Introduction

Vesiculobullous diseases (VBDs) are characterized by the formation of vesicles or bullae [1]. The diagnosis of VBDs can be made histopathologically, clinically, and through immunological investigations [2]. VBDs include pemphigus vulgaris (PV), bullous pemphigoid (BP), pemphigus herpetiformis (PH), mucous membrane pemphigoid (MMP), bullous dermatosis, and epidermolysis bullosa [3].

PV is one of the most common VBDs, which includes a group of autoimmune diseases that are potentially life-threatening and cause blisters and erosions on the skin and mucous membranes [4,5]. Pemphigus vulgaris oral lesions may present several months before skin lesions in more than half of the patients.
The incidence of pemphigus is 1 to 34 cases/million/year [7,8]. The prevalence of pemphigus vulgaris in Iran is estimated to be 30 in 100,000, and its incidence is between 1.2 and 1.6 in 100,000 which is higher than some other countries [9,10].

Bullous pemphigoid is an autoimmune VBD caused by binding of specific antibodies to the basal epithelial cell hemidesmosome antigens in the basement membrane of lamina lucida [1]. The incidence of BP increases with age, and males are more commonly affected [6].

Mucous membrane pemphigoid is a chronic autoimmune sub-epithelial disease that initially involves the mucous membranes of patients over 60 years of age, and leads to mucosal blistering, ulceration, and subsequent scarring [11].

Many previous epidemiological studies have focused on pemphigus, but few have evaluated the total spectrum of VBDs. Few studies have evaluated the epidemiological aspects of all VBDs in Iran [9,12,13].

Esmaili et al. evaluated 140 pemphigus vulgaris patients in Razi Hospital in Tehran [14] and Salmanpour et al. in Shiraz [15] evaluated cutaneous involvement in patients with PV. Daneshpazhooh et al. demonstrated that among 1,402 patients with vesiculobullous and autoimmune diseases, PV was the most common (81.2%) [12]. A 13-year retrospective study in Hamadan by Sobhan et al. showed that 78% of patients had pemphigus vulgaris [13].

The aim of this study was to epidemiologically evaluate patients with chronic VBDs referred to the Oral and Maxillofacial Medicine Department of Dental School of Shiraz University of Medical Sciences during 2006-2016.

Materials and Methods

In this retrospective cross-sectional study, records of all patients with oral VBDs admitted to the Oral and Maxillofacial Medicine Department of Shiraz Dental School during a 10-year period from 2006 to 2016 were evaluated. This study was approved by the ethic committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1396.S452).

A total of 120 patients with various types of VBDs with oral and dermatological manifestations were evaluated in this study. Patients with indefinite histopathological diagnosis and incomplete data were excluded from the study.

The diagnosis was made based on the clinical manifestations and specific histopathological findings by oral medicine specialists. Four diseases were included in this study: PV, BP, PH, and MMP. Data regarding age, sex, local involvement, underlying disease, and type of treatment were recorded and analyzed.

The mean and standard deviation of the values were reported. The Chi-square test was used for qualitative variables. The Spearman’s correlation test was applied to investigate the relationship between epidemiological factors and VBDs. In all statistical tests, P<0.05 was considered significant.

Results

A total number of 120 patients with autoimmune VBDs were included. Tables 1 and 2 show the characteristics of patients with different VBDs including their mean age and gender. Although there was no significant difference among the patient groups with regard to age (P=0.499), there was a significant difference among the patient groups in terms of sex (P=0.001).

The location of involvement and type of medications administered for VBDs in patients are shown in Table 3. The incidence of VBDs differed significantly based on location of involvement (P=0.006). In this study, 45 patients showed involvement of the mucous membranes and skin concomitantly. In 40 patients, mucosal lesions were seen alone, and in one case, cutaneous involvement was seen alone, which was statistically significant.
Corticosteroids (prednisolone) were the first-line and main treatment in all VBD patients. The incidence of underlying diseases in patients with chronic VBDs was as follows: 6 cases (5%) had anemia, 5 cases (4.16%) had diabetes mellitus, 3 cases (2.5%) had hypothyroidism, 3 cases (2.5%) had ischemic heart disease, 2 (1.66%) had hyperlipidemia, and 4 cases (3.33%) had a combination of several diseases including hypothyroidism, diabetes mellitus, mitral valve prolapse, arthritis, and kidney stones.

There was a significant correlation between age of patients and incidence of chronic VBD (P=0.030). However, underlying diseases did not show a significant correlation with the incidence of chronic VBDs (Table 4).
Discussion

VBDs can affect the mucocutaneous tissue, causing discomfort and morbidity for patients. Epidemiological evaluation of these lesions in each population is necessary.

In the present study, the most common VBDs were PV (88.3%), MMP, BP, and HP. Our results are consistent with those of Jowkar et al. [9], and Sobhan et al. [13] in Iran and also similar to studies conducted in most parts of the world, except those conducted in Tunisia, Mali, and Latin America. In these countries, other forms of VBDs, such as fogo selvagem, pemphigus foliaceus, and pemphigus erythematosus were dominant [16-18].

In the current study, the prevalence of different types of vesiculobullous diseases was higher in females (68.3% vs. 31.7%). Also, PV, MMP and HP had a higher frequency in females. This was consistent with the results of studies conducted in most parts of the world, except those conducted in Tunisian, Mali, and Latin America. In these countries, other forms of VBDs, such as fogo selvagem, pemphigus foliaceus, and pemphigus erythematosus were dominant [16-18].

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In contrast to the findings of studies conducted in Switzerland [6], Germany [19] and Kuwait [20], this result was in accordance and similar to studies in Germany [21], Saudi Arabia [22], and Bangladesh [23].

The mean age of patients with PV at the time of diagnosis was 43.14 years. The mean age for PV was similar to what was reported by Sobhan et al. (43.30 years old) [13], Jowkar et al. (45.8 years old) [9] Daneshpazhooh et al. (43.4 years old) [12] and Salmanpour et al. in the Southwest of Iran (38 years old) [15] and Chams-Davatchi et al. (42 years old) [24] and Baican et al. in Northwestern Romania (53 years old) [8].

Histopathological features may be the only characteristic factor in differentiation of various VBDs [25]. Of all patients, 45 showed concomitant mucous membrane and cutaneous involvement. In 40 patients, mucosal lesions were seen alone. Since Oral and Maxillofacial Department of Shiraz Dental School is a referral center for patients with oral lesions, lower referral of patients with skin lesions was expected; also, mucosal involvement may be the first symptom of VBDs which is associated with less severe cutaneous involvement. Therefore, mucosal involvement was associated with involvement of other sites in almost all cases. Of patients with PV, 31% only had oral mucosal involvement, but 37.33% had mucous membrane and cutaneous involvement and 18.15% represented involvement of mucous membranes and other organs concomitantly. Mucosal involvement had a different prevalence rate in chronic VBDs in the studies by Sobhan et al. (42.7%) [13], Farshchian and Pilehvar (34.3%) [26], Salmanpour et al. (59.3%) [15], Chams-Davatchi et al. (62%) [24] and Sadra Eshkevari et al. (63%) [27]; the reason may be that they only reported mucosal involvement in patients.

Prednisolone with different dosages ranging between 35 to 75 mg daily was the first-line medication prescribed for patients with chronic oral VBDs. Jowkar et al. also showed that prednisolone was the first-line treatment for PV (18.6%), BP (50%), and pemphigus foliaceus (38%) [9].

In spite of our comprehensive assessment of epidemiological aspects of VBDs, evaluating patient records may lead to some missing or even wrong data due to human errors.

Determination of the prevalence of VBDs, routinely prescribed medications, and common involvement locations can be helpful for more
perspective for health policymakers and health insurance systems. Also, specifying the involvement location can be of help to minimize misdiagnoses or undiagnosed clinical presentations of disease.

**Conclusion**

The results of this study showed that, similar to the previous studies conducted in Iran, PV had the highest prevalence among chronic VBDs. Also, we observed female preponderance in vesiculobullous diseases (M:F = 1:2.15).

**Conflict of interest**

There was no conflict of interests to declare.

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