5%)	56 cases (39.4%)
	P seborrheic	53 cases (28.2%)	50 cases (35.2%)
	P foliaceous	25 cases (13.3%)	20 cases (14.1%)
	P paraneoplastic	1 case (0.5%)	1case (0.7%)
Isolated mucosal involvement		15 cases (7.9%)	3 cases (2.1%)
PDAI severe		145 cases (77.1%)	96 cases (67.6%)
Evolution	Remission	83 cases (48%)	52 cases (40%)
	Bleaching time	80 days	73 days
	Relapse	52 cases (30%)	37 cases (28%)
	Death	16 cases (16.6%)	17 cases (11.9%)

4. DISCUSSION

Pemphigus is an acquired bullous dermatosis predominantly in female patients, like most autoimmune diseases (lupus, scleroderma, dermatomyositis) [6].

The initiation of autoimmune diseases correlates with sex hormone levels. Conversely, females experience multiple hormonal transitions, such as puberty, menstruation, pregnancy, and menopause. Consequently, the incidence of pemphigus vulgaris is elevated among postmenopausal females [7].

However, a single study by Uzun et al. showed that pemphigus is male-predominant in countries such as Spain and Saudi Arabia [8,9]. On the other hand, the ,Turkish study of Ibrahim et al concluded that men and women show a close rate, which means that autoimmunity is not the only factor in the etiology of this disease [10]. Pemphigus has been associated with various HLA antigens in different populations. This association mainly concerns class II antigens [11]. Genetic factors may therefore play an important role in this disease. In our study, the disease was more prevalent among women.

Few studies have analyzed the epidemiological and therapeutic differences between the two sexes. The survey by Naseer et al. found that men with PV are more likely to develop the disease before age 40, and had more severe skin involvement and showed greater co-expression of anti-Dsg1 and anti-Dsg3 antibodies, in contrast, women develop the disease between the age of 40-49 years and tended to have a predominance of mucosal involvement and a personal and family history of autoimmunity [12]. In our study There was no significant difference age, The association with autoimmune diseases was more frequent in women and isolated mucosal involvement (without skin involvement) was more frequent in women.

Yavuz et al. found that pemphigus vegetans and pemphigus vulgaris were more common in women, while superficial pemphigus (seborrheic and foliaceous) was more common in men [13]. In our study, we observed a predominance of females across all phenotypes of pemphigus.

Lagacé et al reported an overall female predominance (F:M 1-5:1) for pemphigus vulgaris (PV), with conflicting results or equal gender distribution for pemphigus foliaceous (PF) and pemphigus herpetiformis, and with a possibly higher risk of paraneoplastic pemphigus in men [14,15].

Alternatively,no studies have been conducted to evaluate the evolution and prognosis of pemphigus based on gender. In our study, there were no notables variations in terms of evolution or prognosis according to gender.

5. CONCLUSION

Our findings suggest that gender might impact the clinical presentation of pemphigus patients. Specifically, we observed a higher prevalence of pemphigus herpetiformis, pemphigus vegetans, mucosal involvement, severe Pemphigus Disease Area Index (PDAI), and comorbid autoimmune diseases among women. However, our analysis indicates no significant disparities regarding disease progression or prognosis.

CONSENT

It is not applicable.

ETHICAL APPROVAL

This study received approval from the Ethics Committee of Ibn Sina University Hospital Center in Rabat. All research procedures were conducted in accordance with the ethical standards established by this committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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