



# The Epidemiological Pattern of Premalignant and Malignant Epithelial Lesions in Northeast of Iran: A 43-Year Evaluation

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## Abstract

**Background:** Cancer is one of the most common causes of death in human society. Epidemiological information has an important role in planning for prevention, diagnosis and treatment of cancer in communities.

**Objectives:** The aim of this study was to evaluate epidemiological aspects of the premalignant and malignant epithelial lesions during a 43-year period in faculty of dentistry, Mashhad University of Medical Sciences, Iran.

**Methods:** In this retrospective-descriptive study, all archived records in oral pathology department of dental school, Mashhad University of Medical Sciences in northeast of Iran, during the period of 1971 - 2013 were investigated. A total of 11126 pathology reports were evaluated. Age, gender, primary site and histologic type of the lesions were extracted from patient's records. Data were analyzed using SPSS statistical software (V. 21), Chi-square, Fisher's exact and Mann-Whitney tests.

**Results:** Among 11126 patients, 1066 (9.55%) cases had premalignant and malignant lesions, with mean age of  $53.18 \pm 16.45$ , ranging from 11 to 97 years. Squamous cell carcinoma with 86.2% was the most common malignant tumor and lichen planus with 74.6% was the most common premalignant lesion. 523 (49.5%) of the patients were men and 532 (50.5%) were women. Buccal mucosa was the most frequently involved area in malignant tumors (114 cases) and premalignant lesions (274 cases).

**Conclusions:** The epidemiological pattern of premalignant and malignant lesions in Iran is nearly similar to those reported from other studies with differences in some cases. Also the findings of this study show that the routine examination of oral mucosa is important and emphasize the development of screening policies and primary prevention programs for malignant and premalignant oral lesions.

**Keywords:** Epithelial Malignant Tumor, Premalignant Lesion, Oral Cavity, Epidemiology

## 1. Background

Potentially malignant diseases of the oral cavity, with the risk of developing into squamous cell carcinoma (SCC), have been described in literature as pre-cancer, premalignant and potentially malignant lesions. Also, according to the World Health Organization (WHO), lesions and conditions of the oral mucosa with the possibility of changes toward malignancy are called potentially malignant disorders (PMD) (1). These lesions are divided into 5 categories: erythroplakia, lichen planus, oral submucosus fibrosis, actinic cheilitis and leukoplakia. Early diagnosis and proper

treatment of PMD is crucial in preventing OSCC (1). Leukoplakia is one of the most common premalignant lesions of the oral cavity. According to some reports, leukoplakia, with a risk of 4%, and erythroplakia, with a risk of 90%, can develop into squamous cell carcinoma, which is the most common oral cancer (2).

Oral cancer is one of the most common types of cancers and a major health problem in most parts of the world, especially in developing countries. Its annual prevalence has been reported as 275 thousand cases, and about two-third of them are observed in developing countries (3). To-

bacco and alcohol are its main risk factors (4). The annual prevalence of oral cancer and its mortality differs significantly in different races and countries. This can be due to variations in lifestyle, diet, and exposure to different risk factors (5). In the world map of prevalence of this cancer, Iran is located near countries such as Pakistan, India, and Bangladesh (3). According to the WHO, in developing countries, oral cancer is the sixth and tenth common cancer in men and women, respectively (6). Oral cancer is twice more prevalent in men than it is in women. However, the male: female ratio has decreased from 6:1 in 1950 to 2:1 today (6), which is probably due to increased female exposure to carcinogens such as tobacco, alcohol, and sun exposure (7). The prevalence of oral and lip cancer in Iran in 2012 was reported 2.2 and 1.8 in men and women, respectively (8).

Considering the high prevalence of this cancer in Asian countries neighboring Iran such as Afghanistan, Pakistan, and India, the prevalence of this malignancy seems to be significant in Iran compared to European countries (9). Limited studies have been conducted on the frequency of oral mucosa lesions and the related factors in the Iranian population (10).

Moreover, information regarding the prevalence of cancer, forms the scientific basis for planning the prevention, diagnosis and treatment of cancer in communities (6).

## 2. Objectives

The aim of this study was to evaluate the prevalence of epithelial malignant and premalignant lesions over a period of 43 years in patients who referred to Mashhad dental school, Iran (One of the largest referral centers in North-eastern Iran).

## 3. Methods

In This retrospective study, archives from 1971 to 2013 of oral and maxillofacial pathology department in dental school, Mashhad University of Medical Sciences, Iran were reviewed. After reviewing 11126 pathologic reports, all oral and maxillofacial biopsies related to epithelial malignant and premalignant lesions were selected by sampling census method and their diagnoses were confirmed by microscopic reevaluation. The cases with inadequate or invalid demographic information and the cases with unverified histopathological diagnosis were excluded in this study. Cases were divided into malignant and premalignant lesions and all of them were categorized according to Neville classification (11). Clinicopathological data including age,

sex, primary site and histologic type of the lesions were recorded in the checklist. Also the ages of the patients were converted into categorical variables.

Data were analyzed using SPSS software (SPSS Inc, Chicago, IL), Chi-square, Fisher's exact and Mann-Whitney tests. P values less than 0.05 were considered statistically significant.

## 4. Results

In this retrospective study, of the 11126 available cases in archives of Mashhad dental school from 1971 to 2013 (43-year period), 1066 cases (9.55%) (95% confidence interval (CI), 7.79 - 11.31) were premalignant and malignant lesions. 519 cases (48.55%) (95% CI, 46.5 - 52.5) were associated with malignant tumors and 547 cases (51.45%) (95% CI, 47.5 - 53.5) were premalignant lesions.

The mean age of patients was  $53.18 \pm 16.45$ , ranging from 11 to 97 years. The mean age of the patients with malignant and premalignant lesions was  $59.13 \pm 15.07$  and  $47.52 \pm 15.63$ , respectively.

Malignant tumors were more common in seventh decade of life. But the premalignant lesions were more common in the fifth decade of life and two-third of the patients with dysplastic lichen planus lesions were 30 - 60 years old. According to Mann-Whitney test, there was a significant association between age and malignant tumors; also there was a significant association between age and premalignant lesions ( $P < 0.001$ ).

Out of the cases, 523 (49.5%) of cases were men and 532 (50.5%) cases were women. Malignant and premalignant lesions were more common in male (52%) and female (52.8%), respectively. In malignant lesions, highest frequency of the SCC and verrucous carcinoma cases occurred in males but in premalignant lesions most of the lichen planus and leukoplakia cases were seen in females and males, respectively. However, dysplasia changes were more common in females. According to Chi-square test, there was no significant association between gender and malignant tumors ( $P = 0.336$ ), but there was a significant association between gender and premalignant lesions ( $P = 0.009$ ).

Of all malignant tumors, most were located peripherally with the highest frequency of 114 cases (31.5%) in buccal mucosa followed by 93 cases (25.5%) in tongue, 58 cases (15.6%) in gingiva, 37 cases (10.7%) in labial mucosa, 24 cases (6.6%) in floor of mouth and 19 cases (4.7%) in palate. Six cases of malignant tumors were centrally which 5 cases of them were located in the mandible. Obviously all of the premalignant lesions were located peripherally, with the highest frequency of 274 cases (57.3%) being in buccal mucosa, followed by 103 cases (21.5%) in tongue, 47 cases (9.8%)

in labial mucosa, 28 cases (5.9%) in gingival, 17 cases (3.6%) in floor of mouth and 7 cases (1.5%) in palate. Fisher's exact test did not show a significant association between location and malignant tumors ( $P = 0.103$ ), but this association in premalignant lesions was significant ( $P < 0.001$ ).

#### 4.1. Epithelial Malignant Tumors

SCC was the most common type of epithelial malignant tumor, involving 445 cases of malignant lesions (86.2%) (95% CI, 84.13 - 88.27), also the prevalence of this cancer in studied population was 3.9%. Of the cases, histopathologically, most cases of this cancer were grade I (45.16%), followed by grade II (29.21%), grade III (7.19%) and unspecified cases (18.42%). The mean age of patients with SCC was 58.91, which was more common in males (51.1%). Buccal mucosa was the most common location (96 cases, 31%) in oral SCC, followed by tongue (89 cases, 28.6%). The distribution of other malignant tumors according to age, gender and location are shown in [Tables 1 - 3](#).

#### 4.2. Premalignant Lesions

Lichen planus with 408 (74.6%) (95% CI, 71.5 - 76.76) was the most common lesion in this group. Erosive type accounted for 62 (15%) of all lichen planus cases, followed by atrophic 38 (9%), bullous 22 (5%) and unspecified 276 (70%). About one third of the premalignant lesions (130 cases) had dysplasia changes. The mean age of patients with oral lichen planus was 44.65 and females (55.1%) were affected more than males (44.9%). Buccal mucosa was the most common location (228 cases, 62.9%) in oral lichen planus, followed by tongue (69 cases, 19.06%). The distribution of other premalignant lesions according to age, gender and location are shown in [Tables 1 - 3](#).

## 5. Discussion

Cancer is for a major cause of death in human societies. It is the third cause of mortality In Iran (3). This study evaluated the prevalence of malignant and premalignant epithelial lesions over a period of 43 years in patients who referred to Mashhad Dental School.

Among the total 1066 lesions that were examined in the present study, 519 (48.5%) cases were malignant and 547 (51.4%) cases were premalignant lesions. The most common premalignant and malignant lesions were lichen planus and SCC with 408 (74.6%) and 445 (86.2%) cases, respectively.

Similar to our study, in a research which was conducted by Aminzadeh et al. (12), the most frequent oral malignancy group was related to epithelial lesions (72%), and the most common malignancy was reported to be squamous

cell carcinoma, which comprised 90% of epithelial lesions. Also, in a 10-year study by Razavi et al. (6), SCC was reported as the most prevalent oral cancer (60%) and in Shahsavari et al. study (10), the most common oral lesions were epithelial lesions, and SCC (51%) was the most frequent oral cancer. This ratio of oral cancer has been reported about 40% - 60% in African countries and 98% in Australia. Thus, planning for effective treatment and prevention of oral cancer should be a priority for the health care system especially in the field of dentistry (3).

Unlike the present study, among premalignant lesions, Amanat et al. (13) and Sousa et al. (14) reported leukoplakia as the most prevalent premalignant lesion. It is estimated that about 50% of oral cancers occur on the basis of leukoplakia, so clinical attention to this fact is of great importance for prevention of oral cancer (1). But unfortunately, little attention is paid to this issue; therefore, it is recommended that all idiopathic white plaque lesions that remain 3 - 4 weeks after removal of any factor should be examined cytologically and histologically if required (15).

According to our results, among SCC cases, well differentiated SCC was the most frequent (45.16%) histopathological type that is consistent with the study by Anis et al. (16) and that of Andisheh-Tadbir et al. (17). Inconsistent with the results of our study, Effiom et al. (18) and Hernandez-Guerrero et al. (19) reported poorly differentiated SCC (47.6%) and moderate differentiated SCC (61.2%) as the most prevalent histological types of SCC, respectively.

#### 5.1. Sex

In the present study, the frequency of SCC, as the most common epithelial malignancy, was slightly higher in men compared to women (51.1% vs. 48.9%). It is important to point out that with increased malignancy criteria (increased histopathological grade), the frequency of the lesions increased in men and decreased in women.

Among the samples archived in the oral and maxillofacial pathology department of dental school, Mashhad University of Medical Sciences, the majority of previous studies also reported higher prevalence of SCC in men compared to women. Also the results of other studies are consistent with the present study (6, 17, 18, 20-23). One possible explanation for the higher incidence of oral cancer in men can be higher consumption of tobacco and alcoholic products. In this regard, planning for an effective intervention to reduce the consumption of these substances in men is required. Another reason could be high exposure of men to factors such as sunlight, which can lead to cancer of the lip. But also in recent decades the growing tendency of women to consumption of alcohol and cigarettes throughout the world leads to a reduction of male to female ratio in oral cancer (3).

**Table 1.** Distribution of the Histological Types of Malignant and Premalignant Lesions by Age Group<sup>a,b</sup>

Type of Lesion	Frequency	Age Group									Total
		10 - 19	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 79	80 - 89	90 - 99	
<b>Malignant</b>	519 (100)	5 (1.2)	26 (4.8)	35 (6.5)	77 (15.4)	110 (21.8)	144 (28.9)	89 (17.8)	18 (3.5)	1 (0.1)	505 (100)
SCC	445 (86.2)	3 (0.7)	23 (5.3)	30 (7)	69 (15.7)	93 (21.5)	129 (30)	71 (16.4)	14 (3.2)	1 (0.2)	433 (86.3)
Verrucous carcinoma	57 (10.6)	0	1 (1.8)	3 (5.5)	3 (5.5)	15 (27.3)	12 (21.8)	17 (30.9)	4 (7.3)	0	55 (11)
Basal cell carcinoma	7 (1.3)	0	0	2 (28.6)	2 (28.6)	1 (14.3)	2 (28.3)	0	0	0	7 (1.4)
Spindle cell carcinoma	3 (0.6)	2 (66.7)	0	0	1 (33.3)	0	0	0	0	0	3 (0.5)
Clear cell carcinoma	4 (0.7)	0	0	0	2 (50)	0	1 (25)	1 (25)	0	0	4 (0.8)
Melanoma	3 (0.6)	0	2 (3.6)	0	0	1 (14.3)	0	0	0	0	3 (0.4)
<b>Premalignant</b>	547 (100)	17 (3.3)	64 (12.3)	104 (20)	120 (23.1)	112 (21.5)	62 (11.9)	33 (6.3)	6 (1.2)	2 (0.4)	520 (100)
Lichen planus	408 (74.6)	17 (4.3)	55 (14.1)	92 (23.5)	97 (24.9)	76 (19.4)	38 (9.7)	13 (3.3)	2 (0.5)	1 (0.3)	391 (75.1)
Leukoplakia	115 (21)	0	7 (6.5)	11 (10.3)	15 (14)	33 (30.9)	19 (17.8)	18 (16.8)	4 (3.7)	0	107 (20.5)
Epithelial dysplasia	22 (4)	0	2 (10)	1 (5)	8 (40)	3 (15)	5 (25)	0	0	1 (5)	20 (3.8)
Erythroplakia	2 (0.4)	0	0	0	0	0	0	2 (100)	0	0	2 (0.3)

<sup>a</sup>Values are expressed as No. (%).<sup>b</sup>In 41 cases, age of patients was not recorded in the patient's record.**Table 2.** Distribution of the Histological Types of Malignant and Premalignant Lesions by Gender<sup>a,b</sup>

Gender	Type of lesion											
	Malignant							Premalignant				
	SCC	V.C	BCC	Spindle, Cell. Ca	Clear, Cell. Ca	Melanoma	Total	Lichen Planus	Leukoplakia	Epithelial Dysplasia	Erythroplakia	Total
<b>Female</b>	216 (48.9)	24 (42.11)	5 (71)	1 (33)	1 (25)	1 (33)	248 (48)	222 (55.1)	47 (41.6)	15 (71.4)	0	284 (52.7)
<b>Male</b>	227 (51.1)	33 (57.9)	2 (29)	2 (67)	3 (75)	2 (67)	269 (52)	180 (44.9)	66 (58.4)	6 (28.6)	2 (100)	254 (47.3)
<b>Total</b>	443 (100)	57 (100)	7 (100)	3 (100)	4 (100)	3 (100)	517 (100)	402 (100)	113 (100)	21 (100)	2 (100)	538 (100)
<b>P value</b>				0.336						0.009		

<sup>a</sup>Values are expressed as No. (%).<sup>b</sup>In 11 cases, gender of patients was not recorded in the patient's record.**Table 3.** Distribution of the Histological Types of Malignant and Premalignant Lesions by Location<sup>a,b</sup>

Type of Lesion	Frequency	Location									Total	P Value
		Buccal Mucosa	Tongue	Gingiva	Labial Mucosa	Floor of Mouth	Palate	Sinuses	Intraosseous	Others		
<b>Malignant</b>												0.103
SCC	519 (100)	114 (31.5)	93 (25.5)	58 (15.6)	37 (10.7)	24 (6.6)	19 (4.7)	7 (1.9)	6 (1.6)	9 (1.9)	367 (100)	
Verrucous carcinoma	57 (10.6)	17 (40.5)	4 (9.5)	10 (23.8)	7 (16.7)	3 (7.1)	1 (2.4)	0	0	0	42 (11.6)	
Basal cell carcinoma	7 (1.3)	0	0	0	0	0	0	0	0	6 (1.6)	6 (1.6)	
Spindle cell carcinoma	3 (0.6)	0	0	2 (100)	0	0	0	0	0	0	2 (0.5)	
Clear cell carcinoma	4 (0.7)	1 (25)	0	2 (50)	0	0	0	0	1 (25)	0	4 (1.1)	
Melanoma	3 (0.6)	0	0	1 (33)	0	0	2 (6.7)	0	0	0	3 (0.6)	
<b>Premalignant</b>	547 (100)	274 (57.2)	103 (21.5)	28 (5.8)	47 (9.8)	17 (3.5)	7 (1.5)	1 (0.2)	0	1 (0.2)	479 (100)	< 0.001
Lichen planus	408 (74.6)	228 (62.98)	69 (19.06)	20 (5.52)	35 (9.66)	4 (1.10)	4 (1.10)	0	0	1 (0.2)	362 (75.6)	
Leukoplakia	115 (21)	40 (41.7)	27 (28.1)	7 (7.3)	10 (10.4)	10 (10.4)	2 (2.1)	0	0	0	96 (20)	
Epithelial dysplasia	22 (4)	6 (31.6)	7 (36.8)	1 (5.3)	2 (10.5)	2 (10.5)	0	1 (5.3)	0	0	19 (4)	
Erythroplakia	2 (0.4)	0	0	0	0	1 (50)	1 (50)	0	0	0	2 (0.4)	

<sup>a</sup>Values are expressed as No. (%).<sup>b</sup>In 220 cases, location of the lesions was not recorded in the patient's record.

Our results regarding the verrucous carcinoma samples showed high prevalence in men (57.9%) compared to women (42.11%) in this group of the lesions, which is inconsistent with the findings of Candau-Alvarez et al. (24).

The findings of this study indicate that premalignant

lesions, especially lichen planus, as the most common premalignant lesion, is more frequent in women. This is consistent with some studies (25, 26). But in Cebeci et al. study in Turkish, no sex predominance in oral lichen planus was reported (27).

The frequency of leukoplakia in the present study was more in men compared with women (58.4% vs. 41.6%), which is inconsistent with the study by Amanat et al. (13).

### 5.2. Age

In this study, the mean age of the patients was 53.18 years, ranging from 11 to 97 years, and most of the patients were in the seventh decade of life which is similar to the results from Razavi et al. (6).

However, the mean age of patients with SCC in the Anis et al. study (16) and studies conducted by Effiom et al. (18) in Nigeria and Hernandez-Guerrero et al. (19) in Mexico were 54.9 years, 45.3 and 62.5 years, respectively. Also other studies in Iran reported the mean ages of 43.17 and 56.9 years in patients with SCC (10, 17). In our study, the mean age of patients with SCC was 58.9.

According to results of the present study, the prevalence of SCC, as the most prevalent oral malignancy in this part of the country, occurs at a higher age range compared with other areas, which can be due to racial and geographical differences including dietary and health habits and other factors.

In this study, the mean age of patients with verrucous carcinoma was reported as 64.13 years, which was similar to results in a study by Candau-Alvarez et al. (24).

Budimir et al. (26) reported the mean age of patients with lichen planus as 67.23 years that is somewhat older than patients of OLP in present study (44.65), because most patients in Richter et al. study were in 5th or 6th decade of their life.

### 5.3. Location

Among the malignant lesions that were studied in the present study, most of them were located peripherally and 6 cases were located centrally. In a study with smaller sample size, Delavarian et al. (22) reported 41 peripheral and 3 central cases of oral cancer, respectively. In our study, the majority of SCC cases were in the buccal mucosal (31%) followed by tongue (28.6%). Most previous studies conducted by Hernandez-Guerrero et al. (19), Monteiro et al. (20) and Delavarian et al. (22), reported tongue as the most common site of SCC, while in other studies (6, 18, 21) gingival was the most common site of SCC, which is inconsistent with our finding. Thus, according to the distribution of oral cancer in different sites, it is not recommended to focus only on treatment and prevention plans based on one place; all locations must be potentially considered as oral cancer, but with more focus on areas such as the tongue which is more likely to be involved.

The most prevalent site of verrucous carcinoma samples was buccal mucosal (40.5%). Similarly, Candau-Alvarez

et al. (24) reported buccal mucosa as the first site of involvement in verrucous carcinoma cases.

Among the lichen planus lesions examined in this study, buccal mucosa (63%), tongue (19%), labial (9.7%), gingiva (5.5%) floor of mouth and palate (1.1%) were the most prevalent sites of involvement respectively. Similar to our study, Budimir et al. (26) reported that buccal mucosa as the most common site of involvement in the lichen planus lesions.

Also in our study, in leukoplakia cases, buccal mucosa and the tongue were the most commonly affected sites, but Amanat et al. (13) reported the tongue as the most common site of involvement in their study. It is important to mention that among dysplastic changes in this study, buccal mucosa, tongue, and floor of mouth were the most prevalent sites, respectively. Furthermore, it was reported that tongue and floor of mouth are at high risk for transformation into malignancy in leukoplakia.

The limitations of this study include inability to investigate the major risk factors associated with cancer, such as smoking, alcohol consumption and special dietary habits. Also, we could not investigate outcome of patients with premalignant and malignant lesions and effective factors, which was due to lack of relevant data.

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### Footnotes

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