



Demographic and Clinical Characteristics of Pre-Malignant Oral Lesions and their Related Factors in an Iranian Population: A Registry-Based Study

Somayeh Rahmani^{1*}, Maryam Sadat Shirmardi², Maryam Baharvand¹ and Hamed Mortazavi¹

1. Department of Oral Medicine, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran

2. General Dental Practitioner

* Corresponding author

Somayeh Rahmani, DDS

Department of Oral Medicine, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Tel: +98 21 2217 5351

Email: somayehrahmani2016@gmail.com

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Abstract

Background: Oral Potentially Malignant Disorders (OPMDs) can lead to Oral Squamous Cell Carcinoma (OSCC). The sixth most common cancer in the world is OSCC. This study aimed to describe the demographical and clinical characteristics of OPMD patients and their risk factors registered at the Oral Medicine Department of Shahid Beheshti Dental School in 2019-2021.

Methods: The observational-analytical study was conducted using the dental records of 96 consecutive patients using a web-based registration software (OPMDs registry). Information including demographics and clinical features, the type of OPMD, and risk factors were extracted. Data were analyzed using the Chi-square test, T-test, and Fisher's exact test with SPSS version 21.

Results: In this study, 96 patients (average age: 52.41 ± 14.87) including 52 women and 44 men, participated. The most common OPMDs comprised 69 Oral Lichen Planus (OLP) and 15 leukoplakia. The most common location of lesions was the buccal mucosa (74%) with erosions and plaques being the most common morphology types. Most patients with leukoplakia were male, however, majority of the patients with OLP were female ($p=0.001$). In patients with leukoplakia, 66.5% were smokers; hence, a significant relationship between smoking and OPMD was observed ($p=0.001$). Patients with OLP commonly presented with burning symptoms, while patients with leukoplakia were mostly asymptomatic ($p=0.004$).

Conclusion: A significant relationship was observed between gender, clinical symptoms, location of lesions, morphology, and type of OPMDs. Most patients with OPMDs were women with OLP in their buccal mucosa, suffering from burning sensation.

Keywords: Dental records, Mouth mucosa, Risk factors

Introduction

Oral Potentially Malignant Disorders (OPMDs) are a group of lesions in the oral cavity that have a higher risk of developing into cancer or malignant lesions. OPMDs are the leading cause of Oral Squamous Cell Carcinoma (OSCC). Some of the lesions and conditions that fall under OPMDs include leukoplakia, Proliferative Verrucous Leukoplakia (PVL), erythroplakia, Oral Sub mucous Fibrosis (OSF), Oral Lichen Planus (OLP), Lichenoid Contact Reaction (LCR), Discoid Lupus Erythematosus (DLE), epidermolysis bullosa, verrucous carcinoma, Plummer-Vinson syndrome, Verruciform xanthoma, candida leukoplakia, dyskeratosis congenita, and reverse smoking palate. OPMDs show precancerous changes in the oral mucosa (1,2). Leukoplakia is the most common OPMD, with a reported global prevalence of 2.6%. Leukoplakia presents as white patches or plaques in the mouth and does not fit into any specific disease category clinically. Cellular dysplasia and carcinoma in situ changes are observed in 5 to 25% of leukoplakia cases (3).

PVL is a specific type of leukoplakia that affects various areas of the oral cavity, especially the gums and the buccal mucosa. The risk of malignant transformation in this lesion has been reported to be between 63.3% to 100%. Erythroplakia is another OPMD that cannot be classified into any specific disease category clinically or histologically, similar to leukoplakia. Almost all cases of erythroplakia show a significant degree of dysplastic changes, carcinoma in situ, or squamous cell carcinoma (1).

OSF is a chronic disease that can affect any part of the mouth, esophagus, and pharyngeal mucosa.

Patients with OSF have at least a 19-fold increased risk of developing OSCC compared to the general population. OSCC, which originates from OSF, typically occurs in men around the age of 46 years. The risk of malignant transformation in OSF has been reported to be between 2-8% (4).

OLP is a common chronic immunological disease that has various clinical manifestations. The global prevalence of OLP has been reported to be between 0.5 to 2.6%. The risk of malignant transformation in OLP has been reported to be between 0.4 to 3.7% (5). LCR is a delayed hypersensitivity reaction that is caused by contact with dental restorative materials

and is one of the common factors in its occurrence. Clinically, it is similar to OLP. However, this lesion tends to be more unilateral, it and is associated with the causative agent in terms of the site of involvement. Malignant transformation has also been reported for this lesion (2).

Many cases of OSCC arise from OPMDs, and unfortunately, the lack of knowledge about their symptoms delays the diagnosis and treatment process, leading to increased healthcare costs, discomfort, decreased quality of life, and ultimately, mortality (6). Multiple studies have been conducted to investigate OPMDs in terms of their prevalence, risk of malignant transformation, clinical features, and predisposing factors. These studies have pointed to differences in the prevalence of oral cancer in different geographical regions, which may be due to variations in lifestyle, social and cultural habits, and differences in the beliefs of different ethnic groups (7).

Identifying risk factors and breaking harmful habits and behaviors in individuals with OPMDs can interrupt the progression of these disorders toward cancer or prevent their occurrence altogether.

Additionally, raising awareness among patients can have a significant impact on their prognosis (8).

According to the importance of recognizing pre-malignant lesions, their characteristics, and related risk factors, and the lack of sufficient and systematic community, this study aims to investigate the demographic characteristics, risk factors, and clinical manifestations of OPMDs in patients registered in the registry of OPMDs at the School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran during the years 2019-2021 (6).

Materials and Methods

The present study is observational-analytical research conducted based on the information of all the patients registered in the OPMDs registry of the School of Dentistry at Shahid Beheshti University of Medical Sciences. In the registry of OPMDs, the criterion for patient entry has been the confirmation of clinical or histological diagnosis (9).

The study includes 96 patients in the period of 2019-2021. Files with multiple information deficiencies in clinical symptoms and clinical diagnosis and contradictions between clinical symptoms and final

diagnosis, as well as lack of access to patients' information, were excluded from the study.

In this study, variables such as demographic information (gender, age, education level, occupation, blood type, and RH factor), risk factors (smoking, non-smoking tobacco, alcohol consumption, substance abuse, and hookah consumption), family history of cancer, clinical symptoms (symptoms, location, morphology, duration of presence, and dimensions) were examined.

The frequency and relationships between these variables were analyzed using mean and statistical tests such as T-test, Chi-squared, or Fisher's exact test through SPSS software version 21.

Results

Demographic data and risk factors

Out of 96 patients with precancerous lesions of the oral cavity, 52 were female (54.2%) and 44 were male (45.8%). The mean age of patients with precancerous lesions of the oral cavity was 52.41 ± 14.87 years (minimum 16 - maximum 87 years). The mean and standard deviation of age in men was 52.02 ± 15.13 years and in women, it was 52.73 ± 14.79 years. There was no significant difference in age between men and women according to the statistical analysis (t-test, $p=0.82$).

The statistical result of the chi-square test showed a significant relationship between female gender and the type of precancerous lesions of the oral cavity ($p=0.001$).

The results of this study demonstrated that the age groups of 50 to 59 years and 60 to 69 years had the highest frequency among patients with precancerous lesions of the oral cavity with 31.6% and 23.2%, respectively. However, no statistically significant relationship was found between age groups and types of precancerous lesions of the oral cavity ($p=0.28$). Approximately, 72% of the patients with precancerous lesions of the oral cavity had a high school diploma or less. No significant difference was observed between the level of education and types of precancerous lesions of the oral cavity ($p=0.2$). In terms of the employment status, the highest prevalence of precancerous lesions of the oral cavity were found in housewives with a frequency of 41.3% and employed individuals with 39.1%. The results of

the chi-square test revealed a significant relationship between homemaking and types of precancerous lesions of the oral cavity ($p=0.003$).

Among the blood groups, the highest number of patients with OPMDs had the A+ blood group. 35 patients (63%) were Rh+ (patients in the unknown category had no information about their blood group). Among the patients with leukoplakia, the O- and A+ blood groups were common, and among the patients with OLP, the O+ and A+ blood groups were common. However, no statistically significant relationship was found between blood groups and types of precancerous lesions ($p=0.81$). Smoking was the most significant risk factor. As the results showed, 66.5% of the patients with leukoplakia were smokers. The chi-square test indicated a significant relationship between smoking and types of OPMDs ($p<0.001$). None of the patients with leukoplakia had a family history of cancer, and 9% of the patients with OLP had a family history of cancer. However, no statistically significant difference was observed in the chi-square test ($p=0.33$) (Table 1).

Type of OPMDs

The most common OPMDs were OLP (71.8%), leukoplakia (15.6%), and PVL (4.2%) in order.

Among the patients with leukoplakia, the homogeneous type was more prevalent than the non-homogeneous type. The erosive type was the most common type of lichen planus. In leukoplakia, 66.5% of the patients were male, while in OLP, more patients were female (Table 2).

Clinical features

The results of this study showed that 21 patients (21.9%) had a single lesion and 75 patients (78.1%) had multiple lesions in the oral cavity. The most common symptom in the patients was burning (43.2%), with the highest frequency being related to OLP (50%). However, approximately, 40% of all the lesions were asymptomatic, with the highest frequency being related to leukoplakia (80.5%). According to the chi-square test, there was a significant statistical relationship between clinical symptoms and types of OPMD ($p=0.004$) (Table 3).

The most common clinical morphology of the lesions was the erosive type (55.2%). The most common

Table1. Demographic data and risk factors of patient based on different types of OPMDs

Type of OPMD		Leuko-plakia	OLP	LCR	DILR	GVHD	PVL	Others	Total	p-value	
Demography and risk factors										Chi-squared	
Gender	Female	5(33.5%)	43(62.5%)	3(100)	1(100%)	0	0	0	52(54.2%)	0.001	
	Male	10(66.5%)	26(37.5%)	0	0	1(100%)	4(100%)	3(100%)	44(45.8%)		
Blood group and Rh Factor*	O+	0	9(25%)	0	0	1(100%)	0	1(100%)	11(23.4%)	0.810	
	O-	2(33.33%)	6(16.66%)	1(100)	0	0	0	0	9(19.14%)		
	A+	3(50%)	15(41.66%)	0	0	0	1(100%)	0	19(40.42%)		
	A-	0	1(2.77%)	0	1(100%)	0	0	0	2(4.25%)		
	B+	1(16.66%)	4(11.11%)	0	0	0	0	0	5(10.63%)		
	B-	0	1(2.77%)	0	0	0	0	0	1(2.12%)		
Age (yr)	<19	1(7%)	0	0	0	0	0	0	1(1.05%)	0.280	
	20-29	0	5(7%)	0	0	0	0	0	5(5.3%)		
	30-39	3(21%)	7(10%)	0	0	0	0	3(100%)	13(13.7%)		
	40-49	4(28%)	11(15%)	1(33.5%)	0	0	0	0	16(16.8%)		
	50-59	4(28%)	21(30%)	2(66.5%)	1(100%)	1(100%)	1(25%)	0	30(31.6%)		
	60-69	2(14%)	17(24%)	0	0	0	3(75%)	0	22(23.2%)		
	70-79	0	5(7%)	0	0	0	0	0	5(5.3%)		
	<80	0	3(4%)	0	0	0	0	0	3(3.15%)		
Occupation*	Housewife	2(14%)	33(50%)	2(100%)	1(100%)	0	0	0	38(43.1%)	0.003	
	Employed	6(44%)	24(35%)	0	0	1(100%)	2(66.5%)	3(100%)	36(39.1%)		
	Student	2(14%)	2(2%)	0	0	0	0	0	4(4.3%)		
	Retired	2(14%)	7(11%)	0	0	0	0	0	9(9.8%)		
	Unemployed	2(14%)	1(1%)	0	0	0	1(33.5%)	0	4(4.3%)		
Education level*	Illiterate	1(8%)	6(10%)	0	0	0	0	0	7(7.5%)	0.200	
	High school	6(46%)	17(24%)	0	1(100%)	0	3(100%)	1(33.5%)	28(30.1%)		
	Diploma	4(30%)	25(36%)	2(66.5%)	0	1(100%)	0	0	32(34.4%)		
	Academic education	2(16%)	21(30%)	1(33.5%)	0	0	0	2(66.5%)	26(28%)		
Risk factors	Smoking	Yes	10(66.5%)	9(13.5%)	0	0	0	3(75%)	1(33.5%)	23(24%)	<0.001
		No	5(33.5%)	59(85%)	3(100%)	1(100%)	1(100%)	1(25%)	2(66.5%)	72(75%)	
		Former smoker	0	1(1.5%)	0	0	0	0	0	1	
	Non-smoking tobacco	Yes	0	1(2%)	0	0	0	0	0	1(1%)	>0.990
		No	15(100%)	68(98%)	3(100%)	1(100%)	1(100%)	4(100%)	3(100%)	95(99%)	
	Alcohol	Yes	2(14%)	2(2%)	0	0	0	1(25%)	1(33.5%)	6(6.3%)	0.082
		No	13(86%)	67(98%)	3(100%)	1(100%)	1(100%)	3(75%)	2(66.5%)	90(93.8%)	
	Substance abuse	Yes	2(14%)	2(2%)	0	0	0	0	0	4(4.2%)	0.190
		No	13(86%)	67(98%)	3(100%)	1(100%)	1(100%)	4(100%)	3(100%)	92(95.8%)	
	Hookah	Yes	2(14%)	2(2%)	0	0	0	0	0	4(4.2%)	0.190
		No	13(86%)	67(98%)	3(100%)	1(100%)	1(100%)	4(100%)	3(100%)	92(95.8%)	
	Family history of cancer	Yes	0	6(9%)	0	0	0	0	0	6(6.4%)	0.330
No		15(100%)	61(91%)	3(100%)	1(100%)	1(100%)	4(100%)	3(100%)	88(93.6%)		

group variables, 4 cases for occupation, and 3 cases for education level. This study was conducted based on the available information in the registry Oral Potentially Malignant Disorders (OPMD); Proliferative Verrucous Leukoplakia (PVL); Oral Lichen Planus (OLP); Lichenoid Contact Reaction (LCR); Discoid Lupus Erythematosus (DLE); Graft Versus Host Disease (GVHD)1

Table 2. Frequency of OPMDs and gender of participating patients

OPMDs	Gender		Frequency (percent)	Total			
	Female	Male					
Oral lichenoid reactions		Reticular	6	1	7(10.1%)	69(71.8%)	
		Erosive	18	7	25(36.2%)		
		Ulcerative	5	6	11(15.9%)		
		Plaque Type	4	6	10(14.5%)		
		Reticular-Erosive	2	2	4(5.8%)		
	Lichen planus	Reticular-Ulcerative	2	0	2(2.9%)		
		Erosive- Ulcerative	2	1	3(4.3%)		
		Erosive-Plaque type	2	1	3(4.3%)		
		Ulcerative-Plaque type	1	1	2(2.9%)		
		Reticular-Erosive-Ulcerative	0	1	1(1.4%)		
		Erosive- Ulcerative-Plaque type	1	0	1(1.4%)		
		Lichenoid Contact Reaction	3	0	-		3(3.1%)
		Drug-induced Lichenoid Reaction	1	0	-		1(1.1%)
	GVHD Lichenoid Reaction	0	1	-	1(1.1%)		
Leukoplakia		Homogenous	1	9	10(66.7%)	15(15.6%)	
	Non-homogenous	Speckled	2	1	3(20%)		
		Verrucous	2	0	2(13.3%)		
PVL			0	4	-	4(4.2%)	
Others		Non-specific ulcer	0	1	-	1(1.1%)	
		Discoid lupus erythematosus	0	1	-	1(1.1%)	
		Lichenoid dysplasia	0	1	-	1(1.1%)	

Oral Potentially Malignant Disorders (OPMD); Proliferative Verrucous Leukoplakia (PVL);

Table3. Details of various clinical features of OPMDs

Type of OPMD	Leukoplakia	OLP	LCR	DILR	GVHD	PVL	Others	Total	p-value		
Clinical Feature											
Symptoms	Pain	1(6.5%)	1(1.5%)	0	0	0	0	2(2.1%)	0.004	Chi-squared test	
	Burning	1(6.5%)	34(50%)	3(100%)	1(100%)	0	1(25%)	1(33.3%)			41(43.2%)
	Roughness	1(6.5%)	2(2.9%)	0	0	0	1(25%)	0			4(4.2%)
	Pain & burning	0	9(13.2%)	0	0	0	0	0			9(9.5%)
	With no sign	12(80.5%)	22(32.4%)	0	0	0	2(50%)	1(33.3%)			37(38.9%)
	Other *	0	0	0	0	1(100%)	0	1(33.3%)			2(2.1%)

Conts table 3.

Location	Labial mucosa	Upper lip	1(6%)	3(4.3%)	1(33%)	0	0	1(25%)	0	6(6.3%)	0.270	Fishers exact test
		Lower lip	0	10(14.5%)	1(33%)	0	0	1(25%)	1(33%)	13(13.5%)	0.450	
		Dorsal surface	0	10(14.5%)	0	0	0	0	0	10(10.4%)	0.110	
	Tongue	Ventral surface	1(6%)	4(5.8%)	0	0	0	1(25%)	0	6(6.3%)	0.600	
		Lateral border	2(13%)	13(18.8%)	1(33%)	0	0	1(25%)	0	17(17.7%)	>0.990	
	Gingiva		2(13%)	28(40.6%)	1(33%)	0	0	3(75%)	0	34(35.4%)	0.160	
	Buccal mucosa		7(46%)	55(79.7%)	3(100%)	1(100%)	1(100%)	2(50%)	2(66%)	71(74%)	0.006	
	Retromolar pad		1(6%)	7(10.7%)	1(33%)	0	0	1(25%)	0	10(10.4%)	>0.990	
	Palatal mucosa		0	5(7.2%)	0	0	0	2(50%)	0	7(7.3%)	0.630	
	Tuberosity		1(6%)	2(2.9%)	0	0	0	0	0	3(3.1%)	0.500	
	Vestibular mucosa	Maxillary	0	3(4.3%)	1(33%)	0	0	0	0	4(4.2%)	>0.990	
		Mandibular	2(13%)	4(5.8%)	1(33%)	0	0	0	0	7(7.3%)	0.600	
	Alveolar mucosa	Maxillary	0	7(10.1%)	0	0	0	3(75%)	0	10(10.4%)	0.420	
		Mandibular	1(6%)	5(7.2%)	0	0	0	4(100%)	0	10(10.4%)	0.030	
Floor of the mouth		2(13%)	3(4.3%)	1(33%)	0	0	0	0	6(6.3%)	0.270		
Morphology	Plaque		11 (73%)	28 (39.1%)	2 (66%)	1 (100%)	0	4(100%)	2(66%)	48(50%)	0.001	
	Patch		2 (13%)	7 (10.1%)	0	0	1 (100%)	0	0	10(10.4%)	>0.990	
	Papule		2 (13%)	17 (26.1%)	1 (33%)	0	1 (100%)	0	0	21(21.9%)	0.100	
	Erosion		4 (26%)	45 (63.8%)	2 (66%)	1 (100%)	0	0	0	52(55.2%)	0.008	
	Ulcer		0	21 (30.4%)	0	0	0	0	1 (33%)	22(22.9%)	0.005	
	Wickham striae		0	34 (49.3%)	2 (66%)	1 (100%)	0	0	0	37(38.5%)	0.001	
	Macule		0	4 (5.8%)	0	0	0	0	0	4(4.2%)	0.580	
	Others		0	5 (7.2%)	0	0	0	0	2 (66%)	7(7.3%)	0.580	
Duration of lesion (months)	<1		1 (8.2%)	5 (8.9%)	0	0	0	0	0	6(7.7%)	Fishers exact test	
	1-3		2 (16.2%)	6 (10.7%)	0	0	0	0	0	8(10.3%)		
	3-6		0	5 (8.9%)	1 (33%)	0	0	1 (50%)	0	7(9%)		
	6-12		0	9 (16.1%)	1 (33%)	1 (100%)	0	0	0	11(14.1%)		
	>12		4 (33.8%)	20 (35.7%)	1 (33%)	0	0	1 (50%)	1 (33%)	27(34.6%)		
	Un known		5 (41.8%)	11 (19.6%)	0	0	1 (100)	0	2 (66%)	19(24.4%)		
Dimension (the largest diameter (mm))	0-9		5(38.9%)	9(16.1%)	0	0	1(100%)	1 (50%)	0	16(20.3%)	Chi-squared test	
	10-19		3(23.1%)	7(12.5%)	2(66%)	0	0	0	2(66%)	14(17.7%)		
	20-29		2(15.5%)	11(17.9%)	0	0	0	0	0	16(16.5%)		
	30-39		1(7%)	19(33.9%)	0	0	0	0	0	20(25.3%)		
	40 and more		2(15.5%)	10(19.6%)	1(33%)	1 (100%)	0	1 (50%)	1(33%)	16(20.3%)		

*Other include: dry mouth and restricted mouth opening; Oral Potentially Malignant Disorders (OPMD)

morphology in the precancerous lesions was as follows: plaque in leukoplakia (73%), erosion in OLP (63.8%), plaque and Wickham striae in Lichenoid Contact Reaction (LCR) (66%), plaque and Wickham striae in Drug-Induced Lichenoid Reaction (DILR) (100%), papular appearance in Graft Versus Host Disease (100%), and plaque appearance in PVL (100%).

The longest duration of the presence of a lesion in the oral cavity was over 12 months. In OLP, a significant percentage of lesions were present for more than 12 months, while in leukoplakia, a significant percentage of the patients were unaware of the presence of the lesion. The premalignant lesions had different sizes ranging from less than 1 cm to more than 4 cm. In leukoplakia, the dimensions of the lesions were more frequent less than 10 mm, while in OLP, the size of 30 to 39 mm was more frequent. There was no statistically significant relationship between lesion size and OPMD types ($p=0.06$).

The most common involved sites were buccal mucosa (74%) and then gingiva (35.4%). The most common site of lesion occurrence in patients with leukoplakia was buccal mucosa. In patients with OLP, the most common sites of lesion occurrence were buccal mucosa (79.7%) and gingiva (40.6%). Although the frequency of some sites was higher in some disorders, a statistically significant difference was observed only in the buccal mucosa lesions ($p=0.006$). The most common morphology observed in the patients with leukoplakia was plaque, while in the patients with OLP, erosive and Wickham's striae had the highest frequency in terms of morphology. Also, using Fisher's exact test, a significant relationship was found between plaque, erosion, ulcer, and Wickham's striae morphologies in OPMDs (Table 3).

Discussion

The current study analyzed the data of the patients with OPMDs who visited the Department of Oral Medicine, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran from 2019 to 2021 and were registered in the OPMD registry. According to the results, the most common OPMDs were OLP and leukoplakia.

Age

The study classified the age of the patients into 8 age groups (10 to 89 years), and approximately 80% of the patients were over 40 years old. The results indicated that the age groups of 50 to 59 and 60 to 69 were the most common age groups affected by OPMDs. In various studies on OPMDs, the reported age ranges varied from 18 to 86 years. Most patients with OPMDs were over 50 years old and predominantly male (10,11). In a study by Chher *et al* in Cambodia, a significant association was found between age and the occurrence of OPMDs. The most common OPMDs were leukoplakia and OLP, and the age group of 40 to 60 years (42.7%) was the most affected (12). In the present study, the mean age of the patients was 52.41 ± 14.87 years, and no significant difference was observed between the two genders. However, a study by Pires *et al* showed that the mean age of the patients with OPMDs, mainly OLP, was 58 years, and a significant difference was observed between the mean ages of females (60 years) and males (55 years) (13). The higher prevalence of OPMDs in older age groups may be attributed to the cumulative effect of risk factors that have affected the oral mucosa over the years.

Gender

In the present study, women accounted for a higher percentage (54.2%) of the patients with OPMDs, possibly due to the higher rate of women seeking medical attention for health issues and the higher prevalence of autoimmune diseases in women (14). In the study by Chher *et al* and the meta-analysis conducted by Mello *et al*, men accounted for 65.2 and 59.99% of the patients, respectively (11,12). One reason for this difference could be the type and prevalence of disorders in the two studies, as in the current study, OLP was the most common disorder, while in the study by Chher *et al*, leukoplakia was more prevalent. On the other hand, according to the study by Casparis *et al*, OLP and lichenoid lesions were reported as relatively common disorders in women compared to men (12,15). Similarly, in this study, 62.3% of women were affected by OLP, while men accounted for 77.8% of the patients with leukoplakia. The higher prevalence of certain disorders in men could be due to their

higher exposure to risk factors for oral cancer, such as smoking, alcohol consumption, and sunlight exposure (for lip cancer), as well as men engaging in more outdoor activities compared to women. However, these factors are changing, and currently, women are also involved in risky behaviors (11).

Education level

The highest level of education among the patients with OPMDs was diploma and below diploma.

However, in the present study, no statistically significant association was found between these two factors.

In a study by Chher *et al* in Cambodia, approximately 80% of the patients with OPMDs had primary education (12). On the other hand, in a study by Ferreira *et al*, 65.9% of the workers with OPMDs in Brazil had primary education, and contrary to our findings, there was a significant association between lower education levels and the presence of these disorders (16). A lower level of literacy likely leads to less awareness of risk factors and lower income, resulting in fewer visits to doctors.

Blood group and Rh factor

In the current study, among the blood groups, A+ had the highest frequency (34.5%) among the patients with OPMDs, although no statistically significant association was found between blood groups and types of OPMDs. In a systematic review and meta-analysis by Singh and Purohit, the relationship between blood groups and the incidence of OPMDs and oral cancer was investigated.

Their results demonstrated that similar to this study, individuals with blood group A are at a higher risk of developing OPMDs and oral cancer. Additionally, their meta-analysis found that individuals with blood group O have a lower risk of developing oral cancer (17).

In the current study, 36.4% of the patients had blood group O, although there were many missing data in this category, which may explain the discrepancy in the results.

It is important to note that these findings may vary depending on the population studied and other factors. Further research is required to better understand the relationship between blood groups

and OPMDs.

Risk Factors

In this study, among patients with OPMDs, the risk factors of smoking and alcohol consumption were reported in 24% and 6.3% of the patients, respectively. However, the lower prevalence of alcohol compared to smoking may be due to the patients' reluctance to disclose alcohol consumption and the prohibition of alcohol in society. In this study, 66.5% of the patients with leukoplakia and 13.5% of the patients with OLP were smokers. Various risk factors play a role in the development of OPMDs, with the most important ones being tobacco use, alcohol consumption, hookah use, smokeless tobacco, and substance abuse (opioids, methamphetamine, heroin) (9). In the present study, 14% of the patients with leukoplakia reported alcohol consumption. Premalignant lesions in the floor of the mouth and tongue at the ventral and lateral surfaces have the strongest association with alcohol consumption and are likely considered a risk factor due to prolonged contact with alcohol.

Additionally, alcohol may increase the permeability of oral mucosa to carcinogenic substances, which is observed in relation to tobacco use, altering epithelial proliferation. This process progressively increases the risk of developing oral premalignant lesions (18). In the study by Chher *et al*, smoking alone and the combination of smoking and alcohol consumption increased the risk of OPMDs by 3.74 and 5.69 times, respectively (12).

Location of pre-malignant lesions

In this study, the most common sites of pre-malignant lesions were the buccal mucosa and subsequently the gingival mucosa, which is likely due to the high number of the patients with OLP.

Leukoplakia lesions can occur in any area of the oral cavity. The most common areas include the lateral and ventral surfaces of the tongue, the floor of the mouth, the hard and soft palate, and the gingiva/alveolar mucosa (18). In the study conducted by Singh *et al*, as well as Mello *et al*, similar to the present study, the buccal mucosa was found to be the most common site of pre-malignant lesions in the mouth (19,20). However, in the study by Pires *et al*, the lateral border of the tongue was found to be the

most common site. The variation in the involved areas in different studies may be attributed to population differences or difficulties in distinguishing between leukoplakia and other lesions such as frictional hyperkeratosis clinically and pathologically (13). In the current study, the most common sites of lesions in patients with leukoplakia were the buccal mucosa and the mandibular alveolar mucosa, while in patients with OLP in this study, the buccal mucosa and the gingival mucosa at the buccal surface and the lateral surface of the tongue were the most common sites of lesions. The common sites of leukoplakia in Western countries include the lateral surface of the tongue and the floor of the mouth, while in Asian populations, the buccal mucosa and the mandibular buccal vestibule are usually the most common sites of lesions, often due to the consumption of Betel quid in these areas (21). The most common sites of lesions in patients with OLP are bilateral buccal mucosa, margins and dorsal surface of the tongue, and gingiva, while the palate (hard or soft), lips, and floor of the mouth are less affected by OLP lesions (22).

Type of OLP and symptoms

In the current study, 71.8% of the patients had OLP lesions. In addition, 32.4% of the OLP lesions were asymptomatic and 50% had burning sensation, with erosive and ulcerative types reporting the highest frequency of burning. Reticular/papular lesions are rarely symptomatic and patients are often unaware of their presence, while erythematous and erosive/ulcerative lesions usually cause varying degrees of discomfort or pain (22). The reason why more of the patients had symptomatic lesions may be because many patients only sought dental care when they experienced pain or discomfort. In the current study, in the patients with OLP, erosion, and Wickham's striae showed the highest frequency in terms of morphology. Also, erosive and ulcerative types were the most common types of lichen planus. In Oliveira Alves' study in Brazil, 85% of the lesions were white and the reticular form was the most common type of OLP (23). In Hosagadde's study, the most common clinical manifestation in patients with oral cavity lesions was a white spot on the oral mucosa. Other symptoms included red patches, a combination of red and white patches, pain, burning sensation, and

limited mouth opening (24). In this study, the burning sensation was the most common symptom in the patients with OPMDs. In the patients with OLP in this study, the burning sensation was also the most common symptom, while in the Oliveira Alves' study in Brazil, the pain was the most common symptom, especially in the erosive type (23).

Dimension of the lesions

In the current study, the size of pre-malignant lesions was divided into five categories, ranging from less than 10 mm to more than 40 mm. The highest frequency was related to lesions measuring 30 to 39 mm, followed by those less than 10 mm and those greater than 40 mm.

Regarding the leukoplakia lesions, 38.9% of the lesions were less than 10 mm and 15.5% were greater than 40 mm. In the case of OLP lesions, 33.9% of the lesions measured 30 to 39 mm. In the study by Brouns *et al*, among 176 patients with leukoplakia, about 50% had lesions measuring less than 20 mm, 27% had lesions measuring 20 to 40 mm, and 24% had lesions greater than 40 mm (25). In addition, in the study by Speight *et al*, lesions with dimensions larger than 200 mm² were considered a clinical parameter that increases the risk of pre-malignant lesions turning into malignancy (26).

Conclusion

A significant relationship was observed between gender, clinical symptoms, location of lesions, morphology, and type of OPMDs. Most patients with OPMDs were women with OLP in their buccal mucosa, suffering from burning sensation. Due to the novelty of the OPMD registry, the number of available patients was relatively low.

Further studies are recommended. Since the blood group registration was based on the results of patients' blood tests, it was not possible to register the information for the patients who did not show the test results.

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Conflict of Interest

There was no conflict of interest in this manuscript.

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