Oral Involvement In Pemphigus Vulgaris : An Epidemiological Profile

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Abstract: Background and Objectives**:** Pemphigus vulgaris is a chronic autoimmune disease characterized by the formation of intraepithelial blisters in skin and mucosa. In majority of the patients the initial manifestations of pemphigus vulgaris appears in the oral mucosa followed at a later date by cutaneous lesions. Detection of the oral lesions can result in an earlier diagnosis and early treatment thereby decreasing the hospital stay of the patients. Objective: We review the clinical and epidemiological aspects of oral pemphigus vulgaris in patients attending tertiary care centre. Methodology**:** All patients diagnosed as having Pemphigus in the department of skin during last 6 years were included in the study and data analysed. Results : Out of 91 patients diagnosed as having pemphigus during the period of 6 years, pemphigus vulgaris was the most common type (91.2 %) . The mean age of onset was 45 years . Male to female ratio in the patients with pemphigus vulgaris was 1:1.5 . Oral lesions were found in 84 % of patients and it was the first manifestation in 66% of cases. Results & Conclusion**:** Pemphigus vulgaris was the most common condition seen, oral cavity being the initial site of disease presentation. [Asia A NJIRM 2015; 6(5):50-53]

Key Words: Pemphigus vulgaris , Oral cavity, Skin, Tertiary care centre

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Introduction: The word pemphigus comes from pemphix , a Greek word that means blister. Circulating IgG auto antibodies acting against desmoglein I and III cause intra epidermal blisters and acantholysis. Pemphigus vulgaris (PV) is the most common type accounting for approximately 80% of cases worldwide. Pemphigus vegetans, pemphigus foliacues (PF), pemphigus erythematosus, paraneoplastic pemphigus, drug-induced pemphigus, fogo selvagum or endemic pemphigus foliaceus, IgA pemphigus and pemphigus herpetiformis are the other uncommon subtypes of this disease. Pemphigus affects 0.1-0.5/ 100.000 patients per year.

Women are more likely to be affected than men and mean age of onset is approximately 4-6 decades . Juvenile cases have also been rarely reported. Although the certain pathogenesis of pemphigus vulgaris is not totally understood, high frequency of this disease in some races, especially Ashkenazi Jews and Mediterranean and South Asian origin, has been shown to be actually related to HLA-II genes. Additionally the genetic background, environmental factors, such as drugs, foods, chemicals, viruses, physical agents and stress, have been admitted as triggers of pemphigus . A wide variety of drugs such as thiol drugs (captopril, penicillamine, enalapril) and non-thiol drugs (cephalosporins, penicillins, piroxicam) are implicated as cause of Pemphigus Vulgaris [1] .

Histopathologically, there is characteristic formation of suprabasal clefts and appearance of the 'row of tombstone'. The immunofluorescent test is Positive direct immunofluorescence testing is the gold standard for diagnosis. Immunofluorescence testing shows IgG antibodies in more than 75% of the cases.

Pemphigus vulgaris presents with oral lesions in 50 % - 70% of patients [2] . Oral lesions precede skin lesions by months or be the only manifestations of the disease . Intact bullae are rare in mouth . More commonly patients have ill defined, irregularly shaped buccal or palatal erosions which are slow to heal. The erosions extend peripherally with shedding of the epithelium. Other mucosal surfaces may be involved including the conjunctiva, nasal mucosa, pharynx , oesophagus , urethra ,vulva and cervix. Oral lesions of Pemphigus vulgaris need to be differentiated from other dermatological diseases with possible manifestations on oral mucosa including dermatitis herpetiformis , pemphigus erythematosus , bening chronic familial pemphigus , systemic lupus erythematosus , acrodermatitis enteropathica , crohns disease , deficiencies of folic acid , vitamin B 12 etc [3] .

This observational non analytical study was undertaken in patients attending Department of Dermatology to evaluate the prevalence of oral lesions in new patients with Pemphigus vulgaris

and clinico epidemiological factors associated with it.

Material and Methods: The records of all newly diagnosed patients with pemphigus (from 2009 to 2015) were collected from outdoor and indoor units of Department of Skin , venereology and leprology . Age , sex, treatment history, symptoms, the clinical presentation (presence or absence of blisters and ulceration), location of lesions within the oral cavity, duration and their extent within the mouth were documented in all cases. The involvement of other mucosal membranes and/or skin was also noted. The severity of skin involvement was categorized as mild with less than 20 vesicles / erosions , moderate with 20-40 vesicles / erosions and severe in those with above 40 vesicles / erosions . Mucosal involvement was categorized as mild with 1- 5 lesions , moderate with 5- 10 lesions and severe with lesions above 10 or extensive lesions. Tzanck smear and histopathology examination with or without direct immunofluorescence was the method of confirmation of the diagnosis in all cases.

Results: During the study period total 91 cases were diagnosed as having pemphigus . Among these pemphigus vulgaris was seen in 83 (91.2%) patients followed by pemphigus foliaceus in 6 (6.5%) patients and Linear IgA pemphigus in 2 (2.1%) patient. Pemphigus erythematosus, drug-induced pemphigus , paraneoplastic and Pemphigus vegetans were not found in any of the patients . 83 newly diagnosed cases of pemphigus vulgaris were evaluated.

The male to female ratio was 1:1.5 (33 men , 50 women). The minimum age of patient with pemphigus vulgaris was found to be 11 and maximum was 80 year with an average age of 45.9 years. The majority of the cases were in the 45-60 year-age group 27(32.5%) , followed by 24 (29%) in age group 31 yrs- 45 yrs . Table 1 . 27 (32.5%) patients presented in first quarter of the year, 23 (27.7%) patients presented in second quarter of the year, 25 (30%) patients presented in third quarter of the year and 18 (21.6%) patients presented in last quarter of the year. Among them , 13 % 0f the patients were government employees; 17.9%, workers; 15.5%, farmers and 59.07%, housewives. 26 (31%) lived in urban areas and 57 (69%) in rural areas. In our case series of 83 patients pemphigus vulgaris began with localized lesions (73.3%) rather than generalized lesions (26.7%). 23 (27.7 %) patients had mild , 36 (43.3%) had moderate and 24 (28.9%) had severe form of skin disease. Table 2. In 70 (84 %) cases, the oral cavity was involvement sooner or later . 13 (16 %) had only cutaneous involvement, 5 (6%) had only oral involvement and 65 (78%) had both cutaneous and oral involvement.

All the patients with oral involvement presented with erosions or ulcers with pain and burning sensation . Conjuctival mucosa was affected in only one patient . The duration of oral lesions was taken as the period between the time when patient had first noticed lesion and attended to our clinic. The mean duration of pemphigus was 1 month to 13 months. Among 70 patients with oral lesions 26 (37.1%) of patients had mild , 23(32.8%) of patients had moderate and 21 (30%) patients had severe form of oral disease . Table 3 Most commonly affected site was buccal mucosa 46 (55.4%) followed by gingival 12(14.5%), tongue 8(9.6%), palate 8(9.6%), lips 6 (7.2%) and floor of mouth 3 (3.6%).

Table 1: Age and sex distribution of Pemphigus Vulgaris (PV) patients . M/F = Male Female ratio.

AGE GROUP (YRS)	MALE	FEMALE	M+F
0 - 15 yrs	0 (0%)	1 (1.2%)	1 (1.2%)
16 yr - 30 yrs	5 (6%)	12 (14.5%)	17 (20.4%)
31 yrs- 45 yrs	11 (13.3%)	13 (15.7%)	24 (29%)
46 yrs- 60 yrs	12 (14.4%)	15 (18%)	27 (32.5%)
61 yrs and above	05 (6%)	9 (10%)	14 (16.7%)
Total	33 (39.7%)	50 (60.2%)	83 (100%)

Table 2: Severity of skin disease and area of involvement in Pemphigus Vulgaris (PV) patients.

	Mild	Moderate	Severe	Total
Skin	05(6%)	6 (7.2)	2(2.4)	13 (16%)
Oral and skin	13(15.6)	30 (36.1)	22(26.5)	65 (78 %)

Table 3: Age and severity of oral involvement in Pemphigus Vulgaris (PV) patients.

AGE GROUP (YRS)	Mild	Moderate	Severe	Total
0 - 15 yrs	0	1	0	1
16 yr - 30 yrs	6	6	3	15
31 yrs- 45 yrs	5	7	8	20
46 yrs- 60 yrs	8	8	7	23
61 yrs and above	7	1	3	11
Total	26 (37.1 %)	23 (32.8%)	21 (30%)	70 (100%)

Discussion: The average annual incidence of pemphigus ranges from 0.08 cases/100000 individuals in Finland, 0.1-0.5 in USA 0.17 in France, 0.44 in Macedonia , 0 .47 in Bulgaria, 0.93 in Greece , 1.62 in Israel , 0.67 in Shiraz, and 1.6 in Tehran [4]. Among the 91 patients seen, pemphigus vulgaris was the most predominant type of pemphigus seen (83 , 91.2%). followed by pemphigus foliaceus in 6 (6.5%) patients and Linear IgA pemphigus in 2 (2.1%) patient .This corroborates well with other studies . Higher prevalence of pemphigus vulgaris compared with other variants is reported from Shiraz city, Turkey, Saudi Arabia, Bulgaria, France, Greece, India, Bangladesh, Kuwait, Italy and Gilan province [4]. On the other hand, pemphigus erythematosus is more prevalent in Finland and pemphigus foliaceus is the dominant variant in Brazil, South Africa, Mali, Tunisia [4] . In this study the majority of affected patients were aged between 30 and 60 years at the inception, and the condition has been infrequently recorded in individuals younger than 30. The mean age of onset was 45.9 years Previous studies in Saudi Arabia (43.1 year), Mali (46.7 year) and Turkey (43 year) show similar results. In a study done in Pakistan the average age of onset 33.8 which is lower than the results of the present study and reference books. In Africa the mean age of onset was 41.17 ± 15.07. which is significantly lower with unknown reasons. Although pemphigus vulgaris mainly affected middle-aged people, it was reported in 3-year old and 89-year-old patients in some references [5] . Youngest and eldest patients in our study were of 11 and 80 years . Maximum number of cases were observed between 30-60 years (51 %) surprisingly 14 (16.7%) of patients were above 60 years of age . With regard to our range of patients, we can conclude that pemphigus is expected to occur in patients with all age groups.

Male to female ratio of 1:1.5 was higher than the reports from Tunisia (1:4.1), Mali (1:4), Italy (1:2.2 Greece (1:2.2) and similar to other studies in India (1.16), Mediterranean beach of Turkey (1.35), Tehran (1:1.5), Bangladesh (1.3), and Shiraz city (1.22) [6] . Only in Saudi Arabia, a greater number of men were affected by this disorder with male to female ratio of 2.2 :1 . In northern America, Finland, Malaysia, England, France, Bulgaria and south eastern America morbidity rate was the same in the case of both men and women [6)] . In total, we observed female dominance in majority of the literature.

In the present study oral mucous membrane was affected in 70 (84%) cases. In 65 (78%) patients oral as well as skin involvement was noted. These results are compatible with other studies and reference books . In the study of Tehran (capital of Iran), skin and mucous membrane involvement was present at a same time in 70% of patients [7] . In the study of Isfahan (center of Iran) mucous membrane involvement was the first sign in 74% of patients [5] .

In the study of Rasht (north of Iran), the beginning of the disease was from mouth in 63% of patients and in 72.4% of the patients skin and mucous membrane were involved. The mean interval between the onset of mucosal and dermal involvement was less than 5 months in around half of our cases. This interval was 6-9 months in other studies in India and 5-12 months in Croatia [8] . The

most commonly affected site was buccal mucosa 46 (55.4%) followed by gingival 12(14.5%), tongue 8(9.6%), palate 8(9.6%), lips 6 (7.2%) and floor of mouth 3 (3.6%) similar to our study buccal mucosa was the predominant site affected in other studies [8] . In the present series, lesions in buccal mucosa were usually on the line of linea alba which is the most frequent area where dental traumas are detected.

The exacerbation of disease in summer is reported from India and South Africa. A study in Greece confirmed that high temperature and exposure to the sunshine can increase the relapsing risk. Hashimoto showed that excessive heat can increase pemphigus vulgaris antigen expression in the epidermis [9] . However, pemphigus onset was often in the winter in Shiraz city. In our study no significant increase in cases were seen in any of the seasons . Similarly in Gilan province, there was no relationship between the prevalence of the disease and the seasons.

Conclusion: The results of our study demonstrates that pemphigus vulgaris is the most common type of pemphigus seen and it occurs predominantly in females . It is common in the age group above 30 years . It is not uncommon in elders above 60 years . Involvement of skin as well as oral mucosa was the most common presentation of the disease. Buccal mucosa is commonest site of involvement.

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