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Original Article

A five-year epidemiologic study of autoimmune bullous diseases in Southeast of Iran

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Abstract

Background Autoimmune bullous diseases (AIBDs) are a group of chronic blistering diseases that affect mucocutaneous membranes. These diseases are common worldwide and affect males and females of all races. Treatment options include corticosteroids, rituximab, and topical agents. We evaluated the epidemiology of AIBD in Kerman, Iran, over a five-year period.

Methods This retrospective study was conducted on 100 patients diagnosed with an AIBD between 2015-2020. All patients were included in this study by census method. Factors like age, sex, disease type, and age at diagnosis were evaluated. Data analyses were performed using SPSS version 26.

Results One hundred patients participated in this study, and the male-to-female ratio was 1:1.08. The mean age of participants was 51.99±19.52 years, and the mean age at diagnosis was 49.19±8.31. Out of 100 patients, 82 suffered from pemphigus disease (70 pemphigus vulgaris; 12 pemphigus foliaceus), 17 had bullous pemphigoid, and one patient had pemphigus gestationis.

Conclusion In many countries, pemphigus is the most common AIBD. Although AIBDs are uncommon, the diagnosed cases increase with age.

Key words
Autoimmune; Bullous diseases.

Introduction

Autoimmune bullous skin disorders (AIBDs) are a group of uncommon and potentially life-threatening dermatoses specified by the formation of blisters and erosions on the mucocutaneous membrane, which can lead to skin detachment.[1,2] AIBDs occur worldwide but have a disproportionate geographic and ethnic distribution, with a significantly higher prevalence in the Mediterranean region and in those of Ashkenazi Jewish descent.[3,4] These diseases usually occur between the age of 50 and 60, but the mean age at diagnosis can differ significantly based on the country of origin and ethnic background.[5] Evidence shows that AIBDs are caused by the production of antibodies against the structural parts of the skin such as desmosomes and hemidesmosomes.[6]

AIBDs are classified into two categories according to the location of blisters. The first one, intra-epidermal bullous dermatoses, are mainly represented by pemphigus foliaceous and

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pemphigus vulgaris. Less common diseases such as pemphigus erythematosus (PE), IgA pemphigus, paraneoplastic pemphigus, and drug-induced pemphigus are also in this group.[7,8] In intra-epidermal bullous dermatoses, anti-desmoglein antibodies damage the connection between the keratinocytes, so intra-epidermal blisters appear.[9] The second group, sub-epidermal bullous dermatoses, include bullous pemphigoid, followed by less common types such as dermatitis herpetiformis, mucous membrane pemphigoid, and linear IgA bullous dermatosis.[7,8,10] In this group, anti-collagen antibodies damage keratinocyte-dermis adhesions, causing sub-epidermal blisters.[9]

Treatments of AIBD chiefly include corticosteroids and immunosuppressant adjuvants like azathioprine and mycophenolate mofetil. Autoantibodies are the primary mediators of these diseases, so rituximab, a chimeric anti-CD20 monoclonal antibody targeting B- cells, has emerged as an excellent treatment option for refractory AIBDs.[11,12]

Methods

Study design and population This study examined the records of all new patients with AIBDs who were admitted at Afzalipoor Hospital, Kerman, Iran, during 2015-2020. The diagnoses were confirmed based on clinical manifestations, histopathologic characteristics, and direct immunofluorescence. Afzalipour Hospital is southeast Iran's primary tertiary referral center for dermatologic diseases; other hospitals and private dermatology clinics in Kerman refer their AIBD patients to this center for extra care and follow-ups. Patients with incomplete documents and data that could not be recorded through a phone call or physician's appointment were excluded from the study.

The study design and protocol were approved by the Institutional Review Board and Ethics Committee of Kerman University of Medical Sciences, Kerman, Iran.

Data collection Samples were included in the study by census method. The patients and their disease data were extracted from their medical files and were inscribed in the data collection forms. The data gathered included age, sex, nationality, medical background, family history, age at diagnosis, disease duration, disease type (pemphigus or bullous pemphigoid), site involved by the blisters, medications used, extracutaneous manifestations and mucosal involvement (e.g., esophageal and vaginal mucosa), paraclinical findings, death, and relapse frequency. All the data were recorded anonymously, and no identifying information was noted.

Statistical analysis SPSS version 26 software was used for statistical analysis. In this study, the prevalence of pemphigus and related clinical parameters, as well as the incidence rate of the disease, were calculated. Descriptive statistics were reported with frequency (percentage) and mean (standard deviation).

Ethical considerations In this retrospective study, identifying information was not included in the data collection form. Each patient was given a code, and the coded and confidential list was only available to the researcher and supervisor in case of a need to call or follow up with the patient. Hence, the risks of bias and errors in data extraction were minimized.

Results

This study was conducted on 100 patients diagnosed with AIBDs, with a mean age of 51.99±19.52. Overall, 48 (48%) participants were males, and 52 (52%) were females **(Figure 1)**. A total of 2 patients (2%) were aged between 0-20, 27 (27%) between 20-40, 36 (36%)

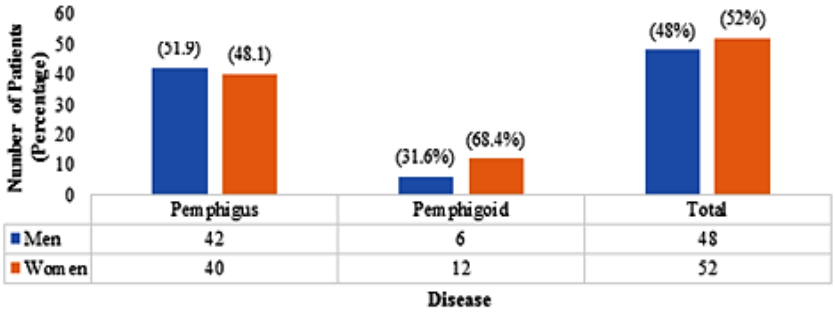

Figure 1 Gender distribution of patients in the study.

Table 1 Summary of the autoimmune bullous diseases in terms of the number of patients, mean age, age range, and sex ratio.

Autoimmune Bullous Disease	Number of patients	Age (Mean±SD) yrs.	Age range, years	M:F ratio
Pemphigus vulgaris	70 (70%)	45.86±17.40	6–83	1:1.05
Pemphigus foliaceous	12 (12%)	47.50±18.68	26–86	1:3
Bullous pemphigoid	17 (17%)	71.52±15.95	35–93	1:1.83
Pemphigus gestationis	1 (1%)	35	35	0:1

M: male, F: female, SD: standard deviation.

Table 2 A summary of the laboratory data of 100 patients with autoimmune bullous diseases.

	Mean	*Standard deviation*
Triglycerides, mg/dl	1221.75	53.41
Cholesterol, mg/dl	166.97	49.54
High-density lipoprotein, mg/dl	43.94	13.9
Low-density lipoprotein, mg/dl	91.63	36.52
White blood cells, ×1000/ml	9.43	3.61
Differential	66.43	13
Platelets, ×1000/ml	272.46	105.17
Erythrocyte sedimentation rate, mm/hr.	22.64	20.73
C-reactive protein, mg/l	18.95	3.56
Aspartate transaminase, u/l	28.88	25.67
Alanine transaminase, u/l	23.38	14.02
Blood urea nitrogen, mg/dl	33.17	13.16
Creatinine, mg/dl	1.15	1.09
Neutrophile/lymphocyte ratio	0.36	0.22

between 40-60, 22 (22%) between 60-80, and 13 (13%) between 80–100. Out of 100 participants, 82 had pemphigus disease (69 pemphigus vulgaris; 12 pemphigus foliaceous, 1 pemphigus gestationis) and 18 had bullous pemphigoid, Each AIBD is summarized in terms of the number of patients, mean age, age range, and sex ratio in **Table 1**.

Regarding education level, 25 people were illiterate, 42 people had a diploma, 22 had a post-graduate diploma, and 11 had a bachelor's degree. The mean age of disease onset was 49.80±19.31 years, and the mean disease duration was 18.66±28.93 months. The mean duration of hospitalization was 6.56±5.35 days. The laboratory data of the participants are summarized in **Table 3**.

The laboratory data, categorized by type of AIBD, is summarized in the table below. As evident, inflammatory factors such as ESR, CRP, and WBC were mostly abnormal.

Hypertension was the most prevalent comorbidity. Diabetes, hyperlipidemia, hyperthyroidism, cardiovascular disease, and psoriasis were next. The prevalence of comorbidities, categorized by the type of AIBD, is shown in **Table 3** and **Figure 2**.

Regarding the location of skin involvement, most patients had skin lesions in the whole body (52%) and trunk (27%). The lower limbs (5%), upper limbs (3%), and face (3%) were less

Table 3 A summary of the laboratory data categorized by the type of autoimmune bullous disease.

		Pemphigus		*Bullous pemphigoid*		*Total*		*P-value*
		Number	*%*	*Number*	*%*	*Number*	*%*	
ESR	Normal	38	46.9	5	26.3	43	43	**0.10**
	Abnormal	44	53.1	13	73.7	57	57	
CRP	Normal	41	50	5	26.3	46	46	**0.05**
	Abnormal	41	50	13	73.7	54	54	
Neutrophile/ lymphocyte	Normal	45	55.6	10	52.6	55	55	**0.81**
	Abnormal	37	44.4	8	47.4	45	45	
WBC	Normal	50	61.7	11	57.9	61	61	**0.75**
	Abnormal	32	38.3	7	42.1	39	39	
Plt	Normal	73	90.1	17	89.5	90	90	**0.93**
	Abnormal	9	9.9	1	10.5	10	10	
ALT	Normal	72	88.9	15	78.9	87	87	**0.24**
	Abnormal	10	11.1	3	21.1	13	13	
AST	Normal	68	84	17	94.7	85	85	**0.23**
	Abnormal	14	16	1	5.3	15	15	
BUN	Normal	67	82.7	16	84.2	83	83	**0.87**
	Abnormal	15	17.3	2	15.8	17	17	
	Normal	67	82.7	16	84.2	83	83	
Cr	Normal	77	93.8	15	84.2	92	92	**0.16**
	Abnormal	5	6.2	3	15.8	8	8	
PPD	Negative	80	97.5	18	100	98	98	**0.49**
	Positive	2	2.5	0	0	2	2	

ESR: Erythrocyte sedimentation rate, CRP: C- reactive protein, WBC: White blood cells, PLT: Platelets, ALT: Alanine transaminase, AST: Aspartate transaminase, BUN: Blood urea nitrogen, Cr: Creatinine, PPD: purified protein derivative.

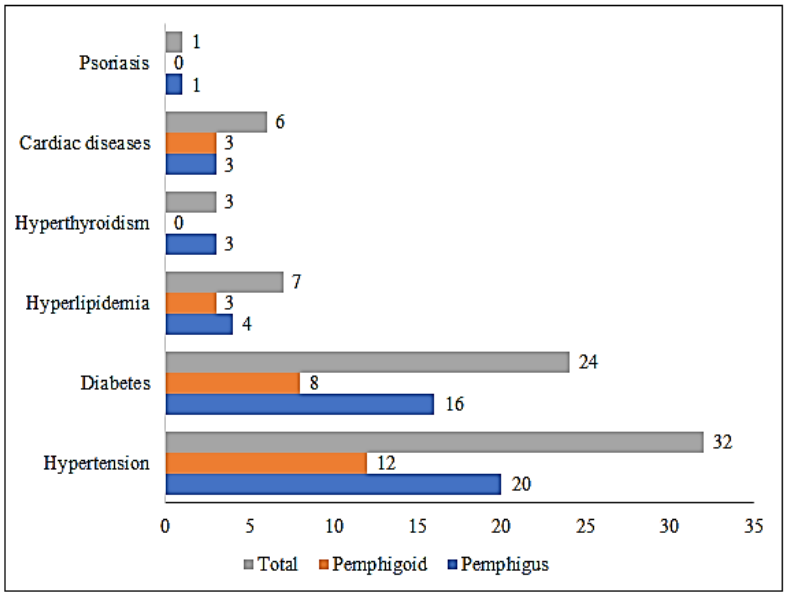

Figure 2 Bar chart for the comorbidities observed in patients with autoimmune bullous diseases.

frequently affected. Mucosal involvement was seen in 70 patients (70%), mostly accounted for by isolated oral mucosa lesions (60 patients). Lesions of the genitalia were seen in 3 patients (3%), while 6 (6%) patients had both oral and genital mucosal lesions. One patient had nasal membrane involvement, and no patient suffered from esophageal lesions. The site of lesion involvement according to the disease type is summarized in **Figure 3** and supplementary **Table 1**. Regarding medications, 92 patients were using prednisolone, 72 were using azathioprine, 12 were taking rituximab, and 60 were applying topical medications as treatment. Some patients use more than one drug as treatment.

Supplementary Table 1 Site of lesion involvement according to the type of autoimmune bullous diseases

	Skin	*Mucosal membrane*	*Skin & mucosal membrane*	*Total*
Pemphigus vulgaris	17 (17%)	3 (3%)	50 (50%)	70 (70%)
Pemphigus foliaceous	8 (8%)	0 (0%)	9 (9%)	17 (17%)
Bullous pemphigoid	5 (5%)	0 (0%)	7 (7%)	12 (12%)
Pemphigus gestationis	1 (1%)	0 (0%)	0 (0%)	1 (1%)

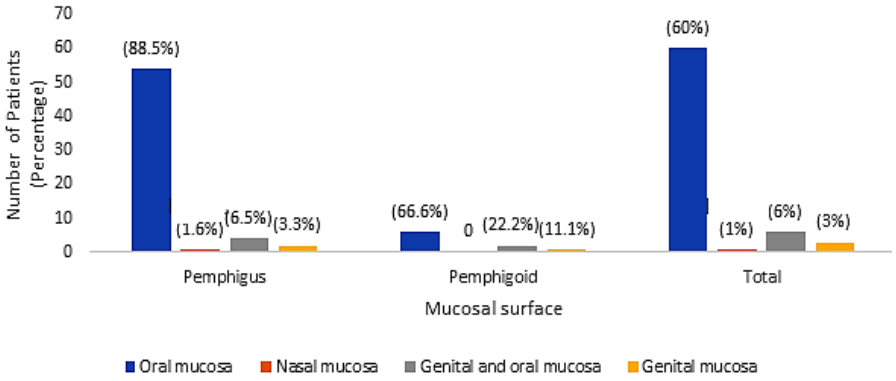

Figure 3 Mucosal involvements in patients with autoimmune bullous diseases.

The information on using medications is summarized in supplementary **Table 2**.

The results obtained after performing statistical calculations showed that the first common site of involvement was the trunk (48 patients) and mouth (16 patients). In terms of hospitalization frequency, 72 patients had been admitted to the hospital once, 14 twice, 9 three times, 4 patients four times, and 1 patient six times. Regarding the season in which they first contracted the disease, 23 patients' first presentations were in spring, 29 in summer, 17 in autumn, and 30 in winter. In terms of additional diseases in AIBD patients, hypertension (31 patients) and diabetes (25 patients) were the most common underlying disorders.

Discussion

Autoimmune bolus diseases (AIBD) are not common. Our study investigated the clinico-epidemiological characteristics of AIBD cases among the Iranian population from southeast Iran between 2015 and 2020. Most previous studies focused on a single disease or a group of AIBD, but our study targeted the whole spectrum of AIBDs.[17-20] We were restricted by using health data that were not collected to answer our specific research questions because of our retrospective approach. Pemphigus vulgaris is the most common AIBD in Iran.[13] Hypertension is the most prevalent comorbidity in patients who suffer from AIBDs.[14] AIBDs can involve the skin and mucosal membranes (esophageal, oral, and vaginal mucosa).[15,16] In this study, 100 AIBD cases were included. In our study, intra-epidermal AIBD accounted for the majority of cases (77%), with pemphigus vulgaris as the most frequent type (65%), which is similar to the results from studies in the north and south of Iran[21-23] and some Middle-Eastern countries including Kuwait,[24] Malaysia,[25] and Turkey[26] in addition to Romania[27] and China.[28] However, in studies from Germany,[29] Switzerland,[30] the United Kingdom,[31] Singapore,[32] and Israel,[33,34] sub-epidermal AIBD (especially bullous pemphigoid) was the most common type. Bullous pemphigoid, pemphigus foliaceous, and pemphigus gestationis were

Supplementary Table 2 Medications used by patients with different types of autoimmune bullous diseases.

	Pemphigus vulgaris		*Pemphigus foliaceous*		*Bullous pemphigoid*		*Pemphigus gestationalis*	
	Number	%	Number	%	Number	%	Number	%
Prednisolone, Azathioprine	22	31.9	2	16.7	2	12.9	0	**0**
Prednisolone, Topical	8	11.6	1	8.3	5	27.8	1	**100**
Rituximab	0	0	1	8.3	0	0	0	**0**
Prednisolone, Azathioprine, Topical	24	33.3	6	50	5	27.8	0	**0**
Azathioprine, Topical	1	1.4	0	0	2	12.9	0	**0**
Prednisolone, Rituximab	2	2.9	0	0	0	0	0	**0**
Topical	0	0	0	0	1	5/6	0	**0**
Topical, Azathioprine, Rituximab	0	0	0	0	2	12.9	0	**0**
Prednisolone, Azathioprine, Rituximab	2	2.9	1	8.3	0	0	0	**0**
Prednisolone	7	10.1	1	8.3	0	0	0	**0**
Prednisolone, Topical, Rituximab	1	1.4	0	0	0	0	0	**0**
Prednisolone, Topical, Rituximab, Azathioprine	3	4.3	0	0	0	0	0	**0**

Table 4 Classification of comorbidities in patients with autoimmune bullous diseases.

		Pemphigus		*Bullous Pemphigoid*		*Total*		*P-value*
		Number	*%*	*Number*	*%*	*Number*	*%*	
Hypertension	Yes	21	24.7	12	63.2	33	33	**0.001**
	No	61	75.3	6	36.8	67	67	
Diabetes	Yes	16	19.8	8	42.1	24	24	**0.04**
	No	66	80.2	10	57.9	76	76	
Hyper lipidemia	Yes	4	4.9	3	15.8	7	7	**0.09**
	No	78	95.1	15	84.2	93	93	
Hyperthyroidism	Yes	3	3.7	0	0	3	3	**0.39**
	No	79	96.3	18	100	97	97	
Cardiovascular disease	Yes	3	3.7	3	15.8	6	9	**0.04**
	No	79	96.3	15	84.2	94	94	
Psoriasis	Yes	1	1.2	0	0	1	1	**0.62**
	No	81	98.8	18	100	99	99	

ranked second to fourth in frequency in our study. The ratio of pemphigus vulgaris to bullous pemphigoid was 3.8:1, which is much lower than the results of previous studies from the north and south of Iran,[21-23] Kuwai,[24] and China.[28]

We found a female predominance in most of the AIBD types, in line with previous studies. The mean age of patients during the disease onset was 49.80±19.31 and the mean age at the referral time was 51.99±19.52, consistent with previous studies except for Germany,[29] Switzerland,[30] and the United Kingdom,[35] where the mean age was higher. Our findings are compared against the epidemiological features of eight studies that have previously investigated the whole spectrum of AIBD in **Table 5**.

Intra-epidermal group

Pemphigus vulgaris In our study, we found that pemphigus vulgaris is the most common intra-epidermal type and ranked first in frequency among the whole spectrum of AIBD (70%), which is in agreement with findings from most countries including Tunisia,[36] Saudia Arabia,[37] Turkey,[26] India,[38] France,[39] Japan,[40] Singapore,[32] Korea,[41] Bangladesh,[42] Bulgaria,[43] Serbia and Montenegro,[44] Greece,[45] Spain,[46] UK,[47] Switzerland,[30] and Israel[34] but in contrast with findings from Brazil,[48] Mali,[49] South Africa,[50] Finland,[51] and South American countries[52] where pemphigus foliaceous, pemphigus

erythematosus, and some endemic types were more common.

We found a male predominance in our study with a male-to-female ratio of 1.25:1, which concurs with data from previous studies from Iran,[20] Kuwait,[24] Saudia Arabia,[37] China,[28] and Bangladesh.[42] However, most countries reported the disease more in females than males.[22,26,27,34,40,53]

Regarding the age of presentation, we found that pemphigus vulgaris had a mean age of 46.1±17.2 years at presentation. This finding is in line with previous reports from Iran,[21-23] Saudia Arabia,[37] Singapore,[32] South Africa,[50] Turkey,[26] and Sudan.[54] However, in some European countries including Germany,[29] Romania,[27] Switzerland,[30] the United Kingdom,[31] and Italy,[53] in addition to Japan[40] and Korea,[41] the disease was reported to present in the sixth and seven decades, which is much higher than our study. Different genetic and environmental factors play an important role in this disease, which can explain the different mean ages of presentation between different countries.

The prevalence of oral mucosa involvement among pemphigus vulgaris patients was 84% in our study. This finding is in agreement with previous reports from Turkey,[55] Slovakia,[56] Korea,[41] Iran,[57] and Italy.[53] However, in some reports from Spain,[58] Brazil,[59] India,[60] Egypt,[61] Greece,[62] and south and north-east Italy,[63,64] the prevalence was near 100%.

The most commonly observed comorbidities among our pemphigus vulgaris patients were hypertension (26%), diabetes (14.4%), hyperlipidemia (4.9%), hyperthyroidism (3.7%), and cardiac disease (3.7%). Other studies also have shown that hypertension, diabetes, and cardiovascular diseases are the most frequent

Table 5 Epidemiological features of nine studies on autoimmune bullous diseases.

	Iran (2015-2020)present study	*Iran (1997-2006)*	*Tunisia (1997-2007)*	*Romania (April 2001-Dec. 2007*	*Germany (Jan. 2001-June 2002)*	*Kuwait (July 1991-Dec. 2002)*	*China (1953-1991)*	*Malaysia (15 years)*	*Iran (2001-2016)*
PV	N=70(70%) Age=45.86 M:F=1:1.05	N = 1138 (81.2%) Age = 43.4 M:F = 1:1.4	N = 56 (32.2%) Age = NR M:F = 1:2.1	N = 55 (47.4%) Age = 53 M:F = 1:1.8	N = 1 (2.4%) Age = 62 M:F = NR	N = 48 (37.5%) Age = 36.5 M:F = 1:0.7	N = 372 (37.8%) Age = NR M:F = NR	N = 84(56.7%) Age = mostly 30-60 M:F = 1:1	N = 298 (50.9%) Age = 40.4 M:F = 1:2.3
PF	N=12(12%) Age=47.50 M:F=1:3	N = 63 (4.5%) Age =42.2 M:F = 1:1.3	N = 34 (19.5%) Age = NR M:F = 1:1.8	N = 9 (7.8%) Age = NR M:F = NR	N = 0 Age = NA M:F = NA	N = 11 (8.6%) Age = 36.9 M:F = 1:2.7	N = 448 (45.6%) Age = NR M:F = NR	N = 0 Age = NA M:F = NA	N = 48 (8.2%) Age = 46.3 M:F = 1:2.2
BP	N=17(17%) Age=71.52 M:F=1:1.83	N = 163 (11.6%) Age = 59.4 M:F = 1:1.4	N = 41 (23.6%) Age = 68.6 M:F = 1:0.6	N = 40 (34.5%) Age = 73 M:F = 1:1.5	N = 27 (65.9%) Age = 64.6 M:F = 1:1.2	N = 27 (21.1%) Age = 66 M:F = 1:5.8	N = 104 (10.6%) Age = 10- 84 M:F = 1:0.7	N = 51(34.5%) Age = mostly 40-80 M:F = 1:1.2	N = 165 (28.2%) Age = 66.0 M:F = 1:0.9
PG	N=1(1%) Age=35	N = 10 (0.7%) Age = 27.7	N = 18 (10.3%) Age = 31.7	N = 1 (0.9%) Age = NR	N = 4 (9.8%) Age = 33	N = 24 (18.8%) Age = 28.6	N = 0 Age = NA	N = 0 Age = NA	N = 8 (1.4%) Age = 29.5

comorbidities.[14] Some have clarified that there is a higher prevalence of hypertension, diabetes, and cardiovascular diseases among patients with pemphigus vulgaris.[65-67]

Pemphigus foliaceus Pemphigus foliaceus was the third most common AIBD, with a frequency of 12%. This is in agreement with reports worldwide except in some parts of the world like Brazil, where an endemic type of pemphigus foliaceous, Fogo selvagem, predominates,[48] and in Mali, where the pemphigus foliaceous was the most common pemphigus.[39] Also, in Tunisia, a predominance of pemphigus foliaceous was seen, especially in young women.[49]

In contrast with pemphigus vulgaris, pemphigus foliaceous was reported more in females than males, with a male-to-female ratio of 1:3. This is in agreement with other reports from Iran,[22] Kuwait,[24] Japan,[40] Brazil,[48] Mali,[49] South Africa[50] and Tunisia.[36] However, in Turkey,[36] Singapore,[32] Israel,[34] and France,[39] the disease was reported more in males than females.

The mean age of presentation for pemphigus foliaceous in our study was 47.5±18.6, which is in line with previous studies from Iran,[22] Mali,[49] and China.[28] However, in Turkey,[26] Singapore,[32] Italy,[53] and Japan,[40] the mean age was higher than in our study.

The frequency of oral mucosa involvement among patients with pemphigus foliaceous was 58.3%, and the most frequent comorbidities were diabetes (50%) and hypertension (16.6%).

Subepidermal group

Bullous pemphigoid In this study, we found that bullous pemphigoid was the most common type among the sub-epidermal AIBD and ranked second in frequency among the whole spectrum of AIBD with a frequency of 17%, which is compatible with previous studies from Iran,[17,21,22] Switzerland,[30] Singapore,[48] Tunisia,[39] Germany,[69] France,[70] Romania,[27] Kuwait,[24] China,[28] and Malaysia.[71]

In our study, bullous pemphigoid was more common in females, similar to previous reports from Iran.[21-23] However, in reports from China,[28] Tunisia,[36] and Germany,[72] a male predominance was observed.

Bullous pemphigoid's mean age of presentation was 71.5±15.9, similar to what was observed in several reports from Iran,[22] Kuwait,[24] Turkey,[26] Germany,[29] and Tunisia.[36] This is slightly lower than reports from western countries, including Switzerland,[30] France,[70] Germany,[69] the United Kingdom,[31] and the United States.[73]

In our patients, we observed a much higher prevalence rate of mucosal involvement than in previous reports. A prevalence of 5.7%, 7.7%, and 14.5% was reported in Singapore,[74] France,[75] and Switzerland.[76] The oral mucosa was the most frequently involved mucosal surface, which agrees with nearly all previous reports. The rate of oral mucosa involvement among bullous pemphigoid patients was 66.6% (12/18); this is much lower than most previous studies, where the rate was between 80.4% and 94.4%.[75-78]

We determined the frequency of comorbidities among patients with bullous pemphigoid. Hypertension (66%), diabetes (44.4%), cardiovascular disease (16.6%), and hyperlipidemia (16.6%) were the most common comorbidities among our patients. Similarly, previous reports have found that hypertension is the most common comorbidity among bullous pemphigoid patients.[14,79-83] Some of these studies showed an increased incidence of cardiovascular diseases among patients with bullous pemphigoid.[83-85]

Limitations This study was conducted on all patients admitted to the hospital, so patients with less severe disease were not included. Considering the study's retrospective nature, we could not evaluate other variables like the body mass index due to incomplete records.

Conclusion

AIBDs are rare diseases that could affect anyone all around the world. These diseases usually happen in people who are over 40. Like previous studies, pemphigus vulgaris was Kerman's most common AIBD. Bullous pemphigoid was the second most common AIBD, usually seen in old patients.

References

1. Chu K-Y, Yu H-S, Yu S. Current and Innovated Managements for Autoimmune Bullous Skin Disorders: An Overview. Journal of Clinical Medicine. 2022;11(12):3528.
2. Behkar A, Garmaroudi G, Nasimi M, Yousefi S, Khosravi H, Kianfar N, et al. Assessing quality of life in patients with autoimmune bullous diseases using the Persian version of Treatment of Autoimmune Bullous Disease Quality of Life questionnaire finds similar effects in women as men. International journal of women's dermatology. 2022;8(1):e004.
3. Rashid H, Lamberts A, Diercks GF, Pas HH, Meijer JM, Bolling MC, et al. Oral lesions in autoimmune bullous diseases: an overview of clinical characteristics and diagnostic algorithm. American journal of clinical dermatology. 2019;20(6):847-61.
4. Schmidt E, Borradori L, Joly P. Epidemiology of autoimmune bullous diseases. Blistering diseases: Springer; 2015. p. 251-63.
5. van Beek N, Zillikens D, Schmidt E. Diagnosis of autoimmune bullous diseases. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2018;16(9):1077-91.
6. Fagundes PPS, Santi CG, Maruta CW, Miyamoto D, Aoki V. Autoimmune bullous diseases in pregnancy: clinical and epidemiological characteristics and therapeutic approach. Anais Brasileiros de Dermatologia. 2021;96:581-90.
7. Heckler I, Hong M, Sinha AA, Venkataraman I. Serological Biomarkers and Their Detection in Autoimmune Bullous Skin Diseases. Dermatology Practical & Conceptual. 2022;12(2).
8. Song A, Lee SE, Kim JH. Immunopathology and immunotherapy of inflammatory skin diseases. Immune Network. 2022;22(1).
9. Kanazawa N. Designation of autoinflammatory skin manifestations with specific genetic backgrounds. Frontiers in Immunology. 2020;11:475.
10. Kridin K. Subepidermal autoimmune bullous diseases: overview, epidemiology, and associations. Immunologic research. 2018;66(1):6-17.
11. Meurer M. Immunosuppressive therapy for autoimmune bullous diseases. Clinics in dermatology. 2012;30(1):78-83.
12. Schmidt E, Hunzelmann N, Zillikens D, Bröcker EB, Goebeler M. Rituximab in refractory autoimmune bullous diseases. Clinical and Experimental Dermatology: Clinical dermatology. 2006;31(4):503-8.
13. Abdolsamadi HR, Abdollahzadeh S, Vaziri PB, Beheshti A, Shafigh E, Vahedi M. epidemiology of pemphigus in Tehran, Iran: a 20-year retrospective study. Journal of Dental Research, Dental Clinics, Dental Prospects. 2007;1(3):108.
14. Sánchez-García V, Pérez-Alcaraz L, Belinchón-Romero I, Ramos-Rincón J-M. Comorbidities in Patients with Autoimmune Bullous Disorders: Hospital-Based Registry Study. Life. 2022;12(4):595.
15. Bickle KM, Roark TK, Hsu S. Autoimmune bullous dermatoses: a review. American family physician. 2002;65(9):1861.
16. Ljubojevic S, Lipozenčić J. Autoimmune bullous diseases associations. Clinics in dermatology. 2012;30(1):17-33.
17. Esmaili N, Hallaji Z, Soori T, Davatchi CC. Bullous pemphigoid in Iranian patients: a descriptive study on 122 cases. Acta Medica Iranica. 2012:335-8.
18. Balighi K, Daneshpazhooh M, Mahmoudi H, Nasimi M, Delavari A, Azizpour A. Clinicoepidemiological Features of 82 Cases of Bullous Pemphigoid in Tehran, Iran. Acta Medica Iranica. 2018:522-5.
19. Ali A, AliReza Y, Gita F. Pemphigus vulgaris in Iran: epidemiology and clinical

profile. SKINmed: Dermatology for the Clinician. 2006;5(2):69-71.
20. Chmurova N, Svecova D. Pemphigus vulgaris: a 11-year review. Bratisl Lek Listy. 2009;110(8):500-3.
21. Jowkar F, Sadat Sadati M, Tavana S, Agah MA. Epidemiology of autoimmune bullous diseases and therapeutic modalities during a 10 year period in Iran. Acta Dermatovenerologica Croatica. 2014;22(4):246-.
22. Daneshpazhooh M, Chams-Davatchi C, Payandemehr P, Nassiri S, Valikhani M, Safai-Naraghi Z. Spectrum of autoimmune bullous diseases in Iran: a 10-year review. International journal of dermatology. 2012;51(1):35-41.
23. Ghiasi M, Daneshpazhooh M, Ismonov M, Chams-Davatchi C. Evaluation of Autoimmune Bullous Diseases in Elderly Patients in Iran: A 10-Year Retrospective Study. Skinmed. 2017;15(3):175-80.
24. Nanda A, Dvorak R, Al-Saeed K, Al-Sabah H, Alsaleh QA. Spectrum of autoimmune bullous diseases in Kuwait. International journal of dermatology. 2004;43(12):876-81.
25. ADAM BA. Bullous diseases in Malaysia: epidemiology and natural history. International journal of dermatology. 1992;31(1):42-5.
26. Uzun S, Durdu M, Akman A, Gunasti S, Uslular C, Memisoglu HR, et al. Pemphigus in the Mediterranean region of Turkey: a study of 148 cases. International journal of dermatology. 2006;45(5):523-8.
27. Baican A, Baican C, Chiriac G, Chiriac MT, Macovei V, Zillikens D, et al. Pemphigus vulgaris is the most common autoimmune bullous disease in Northwestern Romania. Wiley Online Library; 2010.
28. PEIYING J, CHANGGENG S, GANYUN Y. Chronic bullous dermatoses in China. International journal of dermatology. 1993;32(2):89-92.
29. Bertram F, Bröcker EB, Zillikens D, Schmidt E. Prospective analysis of the incidence of autoimmune bullous disorders in Lower Franconia, Germany. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2009;7(5):434-9.
30. Marazza G, Pham H, Schärer L, Pedrazzetti P, Hunziker T, Trüeb R, et al. Incidence of bullous pemphigoid and pemphigus in Switzerland: a 2-year prospective study. British journal of dermatology. 2009;161(4):861-8.
31. Langan S, Smeeth L, Hubbard R, Fleming K, Smith C, West J. Bullous pemphigoid and pemphigus vulgaris—incidence and mortality in the UK: population based cohort study. BMJ [Internet]. 2008; 337: 160–3.
32. Goon ATJ, Tan SH. Comparative study of pemphigus vulgaris and pemphigus foliaceus in Singapore. Australasian journal of dermatology. 2001;42(3):172-5.
33. Kridin K, Bergman R. Ethnic variations in the epidemiology of bullous pemphigoid in Israel. International journal of dermatology. 2018;57(1):34-9.
34. Kridin K, Zelber-Sagi S, Khamaisi M, Cohen AD, Bergman R. Remarkable differences in the epidemiology of pemphigus among two ethnic populations in the same geographic region. Journal of the American Academy of Dermatology. 2016;75(5):925-30.
35. Langan S, Smeeth L, Hubbard R, Fleming K, Smith C, West J. Bullous pemphigoid and pemphigus vulgaris—incidence and mortality in the UK: population based cohort study. Bmj. 2008;337.
36. Zaraa I, Kerkeni N, Ishak F, Zribi H, El Euch D, Mokni M, et al. Spectrum of autoimmune blistering dermatoses in Tunisia: an 11-year study and a review of the literature. International journal of dermatology. 2011;50(8):939-44.
37. Tallab T, Joharji H, Bahamdan K, Karkashan E, Mourad M, Ibrahim K. The incidence of pemphigus in the southern region of Saudi Arabia. International journal of dermatology. 2001;40(9):570-2.
38. Kanwar AJ. Dipankar De. Pemphigus in India Indian Journal of Dermatology, Venereology and Leprology. 2011;77(4):439-49.
39. Bastuji-Garin S, Souissi R, Blum L, Turki H, Nouira R, Jomaa B, et al. Comparative epidemiology of pemphigus in Tunisia and France: unusual incidence of pemphigus foliaceus in young Tunisian women. Journal of investigative dermatology. 1995;104(2):302-5.
40. Barton L, BUTTERBACH-BAHL K, Kiese R, Murphy DV. Nitrous oxide fluxes from a grain–legume crop (narrow-leafed lupin) grown in a semiarid climate. Global Change Biology. 2011;17(2):1153-66.
41. Seo PG, Choi WW, Chung JH. Pemphigus in Korea: clinical manifestations and

treatment protocol. The Journal of Dermatology. 2003;30(11):782-8.
42. Amin MN, Islam AM. Clinical, histologic and immunologic features of pemphigus in Bangladesh. International journal of dermatology. 2006;45(11):1317-8.
43. Tsankov N, Vassileva S, Kamarashev J, Kazandjieva J, Kuzeva V. Epidemiology of pemphigus in Sofia, Bulgaria. A 16-year retrospective study (1980–1995). International journal of dermatology. 2000;39(2):104-8.
44. Golušin Z, Poljački M, Jovanoviç M, Đuran V, Stojanoviç S, Rajiç N. Some epidemiological features of pemphigus chronicus in South Vojvodina: a 12-year retrospective study. International journal of dermatology. 2005;44(9):792-3.
45. Kyriakis K, Tosca A, Lehou J, Hatzis J, Vareltzidis A, Stratigos J. A five year retrospective study on pemphigus and pemphigoid. Australasian journal of dermatology. 1989;30(1):33-6.
46. Coronel-Pérez IM, Rodríguez-Rey E, Pérez-Bernal A, Camacho F. Epidemiology of pemphigus in hospital universitario virgen macarena, seville, spain, 2005-2006. Actas Dermo-Sifiliográficas (English Edition). 2009;100(2):121-5.
47. Wilson C, Wojnarowska F, Mehra N, Pasricha J. Pemphigus in Oxford, UK, and New Delhi, India: a comparative study of disease characteristics and HLA antigens. Dermatology. 1994;189(Suppl. 1):108-10.
48. Chiossi MPdV, Roselino AMF. Endemic pemphigus foliaceus (" fogo selvagem"): A series from the Northeastern region of the state of São Paulo, Brazil, 1973-1998. Revista do Instituto de Medicina Tropical de São Paulo. 2001;43:59-62.
49. Mahe A, Flageul B, Cisse I, Keita S, Bobin P. Pmphigus in Mali: a study of 30 cases. British Journal of Dermatology. 1996;134(1):114-9.
50. Aboobaker J, Morar N, Ramdial PK, Hammond MG. Pemphigus in South Africa. International journal of dermatology. 2001;40(2):115-9.
51. Hietanen J, Salo O. Pemphigus: an epidemiological study of patients treated in Finnish hospitals between 1969 and 1978. Acta dermato-venereologica. 1982;62(6):491-6.
52. Chacón GR, Ortega-Loayza AG, Cyr RM. Historical notes on endemic pemphigus in South America. International Journal of Dermatology. 2012;51(4):477-81.
53. Micali MD G, Musumeci MD M, Letizia, Nasca MD MR. Epidemiologic analysis and clinical course of 84 consecutive cases of pemphigus in eastern Sicily. International journal of dermatology. 1998;37(3):197-200.
54. Suliman NM, Åstrøm AN, Ali RW, Salman H, Johannessen AC. Clinical and histological characterization of oral pemphigus lesions in patients with skin diseases: a cross sectional study from Sudan. BMC oral health. 2013;13(1):1-12.
55. Kavala M, Zindancı İ, Turkoglu Z, Kuru B, Ozlu E, Simsek M. Nineteen-year retrospective evaluation of pemphigus in a single dermatology centre in Istanbul, Turkey. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii. 2020;37(1):23-8.
56. Svecova D. Pemphigus vulgaris: a clinical study of 44 cases over a 20-year period. International Journal of Dermatology. 2015;54(10):1138-44.
57. Javidi Z, Meibodi NT, Nahidi Y. Epidemiology of pemphigus in northeast Iran: A 10-year retrospective study. Indian Journal of Dermatology. 2007;52(4):188.
58. España A, Fernández S, Del Olmo J, Marquina M, Pretel M, Ruba D, et al. Ear, nose and throat manifestations in pemphigus vulgaris. British Journal of Dermatology. 2007;156(4):733-7.
59. GONÇALO RIC, SEVERO MLB, MEDEIROS AMCd, OLIVEIRA PTd, SILVEIRA ÉJDD. Vesiculobullous autoimmune diseases with oral mucosa manifestations: retrospective and follow-up study. RGO-Revista Gaúcha de Odontologia. 2018;66:42-9.
60. Guliani A, De D, Handa S, Mahajan R, Sachdeva N, Radotra BD, et al. Identification of clinical and immunological factors associated with clinical relapse of pemphigus vulgaris in remission. Indian Journal of Dermatology, Venereology and Leprology. 2020;86:233.
61. Fawzy MM, Hegazy RA, Abdel Fattah AF. Ear, nose, and throat involvement in E gyptian patients with pemphigus vulgaris: a step towards a better management. International Journal of Dermatology. 2013;52(10):1268-73.
62. Michailidou EZ, Belazi MA, Markopoulos AK, Tsatsos MI, Mourellou ON, Antoniades

DZ. Epidemiologic survey of pemphigus vulgaris with oral manifestations in northern Greece: retrospective study of 129 patients. International journal of dermatology. 2007;46(4):356-61.
63. Arduino PG, Broccoletti R, Carbone M, Gambino A, Sciannameo V, Conrotto D, et al. Long-term evaluation of pemphigus vulgaris: A retrospective consideration of 98 patients treated in an oral medicine unit in north-west Italy. Journal of Oral Pathology & Medicine. 2019;48(5):406-12.
64. Calabria E, Fortuna G, Aria M, Mignogna MD. Autoimmune mucocutaneous blistering diseases in the south of Italy: a 25-year retrospective study on 169 patients. Journal of Oral Pathology & Medicine. 2020;49(7):672-80.
65. Chiu Y-W, Chen Y-D, Hua T-C, Wu C-H, Liu H-N, Chang Y-T. Comorbid autoimmune diseases in patients with pemphigus: a nationwide case-control study in Taiwan. European Journal of Dermatology. 2017;27(4):375-81.
66. Askin O, Ozkoca D, Kutlubay Z, Mat MC. A retrospective analysis of pemphigus vulgaris patients: Demographics, diagnosis, co-morbid diseases and treatment modalities used. Northern Clinics of İstanbul. 2020;7(6):597.
67. Heelan K, Mahar A, Walsh S, Shear N. Pemphigus and associated comorbidities: a cross-sectional study. Clinical and Experimental Dermatology. 2015;40(6):593-9.
68. Wong S, Chua S. Spectrum of subepidermal immunobullous disorders seen at the National Skin Centre, Singapore: a 2-year review. British Journal of Dermatology. 2002;147(3):476-80.
69. Zillikens D, Wever S, Roth A, Weidenthaler-Barth B, Hashimoto T, Bröcker E-B. Incidence of autoimmune subepidermal blistering dermatoses in a region of central Germany. Archives of dermatology. 1995;131(8):957-8.
70. Bernard P, Vaillant L, Labeille B, Bedane C, Arbeille B, Denoeux J-P, et al. Incidence and distribution of subepidermal autoimmune bullous skin diseases in three French regions. Archives of dermatology. 1995;131(1):48-52.
71. Garred P, Brygge K, Sørensen C, Madsen H, Thiel S, Svejgaard A. Mannan-binding protein—levels in plasma and upper-airways secretions and frequency of genotypes in children with recurrence of otitis media. Clinical & Experimental Immunology. 1993;94(1):99-104.
72. Junga M, Kippesb W, Messer G, Zillikens D, Rzany B. Increased risk of bullous pemphigoid in male and very old patients: a population-based study on incidence. Journal of the American Academy of Dermatology. 1999;41(2):266-8.
73. Parker SR, Dyson S, Brisman S, Pennie M, Swerlick RA, Khan R, et al. Mortality of bullous pemphigoid: an evaluation of 223 patients and comparison with the mortality in the general population in the United States. Journal of the American Academy of Dermatology. 2008;59(4):582-8.
74. Cai S, Allen J, Lim Y, Chua S, Tan S, Tang M. Mortality of bullous pemphigoid in S ingapore: risk factors and causes of death in 359 patients seen at the N ational S kin C entre. British Journal of Dermatology. 2014;170(6):1319-26.
75. Clapé A, Muller C, Gatouillat G, Le Jan S, Barbe C, Pham B-N, et al. Mucosal involvement in bullous pemphigoid is mostly associated with disease severity and to absence of anti-BP230 autoantibody. Frontiers in Immunology. 2018;9:479.
76. Della Torre R, Combescure C, Cortés B, Marazza G, Beltraminelli H, Naldi L, et al. Clinical presentation and diagnostic delay in bullous pemphigoid: a prospective nationwide cohort. British journal of dermatology. 2012;167(5):1111-7.
77. Di Zenzo G, Thoma-Uszynski S, Fontao L, Calabresi V, Hofmann SC, Hellmark T, et al. Multicenter prospective study of the humoral autoimmune response in bullous pemphigoid. Clinical Immunology. 2008;128(3):415-26.
78. Kridin K, Bergman R. Assessment of the prevalence of mucosal involvement in bullous pemphigoid. JAMA dermatology. 2019;155(2):166-71.
79. Banihashemi M, Zabolinejad N, Vahabi S, Razavi HS. Survey of bullous pemphigoid disease in northern Iran. International Journal of Dermatology. 2015;54(11):1246-9.
80. Kibsgaard L, Rasmussen M, Lamberg A, Deleuran M, Olesen A, Vestergaard C. Increased frequency of multiple sclerosis among patients with bullous pemphigoid: a population-based cohort study on comorbidities anchored around the diagnosis

of bullous pemphigoid. British Journal of Dermatology. 2017;176(6):1486-91.
81. Försti AK, Huilaja L, Schmidt E, Tasanen K. Neurological and psychiatric associations in bullous pemphigoid—more than skin deep? Experimental dermatology. 2017;26(12):1228-34.
82. Lee S, Rastogi S, Hsu DY, Nardone B, Silverberg JI. Association of bullous pemphigoid and comorbid health conditions: a case–control study. Archives of Dermatological Research. 2021;313(5):327-32.
83. Bech R, Kibsgaard L, Vestergaard C. Comorbidities and treatment strategies in bullous pemphigoid: an appraisal of the existing litterature. Frontiers in medicine. 2018;5:238.
84. Jeon HW, Yun SJ, Lee S-C, Won YH, Lee J-B. Mortality and comorbidity profiles of patients with bullous pemphigoid in Korea. Annals of Dermatology. 2018;30(1):13-9.
85. Chen Y-J, Juan C-K, Chang Y-T, Wu C-Y, Ho HJ, Tseng H-C. Association between inflammatory bowel disease and bullous pemphigoid: a population-based case–control study. Scientific reports. 2020;10(1):1-7.