

Pemphigus: Clinical study of 68 patients 5 years ago in Aden, Yemen

Amer Omer Bin Al-Zou

Associate Professor, Department of Dermatology, Faculty of Medicine, University of Aden, Yemen

Correspondence:

Dr Amer Omer Bin Al-Zou,

Associate Professor of Dermatology, Faculty of Medicine, University of Aden, Yemen

Email: amer_zou2009@yahoo.com

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Abstract

Background: Pemphigus is a rare disease with an incidence range from 0.5 to 32.0 per 1,000,000 in different geographic areas and ethnic groups.

Objective: To describe the epidemiological and clinical pattern of pemphigus.

Materials and methods: The records of 68 patients diagnosed with pemphigus were reviewed. Documented information of the patients during the period of January 2018 to December 2022 were extracted. Data were analyzed using SPSS version 22.

The collected data were tabulated and statistical analysis was done by estimating rates, means and standard deviations. The chi-square test was used to compare final outcomes. Fisher test was used and p-value < 0.05 was considered as statistically significant.

Results: The total study patients were 68. They were (61.8%) females and (38.2%) males. The mean age at the onset of disease was 49.1 ± 14.4 years. Pemphigus vulgaris was the most common type (88.2%), followed by pemphigus foliaceus (10.3%). The most common site of involvement of pemphigus was in mucocutaneous (72.1%).

Most of the patients (60.3%) were treated by a combination of corticosteroid and azathioprine, ($p = 0.000$). The complete remission of lesions after 2 months was (73.5%).

Conclusion: Pemphigus vulgaris was the most common type. Females were predominant and the patients of the age group ≤ 50 years and the age group > 50 years were to some extent equally affected. The most common site of involvement was mucocutaneous. Most of the patients were treated by a combination of corticosteroid and azathioprine.

Key words: Pemphigus, clinical study, Aden, Yemen

Introduction

Pemphigus is a rare disease with an incidence range from 0.5 to 32.0 per 1,000,000 in different geographic areas and ethnic groups [1]. Pemphigus vulgaris (PV) and pemphigus foliaceus (PF) are the main clinical subtypes of the disease. PV often affects individuals during the fourth and fifth decades of life, and its main characteristics are flaccid blisters and erosions of the mucous membranes and the skin [2].

The most characteristic clinical findings are painful erosions and ulcers in the oral mucosa. In contrast, scaly crusted erosions with an erythematous base are often observed in PF on the seborrheic regions such as the face, scalp, chest, and back without mucosal involvement [3].

Pemphigus is the name of a group of autoimmune pathological entities characterized by the formation of intraepithelial blisters in the skin and/or mucosa [4]. PV is the most common variant of pemphigus, and usually begins with painful ulcerations on oral and other mucosa. The primary skin lesions of PV are flaccid, thin-walled, easily ruptured blisters that appear anywhere on the skin surface [5]. Histological studies of PV lesions usually demonstrate acantholysis in the supra-basilar part of the epidermis [4]. Without appropriate treatment, PV can be fatal because large areas of the skin lose epidermal barrier function, leading to loss of body fluids or secondary bacterial infection [6]. The primary lesions in PF are flaccid, superficial vesicles and bullae of the skin. These lesions some-times may not be seen on examination because of their fragile and subsequent transient nature. More often, only secondary lesions, such as shallow erosions, are seen [7]. There are no mucosal lesions, even with widespread disease. Intra-dermal acantholysis occurs in the granular layer [8]. The diagnosis of the pemphigus group of diseases is based on clinical picture and history, histopathologic diagnosis, and direct and indirect immunofluorescence [9]. Due to the low prevalence of pemphigus and variability of triggers and manifestations, large scale study data on treatment responses are limited [10]. Currently, pemphigus therapy guidelines are based on a limited number of placebo-controlled trials [10,11]. The treatment response can vary among individual pemphigus patients and not rarely several therapy changes are necessary to achieve long-lasting disease control [12], i.e., the absence of symptoms. However, inadequate disease control as well as iatrogenic immunosuppression can lead to infectious and other potentially fatal complications [13].

Objective

To describe the epidemiological and clinical pattern of pemphigus seen at our private clinic in Aden.

Materials and Methods

The records of 68 patients diagnosed with pemphigus in our private Clinic of Dermatology, Aden, Yemen during the period January 2018 to December 2022 were reviewed in a descriptive and retrospective study.

Documented information of the patients included sex, age, residency, site of involvement, type of pemphigus, duration from the onset of the disease and treatment. The following types of pemphigus were considered in this research: (a) Pemphigus vulgaris, (b) pemphigus foliaceus, and (c) pemphigus vegetans. Data was analyzed using SPSS software version 22. The collected data were tabulated and statistical analysis was done by estimating rates, means and standard deviations. The chi-square test was used to compare final outcomes. Fisher test was used and p -value < 0.05 was considered as statistically significant.

Results

The total study patients were 68 diagnosed with pemphigus. The patients included 42 females (61.8%) and 26 males (38.2%) with a female to male ratio 1.6:1. The mean age at the onset of disease was 49.1 ± 14.4 years (range: 24 – 78 years old,). In addition, the age group ≤ 50 years represented 51.5% while the age group > 50 years represented 48.5%. Mean duration since disease onset was 9.3 ± 8.3 months.

Most of the patients were from Aden governorate 28 (41.2%) followed by Lahej governorate with 18 (26.4%), as shown in Table 1 and Figure 1.

Pemphigus vulgaris was the most common clinical variant diagnosed in 60 (88.2%) patients. They were distributed as 40 females (58.8%) and 20 (29.4%) males, followed by pemphigus foliaceus in 7 (10.3%) patients and pemphigus vegetans in 1 (1.5%) patient. The values of sex and types of pemphigus did not show a significant difference ($P = 0.059$), Table 2 and Figure 2.

The most common site involvement of pemphigus was in cutaneous + mucosal (mucocutaneous) 49 (72.1%), distributed in 34 (50%) female patients and 15 (22.1%) male patients, followed by cutaneous involvement 15 (22.1%) then mucosal involvement in 4 (5.8%) patients. There was a statistical relation between site of pemphigus and sex ($p = 0.038$), as shown in Table 2 and Figure 2.

Table 1: Distribution of sex, age and mean duration since disease onset (n=68)

Variables	No	%
Sex:		
Males	26	38.2
Females	42	61.8
Female to male ratio	1.6:1	
Age range (years):	24 – 78	
Mean age all patients:	49.1 ± 14.4	
Age groups (years):		
≤ 50	35	51.5
> 50	33	48.5
Mean duration since disease onset (months):	9.3 ± 8.3	
Residence:		
Aden	28	41.2
Lahej	18	26.4
Abyan	9	13.2
Shabwa	5	7.4
Aldhalae	4	5.9
Hadramout	4	5.9

Figure 1: Proportions of demographic variables of the study patients

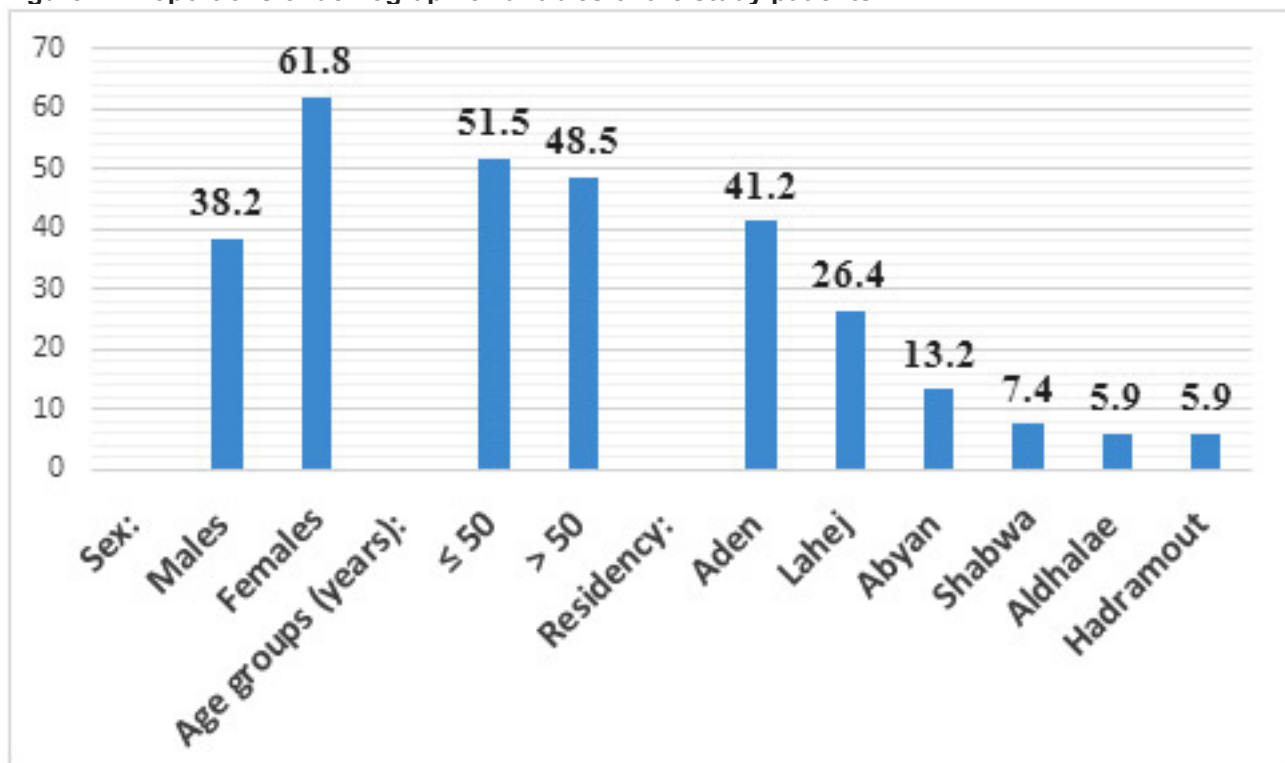


Table 2: Distribution of various variables of the study patients (n=68)

Variables	Sex		Total No	p-value
	Females No (%)	Males No (%)		
Type of pemphigus:				
Pemphigus vulgaris	40 (58.8)	20 (29.4)	60 (88.2)	0.059
Pemphigus foliaceus	2 (2.9)	5 (7.4)	7 (10.3)	
Pemphigus vegetans	0 (0.0)	1 (1.5)	1 (1.5)	
Site of pemphigus:				
Mucocutaneous	34 (50.0)	15 (22.1)	49 (72.1)	0.038
Cutaneous	5 (7.4)	10 (14.6)	15 (22.1)	
Mucosal	3 (4.3)	1 (1.5)	4 (5.8)	

Figure 2: Proportions of pemphigus types and site involvements related to sex

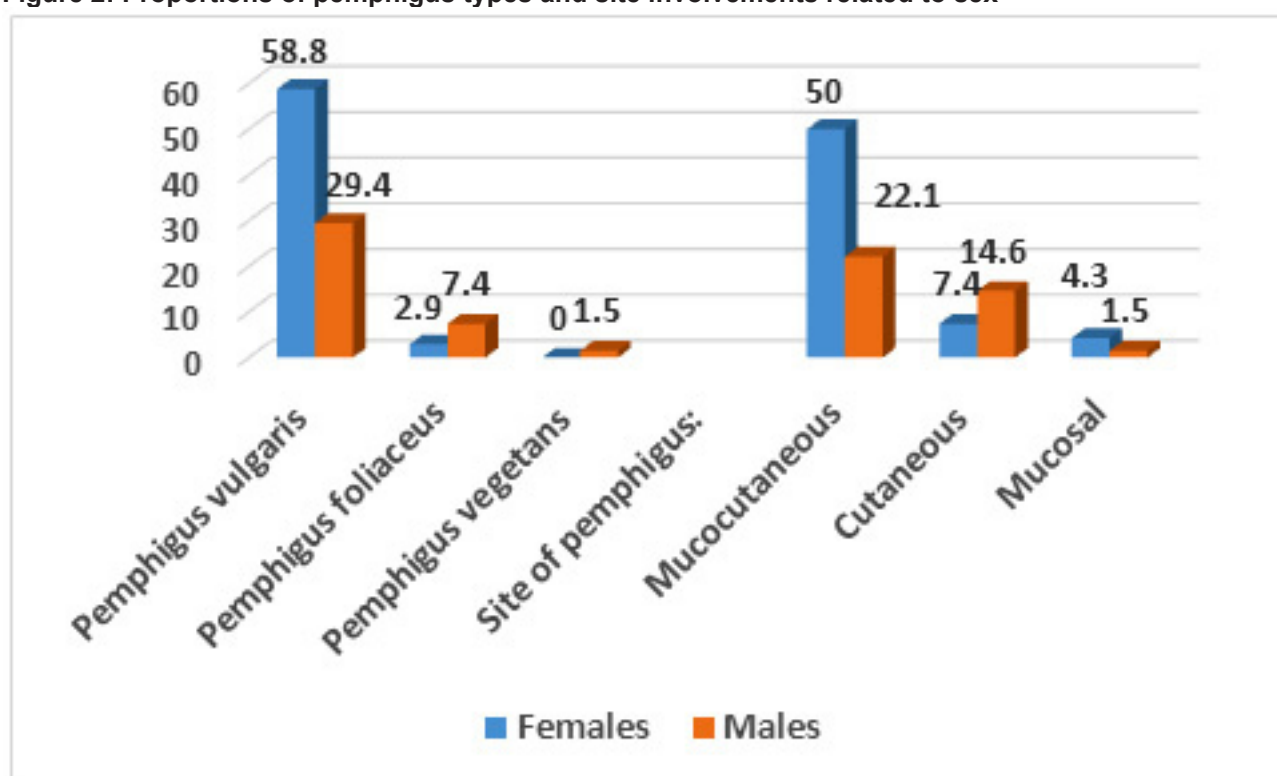


Table 3 revealed the pemphigus treatment of the study patients. Most of the patients 41 (60.3%) were treated by a combination of corticosteroid and azathioprine. Out of them 40 (58.8%) PV patients and 1 (1.5%) PF patients were thus treated, then 12 (17.6%) patients were treated only by corticosteroid distributed as follows: 5 (7.4%) for PV patients, 6 (8.8%) for PF patients and 1 (1.5%) for pemphigus vegetans patient.

Seven (10.3%) of the PV patients were treated by a combination of corticosteroid + azathioprine + dapsone, followed by 4 (5.9%) PV patients were treated by a combination of corticosteroid + azathioprine + mycophenolate mofetil and also, 4 (5.9%) PV patients were treated by a combination of corticosteroid + dapsone. There was a statistical relation between treatment and types of pemphigus ($p = 0.000$). Additionally, we observed in Table 3 the complete remission of lesions after 2 months in 50 (73.5%) of all patients distributed as follows: 44 (64.7%) among PV patients, 5 (7.3%) among PF patients and 1 (1.5%) of pemphigus vegetans patient.

Table 3: Pemphigus treatment of the study patients (n=68)

Treatment	Types of pemphigus			P-value
	PV	PF	PVEG	
Corticosteroid	5 (7.4)	6 (8.8)	1 (1.5)	0.000
C + Azathioprine	40 (58.8)	1 (1.5)	0 (0.0)	
C + Azathioprine + Dapsone	7 (10.3)	0 (0.0)	0 (0.0)	
C + Azathioprine + Mycophenolate + Mofetil	4 (5.9)	0 (0.0)	0 (0.0)	
C + Dapsone	4 (5.9)	0 (0.0)	0 (0.0)	
Total	60 (88.2)	7 (10.3)	1 (1.5)	
CRL (2 months):				0.820
Yes	44 (64.7)	5 (7.3)	1 (1.5)	
No	16 (23.5)	2 (3.0)	0 (0.0)	

C = Corticosteroid, PV = Pemphigus vulgaris, PF = Pemphigus foliaceus, PVEG = Pemphigus vegetans, CRL = Complete remission of lesions



(A) Pemphigus vulgaris with cutaneous and oral erosions



(B) Pemphigus vulgaris



(C) Oral mucosa erosion in Pemphigus vulgaris



(D) Pemphigus foliaceus



(E) Pemphigus vegetans

Discussion

Pemphigus is a heterogeneous group of autoimmune bullous diseases, characterized by autoantibodies targeting intra-epidermal adhesion molecules [14]. Pemphigus vulgaris (PV) and pemphigus foliaceus (PF) are the two major variants of pemphigus. Pemphigus variants other than PV and PF are less frequent [15,16]. The epidemiological characteristics of pemphigus vary according to the clinical variant, geographical regions, and ethnicities [17-19]. PV is considered the most prevalent type of pemphigus, corresponding to 70% of all cases [17,18].

In European countries, the average age at onset of PV varies from 50 to 60 years [20]. Conversely, PV is extremely rare during childhood [21]. PV seems to be more prevalent in female than male patients, with a female/male sex ratio ranging from 1.1 in Finland to 5.0 in the USA [15,18].

In our current study, the patients were 68 and they were 42 (61.8%) females and 26 (38.2%) males with a female to male ratio 1.6:1. Our study findings revealed that pemphigus is predominant in females. Similar findings have been reported by others from Turkey, Iran and South Africa [22-24].

In the current study, the mean age of the patients at the onset of disease was 49.1 ± 14.4 years (range: 24 – 78 years old,). In addition, the age group ≤ 50 years represented 51.5% while the age group > 50 years represented 48.5%. Mean duration since disease onset was 9.3 ± 8.3 months.

In a study carried out in Turkey by Yayli et al [2] their results were convergent to our findings. They reported that a female predominance with a female to male ratio of 1.41:1. The mean age of onset was 48.92 ± 15.02 years. There was a difference in the mean time period between the onset of the disease and the definite diagnosis. In our study was 9.3 ± 8.3 months and in their study it was 6.45 ± 8.32 months. This may be due to the level of medical services provided, as well as health awareness among citizens.

Pemphigus largely affects patients between the ages of 50 and 60, although the mean age at diagnosis can differ significantly based on the country of origin and ethnic background. In some Western Asian nations such as Kuwait, the mean age at diagnosis is 36.5 years, whereas in European nations such as Bulgaria, the mean age at diagnosis is 72.4 years [25].

In the current study, we found the pemphigus vulgaris was the most common clinical variant diagnosed in 60 (88.2%). They were distributed as 40 female patients (58.8%) and 20 (29.4%) male patients, followed by pemphigus foliaceus in 7 (10.3%) patients and pemphigus vegetans in 1 (1.5%) patient. The values of sex and types of pemphigus did not show a significant difference ($P = 0.059$).

Michailidou et al [26] mentioned that pemphigus vulgaris is the most common type accounting for approximately 80% of cases worldwide. Abdolsamad et al [27] reported that pemphigus vulgaris was the most common clinical subtype, identified in 1,422 patients (91.15%) followed by pemphigus foliaceus in 100 patients (6.4%), and pemphigus vegetans in 37 patients (2.3%).

In the present study, we found the most common site of involvement of pemphigus was in cutaneous + mucosal (mucocutaneous) (72.1%), followed by cutaneous involvement (22.1%) then mucosal involvement in (5.8%) patients. There was a statistical relation between site of pemphigus and sex ($p = 0.038$).

The mention and distribution of the disease site in our study was limited and differed from the distribution mentioned by Abdulsamad et al [27] from Iran. They reported that in (44.9%) patients, pemphigus affected oral mucosa exclusively. (9.6%) patients had only skin lesions, (16.7%) patients had oral and skin lesions, and (9.6%) patients manifested lesions in the other mucous membranes such as esophagus, and vagina without any skin lesions. In the remaining (19.2%) patients, skin and other mucous membranes except oral mucosa were involved.

Ann SS [28] reported in his study that in 28 (51.9 %) patients, onset was on skin, 23 had it on mucosa and both skin and mucosa in 3 patients. Anterior chest wall (18.5 %) was the common site of onset on skin and on scalp in 4 patients.

In the present study, the pemphigus treatments of the study patients were tabulated in Table 3.

Most of the pemphigus patients (60.3%) were treated by a combination of corticosteroid and azathioprine. Out of them 40 (58.8%) PV patients and (1.5%) PF patients were thus treated, then 12 (17.6%) patients were treated only by corticosteroid, distributed as follows: (7.4%) of PV patients, (8.8%) of PF patients and (1.5%) of pemphigus vegetans patients.

Seven (10.3%) of the PV patients were treated by a combination of corticosteroid + Azathioprine + dapsone, followed by (5.9%) PV patients were treated by a combination of corticosteroid + azathioprine + mycophenolate mofetil and also, (5.9%) PV patients treated by combination of corticosteroid + dapsone. There was a statistical relation between treatment and types of pemphigus ($p = 0.000$).

Baican et al [29] reported in their study, which was conducted in Romania, that out of 108 patients, only 28.7 % received corticosteroids alone and the majority of the cases were given corticosteroids along with Azathioprine, Cyclophosphamide, Methotrexate or intravenous immunoglobulins.

Additionally, we observed in our study after 2 months complete healing of lesions (73.5%) of all patients were distributed as follows: (64.7%) among PV patients, (7.3%) among PF patients and (1.5%) of pemphigus vegetans patients.

Bystryn et al [30] mentioned that the approach to the treatment of PV and PF is similar. Treatment is aimed at achieving a rapid and sustained remission with the resolution of cutaneous lesions and elimination of circulating

antibodies, with the eventual goal of maintenance with low-dose therapy, or ideally tapering off all treatment.

The management approach of PV may be considered in 2 general phases: remission induction and remission maintenance. In moderate to severe cases, systemic corticosteroids with adjuvant immunosuppressants are the primary therapy [31].

Clinical response may be observed within days of starting treatment, although cessation of new blister formation may take a few weeks, with complete healing occurring at 6–8 weeks [32].

Conclusion

Pemphigus presents with superficial erosions in the skin and oral mucosa. The study revealed that pemphigus vulgaris is the most common type of pemphigus. Females were predominant and the patients of the age group ≤ 50 years and the age group > 50 years were to some extent equal. The most common site of involvement of pemphigus was in mucocutaneous. Most of the patients were treated by a combination of corticosteroid and azathioprine. Further studies are needed to determine the incidence and prevalence of this disease in Aden governorate and the surrounding areas.

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