

Epidemiology of Pemphigus in Fez, Morocco: A 10 year Prospective Across Study

Ghita Senhaji^{1*}
Hanane Bay Bay¹
Ouiame El Jouari¹
Amina Lamouaffaq¹
Zakia Douhi¹
Sara Elloudi¹
Fatima Zahra Mernissi¹

¹Department of Dermatology, University Hospital Hassan II, Fez, Morocco.

Abstract

Introduction: Pemphigus is a group of rare, potentially life-threatening, autoimmune blistering diseases involving the skin and mucosa. It results from autoimmune response directed against desmoglein (Dgl) 3 and/or Dgl 1 leading to loss of cell-cell adhesion, and thus to intra-epidermal blister formation. This group comprises pemphigus vulgaris, which is the most common form, and its variant pemphigus vegetans, superficial pemphigus (pemphigus foliaceus and pemphigus erythematosus), paraneoplastic pemphigus, and IgA pemphigus. It had shown to have an uneven geographical distribution. However, owing to the relative rarity of this disease, only a limited number of large epidemiological studies are available.

Objective: To determine and evaluate the epidemiological and clinical features of Pemphigus in the Moroccan city of Fez, as well as to analyze its incidence.

Materials and methods: We performed a unicentric prospective study including all patients with newly registered Pemphigus attending the dermatology department of Fez in Morocco during the period from January 2008 to June 2018 (over 10 years). Patient inclusion criteria comprised a diagnosis of pemphigus based on the typical clinical features of the disease and histopathologic sometimes confirmed by direct immunofluorescence (DIF) findings based on revised diagnostic criteria. Indirect immunofluorescence (IIF) was performed in a number of patients.

Results: 150 cases of pemphigus were included with a mean age of 50 years and a female to male ratio of 1.77. There were a predominance of deep forms of pemphigus with pemphigus vulgaris being the most frequent subtype. 27% of all patients presented with comorbidities like hypertension and neurological disorders who were the most frequent ones. Initial presentation included both skin and mucosal involvement in 63% of the patients, whereas 30% of them had exclusive cutaneous lesions and only 7% of them had exclusive mucosal involvement. The diagnosis for all the patients was confirmed by histologic examination, with DIF test performed in 88% of cases, and proved positive for intercellular immunoglobulin G deposits in 81% of cases.

Conclusion: We present a prospective study that evaluates the epidemiology of pemphigus in the Moroccan population of Fez. The results of our study demonstrate a high incidence of pemphigus vulgaris in Fez. However, future studies are needed to provide more precise insights into the epidemiology of pemphigus in Morocco.

Article Information

Article Type: Research
Article Number: JCCRT120
Received Date: 01 May 2019
Accepted Date: 18 May 2019
Published Date: 21 May 2019

***Corresponding author:** Senhaji Ghita, Doctor, Department of Dermatology, University hospital Hassan II, Fez, Morocco. Tel : +212 600075857, Email : [ghitasenhaji88\(at\)gmail.com](mailto:ghitasenhaji88(at)gmail.com)

Citation: Senhaji G, Bay HB, Jouari OE, Lamouaffaq A, Douhi Z, et al (2019) Epidemiology of Pemphigus in Fez, Morocco: A 10 year Prospective Across Study. J Clin Case Rep Trials. Vol: 2, Issu: 1 (08-14).

Copyright: © 2019 Senhaji G, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Keywords: Pemphigus, Autoimmune Blistering Disease, Pemphigus Vulgaris, Epidemiology, Prospective Study, Clinical Features.

Introduction

Pemphigus is a group of rare, potentially life-threatening, autoimmune blistering diseases involving the skin and mucosa [1]. This group comprises pemphigus vulgaris (PV), which is the most common form, and its variant pemphigus vegetans, superficial pemphigus (pemphigus foliaceus [PF] and pemphigus erythematosus [PE]), paraneoplastic pemphigus (PNP), and IgA pemphigus [2]. The diseases result from autoimmune response directed against desmoglein (Dgl) 3 and/or Dgl 1 leading to loss of cell–cell adhesion [3], and thus to intra-epidermal blister formation, which is the clinical hallmark of the disease [1]. Furthermore, both genetic and environmental factors have been associated with the occurrence of auto-immune pemphigus [4]. Owing to the relative rarity of the disease, only a limited number of large epidemiological studies are available [1]. In fact, the incidence of pemphigus varies by geographic area and ethnic groups [5], and it generally ranges from 0.5 to 16.2/1,000,000 per year [2]. We performed a unicentric epidemiological prospective study in our department. The purpose of this study was to determine and evaluate the epidemiological and clinical features of Pemphigus in Fez, as well as to analyze its incidence.

Materials and Methods

We conducted a unicentric prospective study including all patients with newly registered Pemphigus attending the dermatology department during the period from January 2008 to June 2018 (over 10 years). The study was carried out at the dermatology department of the University Hospital Hassan II in Fez, Morocco. Patient inclusion criteria for the prospective analysis comprised a diagnosis of pemphigus based on the typical clinical features of the disease, confirmed by histopathologic and sometimes direct immunofluorescence (DIF) findings based on revised diagnostic criteria. Indirect immunofluorescence (IIF) was performed in a number of patients. In patients with mucosal lesions only, a biopsy was obtained from intraoral lesions and DIF was performed on perilesional normal mucosa. The patients were classified in deep pemphigus (vulgaris or vegetative) and superficial (seborrhic, foliaceus or herpetiform) according to the clinical aspect of the cutaneous lesions and the location of the bullous detachment on histological examination for instance, supra basal acantholysis for deep pemphigus and subcorneal for superficial pemphigus. Tzanck smear was performed in all patients. Each patient was subjected to a detailed review of clinical history, similar familial diseases, drug intake, other autoimmune diseases and a complete physical examination. Various clinical parameters were studied, including age, sex, age at onset of the disease, duration of the disease, anatomic sites affected at the onset of disease and subsequently, the percentage of skin involvement.

The comorbidities were documented prior to initiation of prednisone therapy, therefore excluding the possibility

of adverse effects due to glucocorticosteroids. Data were compiled as Excel files and analyzed using the statistical software package SPSS 17.0.A P-value of < 0.05 was considered to indicate statistical significance. The study was approved by the Ethics Committee of the Medical University of Fez in Morocco.

Results

In the period studied, a total of 150 cases of pemphigus were included, which represent almost 60 % of total bullous dermatitis, with a mean age of 50 ± 14.7 years. Ninety-six patients were female (64%), and 54 were male (36%), with a female to male ratio of 1.77. 80 % of the patients presented with deep forms of pemphigus, while only 20 % had superficial forms. In fact, there were 104 cases of pemphigus vulgaris, 10 cases of pemphigus vegetans, 23 cases of seborrhic pemphigus and 7 of pemphigus foliaceus. Other types of pemphigus like IgA pemphigus, pemphigus herpetiformis, or paraneoplastic, bullous pemphigus were diagnosed only in 6 cases (Figure 1).

Females constituted the majority of patients in PV and PF groups. Moreover, residents of urban areas constituted the majority of pemphigus patients.

The majority of patients were in their fourth and fifth decades (83 patients, 55%), whereas 34 cases (23%) occurred in individuals older than 60 years, and 33 cases (22%) in patients less than 40 years of age. The mean age at the onset of the disease was 49.4 ± 15 years (range, 16– 80 years) for women and 52.1 ± 14.1 years (range, 24–92 years) for men. Although men were approximately 3 years older, the difference was not statistically significant (Figure 2).

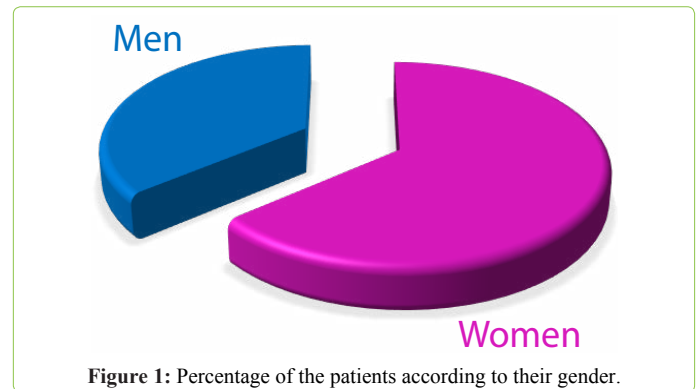


Figure 1: Percentage of the patients according to their gender.

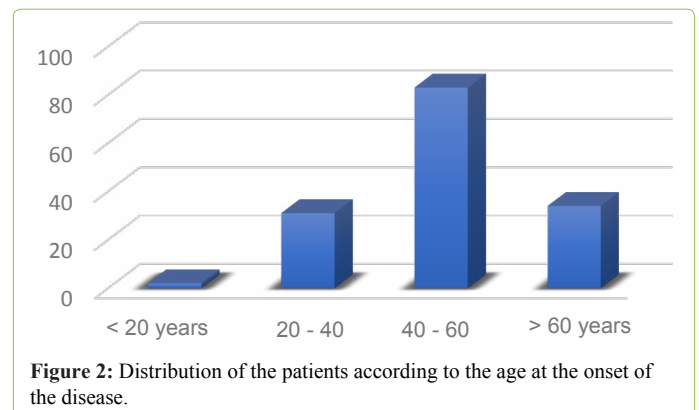


Figure 2: Distribution of the patients according to the age at the onset of the disease.

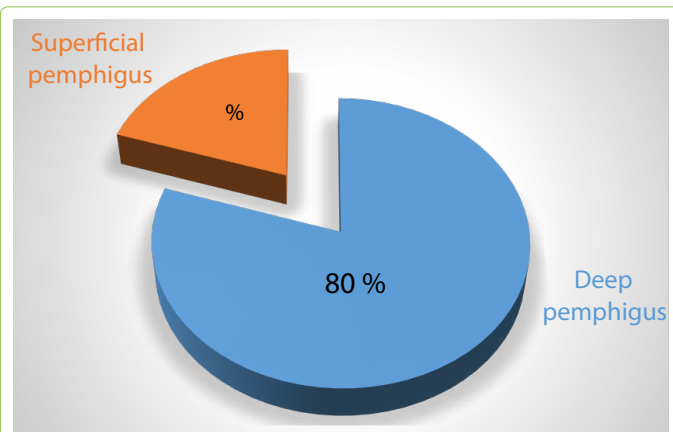


Figure 3: Percentage of pemphigus patients according to the clinical form.

Patients had been seen at two weeks to three years with median was 8 months after the onset of symptoms. None of the patients hadn't taken drugs in the weeks preceding the onset of pemphigus and none of them had a family history of pemphigus.

Overall, 40 patients (27% of the 150 pemphigus patients) presented with other comorbidities. The most common were hypertension (n = 6; 4%), neurological disorders (n = 5; 3%), diabetes (n = 4; 2.6%) and tuberculosis (n = 4; 2.6%), but a sizeable diseases with an autoimmune background were also noted (n = 6; 4%). These diseases included thyroid disease (n = 3; 2%), dermatomyositis (n = 1; 0.6%), rheumatoid arthritis (n = 1; 0.6%) and vitiligo (n = 1; 0.6%) (Figure 3).

At presentation to our dermatology department, both skin and mucosal involvement was observed in 95 patients (63%). Cutaneous lesions without the involvement of the mucous membranes were seen in 45 patients (30%), and exclusive mucosal involvement was present in 10 patients (7%). None of the patients presented initially with generalized disease. The major functional sign was pruritus, and was noted in 50 cases (33%). The Nikolsky sign was positive in 101 of patients (67%).

Lesions on the skin were most frequently documented on the thorax or limbs (each: n = 114 patients, 76%). The disease presented in other parts of the body (face) in 71 cases (47%). All patients with mucosal lesions only were followed up for at least 6 months, and none developed cutaneous lesions similar to pemphigus. Mucosal lesions in the oral cavity were seen in 97 patients (65%), independently of the severity of disease. Mucosal membranes other than those of the oral cavity were affected in 60 (40%) patients in genital membranes, and in 19 cases (13%) in conjunctival site. Phanerial involvement was seen in 90 patients, most frequently with scalp lesions, whereas 43 patients had a nail changes. All these lesions were dominated by erosions, seen in 138 cases (92%), other less common lesions included blisters, pustules and vesicles.

The diagnosis for all 150 patients was confirmed by histologic examination, which showed suprabasal acantholysis in deep forms of pemphigus, and sub epidermal blisters in superficial forms. DIF test was performed in

132 patients (88%), and proved positive for intercellular immunoglobulin G deposits in 81% of cases. IIF was performed in 17 patients; none of them had a negative result.

Discussion

Pemphigus is a disease showing an uneven geographical distribution [6]. It is currently thought that it is much more frequent in midlatitude, subtropical and tropical climates [7]. Furthermore, Mediterranean countries seem to occupy a particular place in its epidemiology [7]. However, in Morocco, the incidence of pemphigus has not been estimated yet [8]. Nevertheless, the high number of patients included in the previous studies reported in Morocco suggests a relatively high incidence.

There was a female predominance in our study, which was in accordance with earlier reports coming from Iran [9], Midi-Pyrénées [4], Poland [3], Marrakesh [10], Taiwan [5], Serbia [2], Sofia [7], Vojvodina [11], Turkey [12], Macedonia [13] and Casablanca [8], where the female to male sex ratios were respectively 1.59, 1.17, 2.88, 3.2, 1.33, 1.44, 1.11, 1.55, 1.35, 1.33 and 1.8. However, other studies reported an equal sex predisposition in patients from USA [14]. Nevertheless, a male predominance is less common and has only been reported in few studies like in Spain were male to female ratio was of 1.22 [15], and Saudi Arabia: 2.2 [16]. Previous studies on the triggering factors in pemphigus have suggested that the traditional cosmetics used by women may favor this disease, in addition to hormonal and genetic factors [8], thus explaining this female predominance in the majority of studies reports.

The majority of our patients were in their fourth and fifth decades, with a mean age of 50 years. These results were comparable to most reports from other countries including Iran [9], Taiwan [5], Sofia [7], Vojvodina [11] and Macedonia [13]. Only few reports noted a predominance of younger pemphigus like studies from Marrakech [10], Turkey [12] and Casablanca [8]. The mean age of onset of pemphigus was higher in men than in women in our study (52.1 in men versus 49.4 in women). This was also reported in another study from Macedonia where the age of onset were of 54 years for men and 52 years for women [13]. However, other studies from Sofia [7] and Vjovodina [11] reported the opposite with a higher age of onset in women (64.20 versus 59.19) [7], and (56.7 vs 54.6) [11]. While all these studies had shown no statistical significant difference on the age of onset. Only one report from Tunisia showed a statistically significant difference, with men being almost 20 years older than women [17].

The incidence of pemphigus was significantly higher among residents of urban areas than those of rural areas, which was also seen in studies from Macedonia [13]. However, in the studies conducted in Marrakech [10] and Poland [3], in contrast to our findings, the incidence of pemphigus was higher in rural than urban areas.

Over 27% of our patients presented with comorbidities before the initiation of treatment. The most common in our series were hypertension, neurological disorders, diabetes and autoimmune diseases. Another study from Vjovodina

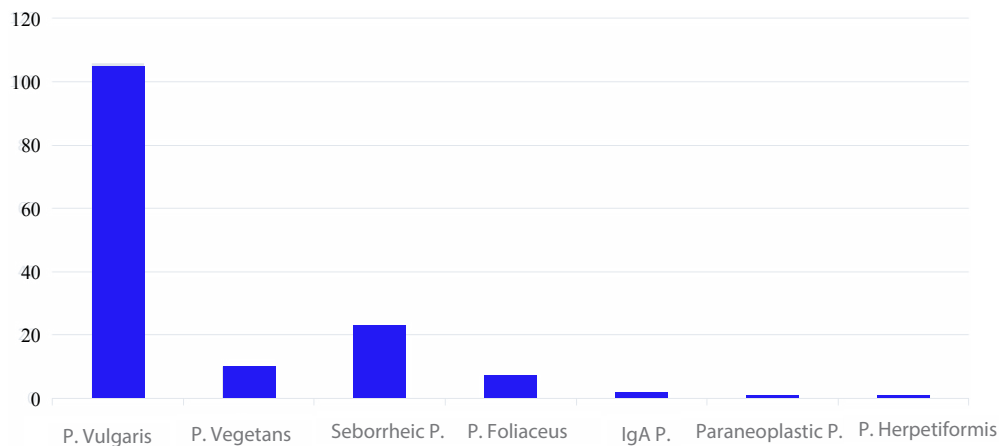


Figure 4: Distribution of the clinical phenotypes of pemphigus in our study.

have shown little similarities, with hypertension and diabetes mellitus being the most associated comorbidities, present in 17.6%, and 9.8% of cases respectively [11]. However, a study report from Turkey have shown a significant association with autoimmune diseases and psychiatric disorders such as depression and obsessive-compulsive disorder [12].

Pemphigus vulgaris is the most common clinical variant of the disease found in our study. This is in perfect concordance with data coming from most European and Mediterranean studies, as in Iran [6], Midi-Pyrénées [4], Serbia [2], Sofia [7], Vjvodina [11], Turkey [12] and Macedonia [13]. On the other hand, there were a predominance of other types of pemphigus reported in the literature, like pemphigus erythematosus in Casablanca [8] and foliaceus pemphigus in Marrakesh [10], which cities are in the south and middle of Morocco in contrast to our city which is in the north of Morocco, and Tunisia [17]. In 30% of cases with pemphigus, we detected only skin lesions, while 63% of all our patients presented with skin and mucous membrane lesions. Studies that show similarities on location of lesions, with predominance of muco-cutaneous lesions, are conducted in Sofia [7] and Vjvodina [11]. Other reports showed other distribution of clinical lesions with a majority of patients having exclusive cutaneous lesions like in Midi-Pyrénées (where 46% having exclusive cutaneous involvement and only 37% having both cutaneous and mucous membranes) [4], and Marrakech (62% of exclusive cutaneous lesions and only 8% of muco-cutaneous lesions) [10], and the majority of them having initial mucosal lesions in the study conducted in Turkey [12]. Lesions on the skin were most frequently documented on the thorax or limbs (76% each) in our study. A similar finding was seen in a study report from Iran were 61.4% of patients presented with lesions on the thorax [9] (Figure 4).

Conclusion

Pemphigus is a serious disease requiring a heavy and chronic management. We present a prospective study that evaluates the epidemiology of pemphigus in the Moroccan population of Fez. The results of our study demonstrate a high incidence of pemphigus vulgaris in Fez. Additionally, although minor differences were noted, the results of this

study are in relatively good agreement with the literature. However, future studies are needed to provide more precise insights into the epidemiology of pemphigus in Morocco.

References

- Baum S, Astman N, Berco E, Solomon M, Trau H, et al (2016) Epidemiological data of 290 pemphigus vulgaris patients: a 29-year retrospective study. *Eur J Dermatol* 26: 382-387.
- Milinković MV, Janković S, Medenica L, Nikolić M, Reljić V, et al (2016) Incidence of autoimmune bullous diseases in Serbia: a 20-year retrospective study. *J Dtsch Dermatol Ges* 14: 995-1005.
- Serwin AB, Koper M, Flisiak I (2018) Incidence of pemphigus vulgaris and pemphigus foliaceus in North-East Poland (Podlaskie Province) – a 15-year (2001–2015) bicentric retrospective study. *Int J Dermatol* 57: 933-937.
- Thomas M, Paul C, Berard E, Fortenfant F, Mazereeuw-Hautier J et al (2010). Incidence of Auto-Immune Pemphigus in the Midi-Pyrénées Region in 2002–2006. *Dermatology* 220: 97-102.
- Huang YH, Kuo CF, Chen YH, Yang YW (2012) Incidence, Mortality, and Causes of Death of Patients with Pemphigus in Taiwan: A Nationwide Population-Based Study. *J Invest Dermatol* 132: 92-97.
- Salmanpour R, Shahkar H, Namazi MR, Rahman-Shenas MR (2006) Epidemiology of pemphigus in south-western Iran: A 10-year retrospective study (1991–2000). *Int J Dermatol* 45: 103-105.
- Tsankov N, Vassileva S, Kamarashev J, Kazandjieva J, Kuzeva V (2000) Epidemiology of pemphigus in Sofia, Bulgaria. A 16-year retrospective study (1980–1995). *Int J Dermatol* 39: 104-108.
- Benchikhi H, Ghafour S, Disky A, Bichra L, Nejjam F, et al (2008) Pemphigus: analysis of 262 cases. *Int J Dermatol* 47: 973-975.
- Esmaili N, Chams-Davatchi C, Valikhani M, Daneshpazhooch M, Balighi K, et al (2007) Pemphigus vulgaris in Iran: a clinical study of 140 cases. *Int J Dermatol* 46: 1166-1170.
- Amal S, Hocar O, Zidane W, Laissaoui K, Squalli DH (2005) Epidemiologic study of pemphigus in Marrakech: 134 cases. *Ann Dermatol Venereol* 132: 1008-1009.
- Golusin Z, Poljacki M, Jovanović M, Ethuran V, Stojanović S, et al (2005) Some epidemiological features of pemphigus chronicus in South Vojvodina: A 12-year retrospective study. *Int J Dermatol* 44: 792-793.
- Uzun S, Durdu M, Akman A, Gunasti S, Uslular C, et al (2006) Pemphigus in the Mediterranean region of Turkey: A study of 148 cases. *Int J Dermatol* 45: 523-538.
- Vlckova-Laskoska MT, Laskoski DS, Kamberova S, Caca-Biljanovska N, Volckova N (2007) Epidemiology of pemphigus in Macedonia: A 15-year retrospective study (1990–2004). *Int J Dermatol* 46: 253-258.

14. Woldegiorgis S, Swerlick RA (2001) Pemphigus in the south eastern United States. *South Med J* 94: 694-698.
15. Alcaide-Martin AJ, Gallardo-Perez MA, Castillo-Muñoz R, et al. (2010) Epidemiologic study of 20 cases of pemphigus at Hospital Clínico Universitario Virgen de la Victoria de Málaga. Spain. *Actas Dermosifiliogr* 101: 524-533.
16. Tallab T, Joharji H, Bahamdan K, Karkashan E, Mourad M, et al (2001) The incidence of pemphigus in the southern region of Saudi Arabia. *Int J Dermatol* 40: 570-557.
17. Bastuji-Garin S, Souissi R, Blum L, Turki H, Nouria R et al. (1995) Comparative epidemiology of pemphigus in Tunisia and France: unusual incidence of pemphigus foliaceus in young Tunisian women. *J Invest Dermatol* 104: 302-305