

Epidemiology of Pemphigus in Tehran, Iran: A 20-Year Retrospective Study

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Abstract

Background and aims. Pemphigus is a chronic autoimmune and vesiculobollos disease that can affect skin and different mucous membrane surfaces. Primary manifestations occur in oral cavity in almost 60% of cases. The purpose of the present study was to evaluate the epidemiology of pemphigus in Tehran, Iran in a 20-year period.

Materials and methods. A retrospective study was conducted on the records of 1560 patients diagnosed with different types of pemphigus in Razi Hospital of Dermatology in Tehran from March 1985 to March 2005. A questionnaire was prepared to collect information regarding age, sex, bedridden duration, pemphigus subtype, sites of involvement, recurrence and mortality rate. Data was analyzed using chi-square test with significant level of $P < 0.05$.

Results. There was a female predominance with a male to female ratio of 1:1.53. In nearly half of the patients, only the oral mucous membranes were affected. One hundred and fifty had only skin lesions and 261 cases had both skin and oral mucosal lesions. Involvement of esophageal and vaginal mucous membranes without skin lesions was observed in 150 patients and 298 cases had esophageal and vaginal mucosal involvement as well as skin lesions. Pemphigus vulgaris was the most common type, with the mean age of 44.6 years. Oral mucous membrane was the most frequent location where pemphigus vulgaris was observed. 1265 patients recovered which 52.2% of them had only oral lesions. Average of bedridden duration was 2.9 months. The highest recurrence rate was seen in patients with skin lesions exclusively. There was a significant difference between recurrences of lesions and location of involvement ($P < 0.05$). Thirty six patients had died from of the disease.

Conclusion. The mean age of the disease onset in the present study was found to be a decade earlier than the other parts of the world. Recurrence and mortality rates were lower in patients with only oral lesions and their prognosis was better.

Key words: Epidemiology, Iran, pemphigus, vesiculobullous.

Introduction

Pemphigus is a chronic bullous disease with autoimmune nature,¹⁻³ that can affect skin and mucous membranes.⁴⁻⁶ Pathogenesis of pemphigus is mediated by autoantibodies that react with the desmosomal glycoproteins present on the cell surfaces of the keratinocytes.⁶⁻⁹ Prevalence of oral lesions in different studies varies from 50%^{1,6} to 90%.⁵ Oral manifestations are the first clinical signs in 60% of cases.^{10,11} Severity and subtype of pemphigus can determine its prognosis.^{2,5} Morbidity and mortality rates have been decreased to 5-10% following corticosteroid therapy.^{1,2,6,8} The average prevalence of pemphigus is 0.5-3.1 in 100,000 individuals; and pemphigus vulgaris is the most common subtype.^{1-3,5,9,12} Hietanen & Salo¹² performed an epidemiological study in England and found that the prevalence rate of the disease was 0.76%, the male to female ratio was 0.9:1 and the average age of the patients was 57 years. They reported oral manifestations as the first sign of disease in 78% of cases. Morbidity and mortality rates were reported 6.8% and average bedridden duration in hospital was 16.4 days. In another epidemiological study, the male-to-female ratio was found to be 1:1.¹³ The author also reported that 30% of the patients showed only mucosal lesions and 70% had mucosal and skin lesions. In one study the prevalence of pemphigus in Bulgaria was reported to be 0.047% with 51% of patients being older than 20 years.⁹ In that study, pemphigus vulgaris was the most common clinical subtype followed by pemphigus erythematosus. Several investigations have been conducted on pemphigus pathogenesis and its clinical course in many other countries.^{4,5,9,12} Pemphigus is still a life-threatening disease despite recent improvements in its treatment. Therefore it is critically important to diagnose pemphigus before the expression of skin manifestations. The aim of the present study was to retrospectively evaluate the findings derived from the records of the pemphigus patients with regards to the demographic, clinical, and epidemiological characteristics of this disease in a 20-year period.

Materials and Methods

The records of 1560 patients diagnosed with pemphigus in Pemphigus Department of Razi Hospital of Dermatology, Tehran, Iran were reviewed in a descriptive and retrospective study. Documented information of bedridden patients during the period of 1985 to 2005 was extracted. These included sex, age, bedridden duration, pemphigus subtype, sites of involvement, recurrence and mortality rates. Patients were divided into nine groups according to the age: group 1, younger than 12 years old; group 2, 12-20 years old; group 3, 21-30 years old; group 4, 31-40 years old; group 5, 41-50 years old; group 6, 51-60 years old; group 7, 61-70 years old; group 8, 71-80 years old; and group 9, 81-90 years old. The following types of pemphigus were considered in this research: (a) Pemphigus vulgaris, (b) pemphigus foliaceus, and (c) pemphigus vegetans. No case of pemphigus erythematosus was detected. At the onset of the disease, the primary site of involvement was as follows:

- Oral mucosa only
- Skin surfaces only
- Skin and oral mucosal involvement
- Other mucous membranes such as esophagus and vaginal mucosa without oral mucosa and skin involvement
- Mucous membrane and skin involvement except oral mucosa

Data was analyzed using SPSS software. The chi-square test was used to compare final outcomes. Confidence rate higher than 95% was considered as significant ($P < 0.05$).

Results

From 1560 patients with pemphigus, 615 (39.4%) were male and 945 (60.6%) were female with a male to female ratio of 1:1.53.

In 701 (44.9%) patients, pemphigus affected oral mucosa exclusively. 150 (9.6%) patients had only skin lesions, 261 (16.7%) patients had oral and skin lesions, and 150 (9.6%) patients manifested lesions in the other mucous membranes such as esophagus, and vagina without any skin lesions. In the remaining 298 (19.2%) patients, skin and other mucous membranes except oral mucosa were involved (Table 1).

Pemphigus vulgaris was the most common clinical subtype, identified in 1422 patients (91.15%) followed by pemphigus foliaceus in 100 patients (6.4%), pemphigus vegetans in 37 patients (2.3%), and pemphigus vulgaris accompanied by pemphigus vegetans in one patient (0.06%).

12 Patients were younger than 12 years old and the majority of the patients (31.6%) were in the fifth decade of their lives (Table 1). 48.9% of male patients and 42.3% of female patients had only oral lesions. The distribution of the patients according to the involved area and sex is given in Table 2.

From 701 patients with oral involvement, 668 (95.3%) had pemphigus vulgaris with 43.1% of them being males and 56.9% females. In addition, 18 (2.6%) had pemphigus foliaceus and 15 (2.1%) had pemphigus vegetans (Table 3).

Among 1422 patients diagnosed with pemphigus vulgaris, 47% had only oral involvement. Oral lesions also existed in 18% of the 100 pemphigus foliaceus patients and in 2.5% of the 37 patients with pemphigus vegetans.

Table 1. Distribution of the patients according to the age group and location of involvement

Location Age group	Oral mucosa	Skin	Skin plus oral mucosa	Other mucous membranes	Other mucosa plus skin	Total
	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)
1	5 (41.7)	2 (16.7)	1 (8.3)	1 (8.3)	3 (25)	12 (100)
2	54 (81.8)	3 (4.5)	1 (1.5)	7 (10.6)	1 (1.6)	66 (100)
3	135 (69.6)	12 (6.2)	7 (3.6)	22 (11.3)	18 (9.3)	194 (100)
4	168 (57.7)	12 (4.1)	30 (10.3)	42 (14.4)	39 (13.5)	291 (100)
5	226 (45.8)	40 (8.1)	79 (16)	48 (9.7)	100 (20.4)	493 (100)
6	88 (29.7)	33 (18.1)	78 (26.4)	14 (4.7)	83 (21.1)	296 (100)
7	19 (14.5)	31 (23.7)	35 (26.7)	14 (10.7)	32 (24.4)	131 (100)
8	5 (6.8)	15 (20.3)	30 (40.5)	2 (2.7)	22 (29.7)	74 (100)
9	1 (33.3)	2 (66.7)	0 (0)	0 (0)	0 (0)	3 (100)
Total	701 (44.9)	150 (9.6)	261 (16.7)	150 (9.6)	298 (19.2)	1560 (100)

Table 2. Distribution of the patients according to the involved area and sex

Location	Sex	Men	Women	All patients
		Number (%)	Number (%)	Number (%)
Oral mucosa		301 (48.9)	400 (42.3)	701 (44.9)
Skin		50 (8.1)	100 (10.6)	150 (9.6)
Oral mucosa plus skin		100 (16.3)	161 (17)	261 (16.7)
Other mucous membranes		69 (11.2)	81 (8.6)	150 (9.6)
Other mucous membranes plus skin		95 (15.4)	203 (21.5)	298 (19.2)
Total number		615 (100)	945 (100)	1560 (100)

Table 3. Distribution of the patients according to the type of pemphigus and location of involvement in males and females

Location Type of pemphigus	Oral mucosa		Skin		Oral mucosa plus skin		Other mucous membranes		Other mucous membranes plus skin	
	Men (%)	Women (%)	Men (%)	Women (%)	Men (%)	Women (%)	Men (%)	Women (%)	Men (%)	Women (%)
Pemphigus vulgaris	288 (43.1)	380 (56.9)	46 (33.6)	91 (66.4)	86 (37.1)	146 (62.9)	65 (46.8)	74 (53.2)	74 (30.1)	172 (69.9)
Pemphigus foliaceus	5 (27.8)	13 (72.2)	1 (9.1)	10 (90.9)	12 (46.2)	14 (53.8)	3 (42.9)	4 (57.1)	15 (39.5)	23 (60.5)
Pemphigus vegetans	8 (53.3)	7 (47.7)	1 (50)	1 (50)	1 (50)	1 (50)	1 (25)	3 (75)	6 (42.8)	8 (57.2)
Total	301	400	50	100	100	161	69	81	95	203

Complete clinical remission was observed in 74.2% of the patients with oral mucosal involvement. 175 individuals (25%) had partial recovery, and 6 Patients (0.8%) did not

have any improvement. The association between locations of involvement and recovery rates is shown in Table 4.

Table 4. Distribution of the patients according to remission of lesions and location of involvement

Location Healing	Oral mucosa	Skin	Oral mucosa plus skin	Other mucous membranes	Other mucous membranes plus skin
	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)
Complete remission	520 (74.2)	47 (31.3)	72 (27.5)	103 (68.7)	101 (33.9)
Partial remission	175 (25)	79 (52.7)	157 (60.2)	44 (29.3)	157 (52.7)
No remission	6 (0.8)	24 (16)	32 (12.3)	3 (2)	40 (13.4)
Total	701 (100)	150 (100)	261 (100)	150 (100)	298 (100)

Average of bedridden duration was 2.9 months in all groups with the range of 0.2-8 months. Patients with manifestations in other mucous membranes except oral mucosa had minimal average of bedridden duration (2.08 months). The longest period was seen in patients with skin lesions (average of 3.89 months).

Recurrence of lesions was observed in the records of 47 patients with only oral involvement (6.7%), 62 patients with only skin lesions (41.3%), 105 patients with skin and oral involvements (40.2%), and 8 patients (5.3%) with other mucous membranes involvement except oral mucosa. In addition, in 91 (30.5%) patients with other mucosal involvements accompanied by skin lesions, recurrence was observed. There were significant statistical differences between various sites of pemphigus involvement and recurrence rates.

From 1560 patients, 36 (2.3%) had died; the most common cause of death was septicemia (87%). Among the deceased patients, 8.3% suffered from oral lesions only, 13.8% skin lesions only, 30.6% oral and skin lesions, 5.6% other mucous membranes involvement, and 41.7% from other mucous membranes involvement accompanied by skin lesions.

Discussion

The majority of the patients in the present study were 40-50 years old (with mean of 44.6 years). A similar observation regarding age has been reported from other studies in Khuzestan⁶ (42.5 years), Tehran¹⁰ (42 years), and Kerman¹⁴ (46 years). It is important to mention that the mean age of patients with pemphigus in the other parts of the world is higher than the present study (Hietanen & Salo¹², 57 years; Qasem et al¹⁵, 63 years). Therefore, an earlier age of onset has been observed in Iran and the reason is still unknown. Many researchers considered that there is a fairly strong genetic background to pemphigus vulgaris.^{6,10,14}

At the present study, most of the patients in age groups of 1-6 had only oral lesions. On the other hand, in groups 7 and 8, pemphigus affected both oral mucous membranes and skin. In the remaining patients in group 9, skin was most the affected site. It could be concluded that as age increases, more skin

lesions are observed in pemphigus. This may be due to the late diagnosis of disease when oral signs disappear and skin signs persist.¹⁶ Additional evaluation is required in this regard.

There was a female predominance with a male to female ratio of 1:1.53, with a statistically significant difference ($P = 0.03$). One explanation for the higher incidence of disease in females may be that women are more likely to seek medical attention. This finding is in accordance with the results of Hietanen & Salo¹² and Mignogna et al¹⁷ in which this ratio was reported 0.9:1 and 1:2, respectively. In other studies, an equal ratio was reported; however, they stated that the rate of females was higher in the patients older than 79 years.^{11,13}

In the present study, pemphigus vulgaris was the most observed clinical variant (91.15%). This finding was in line with the results of another long-term study.¹⁸ The average bedridden duration was 2.9 months. The longest hospitalization period was recorded in patients with only skin lesions (3.89 months). In other studies, bedridden duration of pemphigus patients was reported to be 6.4 months and 4.8 months.^{12,15} The differences in treatment possibilities in various countries may be the main cause of different bedridden durations.

In the present study, there was a 20.1% mean recurrence rate with the highest rate seen in patients with skin manifestation (41.3%). It seems impossible to detect recurrent lesions exactly due to limitations in the study period, which could be the reason why there are not many reports of recurrences in other studies. The highest mortality rate in this study was found in patients with skin and other mucous membranes involvement (41.7%), and the least was seen in patients with only mucous membrane lesions (5.6%). The overall mortality rate in the present study was 2.3%. This figure was reported to be 15%, 0%, and 6.8% in other studies.^{11,15,19} In fact, the mortality rate could be higher, since data was recorded during bedridden time in hospital and not afterwards. Therefore, the association between mortality rate and location of involvement can not be significant due to the bias mentioned ($P > 0.05$). Similar observations have been made by Herbst & Bystryń²⁰ that stated mortality rate was

higher in patients with skin and mucosal involvement. The authors emphasized that mortality rate was lower in patients with mucosal lesions compared to those with skin lesions. One explanation for the lower mortality rate in patients with mucosal lesions may be the early diagnosis of these types of pemphigus and higher efficacy of drugs prescribed at this stage with lower doses and limited complications.²¹

Conclusion

Oral involvement in majority of pemphigus cases occurs prior to skin lesions. Recurrence

and mortality rates are lower in patients with only oral lesions and they have a better prognosis. Therefore, early diagnosis and treatment of oral isolated pemphigus is of great importance for a dentist since it can inhibit progressive course of disease, decrease recurrences as well as mortality rates, and improve prognosis.

Acknowledgements

The authors would like to thank the staffs at Razi Hospital of Dermatology for their kind cooperation in data collection.

References

- Weinberg MA, Insler MS, Campen RB. Mucocutaneous features of autoimmune blistering diseases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1997;84:517-34.
- Elpern D, Foong H, Williams T. A man with recurrent widespread blisters. *J Am Acad Dermatol* 2004;6:974-6.
- Scully C, Challacombe SJ. Pemphigus vulgaris: Update on etiopathogenesis, oral manifestations and management. *Crit Rev Oral Biol Med* 2002;13:397-408.
- Kyriakis K, Tosca A, Lehou JA. Five year retrospective study on Pemphigus and pemphigoid. *Australas J Dermatol* 1989;30:33-36.
- Goon AT, Tan SH. Comparative study of Pemphigus vulgaris and Pemphigus foliaceus in Singapore. *Australas J Dermatol* 2001;42:172-5.
- Yaghibi R. Pemphigus in Khouzestan: Study of 111 cases. *Iran J Dermatol* 2000;3:50-55.
- Nekong AS, Foster CS. Eye and mouth involvement in autoimmune disease. *Clin Dermatol* 2001;19:742-49.
- Sirois D, Leigh JE, Sollecito TP. Oral Pemphigus vulgaris preceding cutaneous lesions: recognition and diagnosis. *J Am Dent Assoc* 2000;131:1156-60.
- Tsankow N, Snezhina V, Jivko K. Epidemiology of Pemphigus in Sofia, Bulgaria. A 16 year retrospective study (1980-1995). *Int J Dermatol* 2000;39:104-108.
- Shams CH, Davatchi M, Daneshpajoo M. Pemphigus: Analysis of 1206 cases. *Int J Dermatol* 2005;10:51-3.
- Ahmed AR, Moy R. Dead in Pemphigus. *J Am Acad Dermatol* 1982;7: 221-8.
- Hietanen J, Salo OP. Pemphigus: An epidemiological study of patients treated in Finnish hospital between 1969-1978. *Acta Derm* 1982;62:491-5.
- Tenner E, Koch PJ, Mahoney MG. Pemphigus and ocular involvement. *Euro J Dermatol* 2001;11:141-43.
- Shamsadini S, Fekri AR, Esfandiarpour I, Saryazdi S, Rahnama Z, Zandi S, et al. Determination of survival and hazard functions for pemphigus patients in Kerman, a southern province of Iran.. *Int J Dermatol* 2006; 45:668-71.
- Qasem A, Nonda A, Nazeeha M, Dvarak R. Pemphigus in Kuwait. *Int J Dermatol* 1999; 38:351.
- Harman KE, Seed PT, Gratine MJ. The severity of cutaneous and oral pemphigus is related to desmoglein 1 and 3 antibody levels. *Br J Dermatol* 2001;144:775-80.
- Mignogna MD, Lo Muzio L, Mignogna RE, Carbone R, Ruoppo E, Bucci E. Oral pemphigus: long term behaviour and clinical response to treatment with deflazacort in sixteen cases. *J Oral Pathol Med* 2000;29:145-52.
- Scully C, Paes De Almeida O, Porter SR, Gilkes JJ. Pemphigus Vulgaris: The manifestation and long-term management of 55 patients with oral lesions. *Br J Dermatol* 1999;140:84-9.
- Mikali G, Musumeci ML, Nasca MR. Epidemiologic analysis and clinical course of 84 consecutive cases of pemphigus in eastern Sicily. *Int J Dermatol* 1998;37:197-200.
- Herbst A, Bystry JC. Pattern of remission in pemphigus vulgaris. *J Am Acad Dermatol* 2000;42:422-7.
- Stanley JR. Therapy of pemphigus vulgaris. *Arch Dermatol* 1999;135:76-8.