

## Epidemiology of oral and pharyngeal cancers: A retrospective study in Kermanshah, Iran

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### Original Article

#### Abstract

**BACKGROUND AND AIM:** The aim of this study was to determine the incidence and relative frequency of oral and pharyngeal cancers in Kermanshah, Iran, from March 1993 until March 2006.

**METHODS:** The data used in this epidemiologic study were extracted directly from pathology records registered in 12 (all) public and private pathology centers of Kermanshah province during the 13-year study period. The medical data of 13,323 cases of cancer were studied.

**RESULTS:** During the 13-year period of this study, 350 new malignant cases occurred in the oral cavity and pharynx. 247 (70%) were men and 103 (30%) were women. The mean age for oral and pharyngeal cancers was 57 [standard deviation (SD) = 17.09] with male to female ratio 2.39:1. The most common oral and pharyngeal cancers were squamous cell carcinoma (SCC) with 283 patients. 211 (74.6%) of the patients were men and 72 (25.4%) of them were women; the mean age of SCC was 60 (SD = 16) with male to female ratio 2.93:1. The two most common sites of involvement were lips [166 (47.5%)] and tongue [25 (7.14%)]. The overall incidence rate of oral and pharyngeal cancers was 1.47 per 100000 populations.

**CONCLUSION:** In summary, the incidence risk of oral and pharyngeal cancers in people living in Kermanshah province is similar to the most other provinces of Iran. However, this study showed that the rank of oral and pharyngeal cancers among males (9<sup>th</sup> most common cancer) is low when compared to other regions of Iran and other countries such as India, Australia, and France.

**KEYWORDS:** Epidemiology; Oral Cancer; Pharyngeal Cancer; Iran

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**O**ropharyngeal cancers (OPCs), globally, are the sixth most common cancer.<sup>1,2</sup> OPC includes tumors of the lips, tongue, gingiva (gums), floor of the mouth, soft and hard palate, tonsils, salivary glands, oropharynx, nasopharynx, hypopharynx, and other less frequent sites.<sup>3-6</sup> Squamous cell carcinoma (SCC) is the most common malignant neoplasm of the oral cavity and represents

about 90% of all oral malignancies.<sup>7,8</sup> It is necessary to remind that variation of OPCs per geographic region around the world is large. The incidence rate is higher in developed countries than in developing countries. However, in countries of Southern Asia, such as India, oral cancer is the most common cancer affecting males and third cancer affecting females, after breast and cervix uteri tumors.<sup>9</sup>

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OPCs are resulted mainly due to the widespread use of tobacco and alcohol.<sup>2,10</sup> Other risk factors such as viral infection (human papilloma virus, Epstein-Barr virus, and human T-cell lymphotropic virus), nutritional deficiency (iron, vitamin A and C), environmental factors, familial aggregation, and genetic susceptibility, could also have specific effect on the incidence of oral and pharyngeal cancers.<sup>2,4,9,11,12</sup> OPCs can be seen in places where tobacco is consumed (chewing or smoking) with alcohol or without it. The incidence of OPCs depends on gender, age, culture, and even in developed countries.<sup>1,2</sup> For example, the use of betel quid is common in parts of Asia that the major risk factor for oral cancer and cancer incidence there are high.<sup>11</sup> In the majority of studies in Iran, smoking including cigarette, hookah, and tobacco consumption was found to be a risk factor.<sup>13</sup>

Due to the high level of morbidity and mortality oral cancer in the world and the variety of its incidence in different geographical areas and even in some cases in an area due to different age groups, gender, habits, is very variable.<sup>2,7,11</sup> Hence, should be highlighted to epidemiology of it to catch data that is required for effective programs and interventions. Considering lack of epidemiological study in Kermanshah, the researchers conducted this study.

Kermanshah is located in the western part of the Islamic Republic of Iran, bordering by Iraq and has a large population of Kurdish ethnics. The total population of the province is 1800000, nearly half living in the provincial capital, Kermanshah city.<sup>14</sup>

## Methods

Based on nature of research and due to principles highlighting in Medline, this is cross-sectional study that surveyed for the first time in Kermanshah province from 1993 to 2006 in one of the above-mentioned sites.

As shown in table 1, all tumors were categorized according to the International Classification of Diseases (ICD-10) codes for

morphology.<sup>15</sup> The case selection for this study included any diagnosed oral SCC (OSCC) and other malignant neoplasms. Tumors of the skin of the lip, hematologic malignancies, and metastatic tumors to the jaws or oral mucosa were excluded from this study. Since there was no comprehensive cancer registry in Kermanshah province until 2002, the data used in this epidemiological study were extracted directly from pathology records registered in 12 public and private pathology centers of Kermanshah province by oral medicine assistant. The cases with grossly incomplete information and double registered cases were carefully reviewed and excluded from the study.

The method applied is a description of variables including sex, age, and histological type. Population estimates were derived based on data obtained from 1996 census and population growth rate, provided by the Iranian Census Bureau. The crude and age-adjusted incidence rates for oral and pharyngeal cancers, standardized to the world population, were calculated and expressed per 1 million populations. Meanwhile, the frequency and ranking of the 10 most common body cancers were calculated. To assess the effects of age and sex and also checking the time variation, the risks ratio was estimated using negative binomial method. The 95% confidence intervals (CI) were estimated for incidence risks ratio. The 95% CI of all rates were analyzed using STATA data analysis and statistical software (version 8, StataCorp LP, Texas, USA)

## Results

In Kermanshah, during the study period from 1993 to 2006, a total number of 13323 new cancer cases were diagnosed. The most common cancer was skin malignancy [16.7% (n = 2235)]. The 19 most common OPCs are presented in table 1. Among males, the first two outstanding cancers were stomach (10.0%) and bladder (6.3%), whereas in females these ranked third and ninth, respectively.

**Table 1.** Site description of the oral cavity and pharynx

ICD-10	Site	Includes
C00	Lip	External upper and lower lip, inner aspect of upper and lower lip, commissure of lip
C01	Tongue	Base of tongue
C02	Tongue	Dorsal surface of tongue, border of tongue, ventral surface of tongue, anterior two-thirds of tongue
C03	Gum	Upper and lower gum, alveolar (ridge) mucosa gingiva
C04	Floor of mouth	Anterior floor of mouth, lateral floor of mouth
C05	Palate	Hard and soft palate, uvula
C06	Mouth unspecified	Buccal mucosa, vestibule of mouth, retromolar area
C07	Parotid gland	Parotid gland
C08	Unspecified major salivary gland	Submandibular gland, sublingual gland
C09	Tonsil	Tonsillar fossa, tonsillar pillar (anterior) (posterior)
C10	Oropharynx	Vallecula, anterior surface of epiglottis, lateral and posterior wall of oropharynx, branchial cleft
C11	Nasopharynx	Anterior and posterior wall of nasopharynx, superior and lateral wall of nasopharynx
C12	Pyriform sinus	Pyriform fossa
C13	Hypopharynx	Postcricoid region, aryepiglottic fold, hypopharyngeal aspect, posterior wall of hypopharynx
C14	Other and ill-defined sites	Pharynx, waldeyer's ring

ICD: International Classification of Diseases

In females, breast cancer was the most common malignancy (8.5%). During the 13-year period of this study, 350 (2.6%) new malignant cases occurred in the oral cavity and pharynx. The majority of oral and pharyngeal cancers (80.9%) were OSCCs group; approximately, 19.1% of cancers were other tumors. 67.0% of cancers occurred in the oral cavity, 22.0% in the pharyngeal region, and 11.0% in the salivary glands. Other tumors histological types included: lymphomas (7.4%), nasopharyngeal carcinoma (4.3%), mucoepidermoid carcinoma (3.7%), adenoid cystic carcinoma (3.4%), and adenocarcinomas (2.6%) (Table 2). The male to female ratio for OSCC and other

tumors are 2.93:1 and 3:1, respectively.

About 268 cases (76.6%) were SCC (excluding 15 cases of nasopharyngeal carcinoma) (Table 2). The most common site for this histologic type in the oral cavity was the lip [(62.0%), n = 166] followed by the tongue [(9.3%), n = 25] (Table 3).

In this study, OPCs occurred in patients between 1 and 96 years of age. The mean age for OPCs was 57 [standard deviation (SD) = 17.09]. The mean age of OPCs was 60 among males (SD = 16) and 54 in females (SD = 18). Statistically significant differences were found in the risk of OPCs between male and female (P = 0.001); the incidence of OPCs was 1.47 per 100000 populations (Figures 1 and 2).

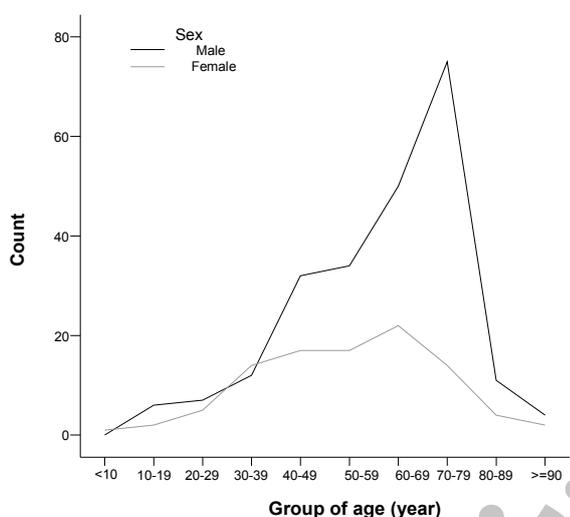
**Table 2.** Distribution of oral cavity and pharynx cancers classified by sex and histological types

Histology	Male	Female	Total
	n (%)	n (%)	n (%)
SCC	199 (74.3)	69 (25.7)	268 (76.6)
Lymphoma	16 (61.5)	10 (38.5)	26 (7.4)
Nasopharyngeal carcinoma	12 (80.0)	3 (20.0)	15 (4.3)
Mucoepidermoid carcinoma	7 (53.8)	6 (46.2)	13 (3.7)
Adenoid cystic carcinoma	4 (33.3)	8 (66.7)	12 (3.4)
Adenocarcinoma	5 (55.6)	4 (44.4)	9 (2.6)
Acinic cell tumor	1 (50.0)	1 (50.0)	2 (0.6)
Malignant melanoma	0 (0.0)	1 (100)	1 (0.3)

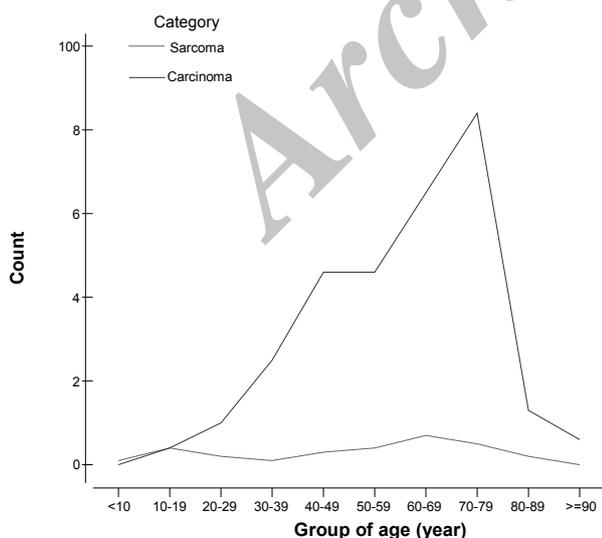
SCC: Squamous cell carcinoma

**Table 3.** Mean age and sex distribution of oral squamous cell carcinoma (SCC) classified by location

Site	Mean age (year)		Male	Female	Total	M/F ratio
	Male	Female	n (%)	n (%)	n (%)	
Upper lip	68	59	4 (2)	10 (20)	14 (7)	0.4
Lower lip	65	57	102 (63)	18 (35)	120 (56)	5.7
Lip unspecified	62	64	29 (18)	3 (3)	32 (15)	9.6
Lip, total	65	60	135 (83)	31 (61)	166 (78)	4.35
Tongue	63	69	14 (9)	11 (22)	25 (12)	1.3
Gingiva	60	82	4 (3)	1 (2)	5 (2)	4
Floor of mouth	81	58	2 (1)	2 (4)	4 (2)	1
Palate	65	33	3 (2)	3 (6)	6 (3)	1
Buccal mucosa	40	0	1 (1)	0 (0)	0 (1)	-
Oral, unspecified	58	58	3 (2)	3 (6)	6 (3)	1
Total	62	60	162 (100)	51 (100)	213 (100)	3.17

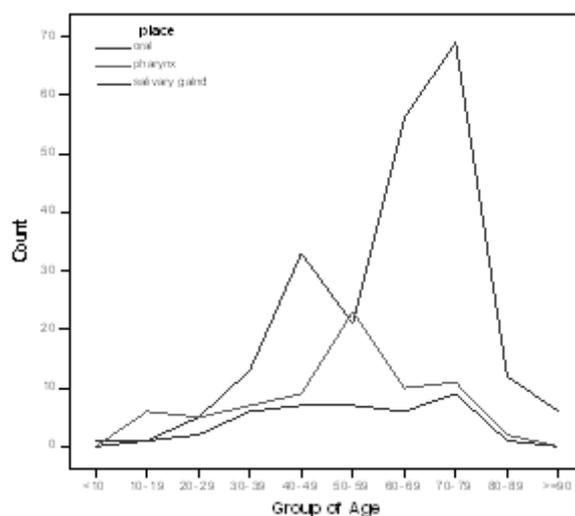


**Figure 1.** The temporal variation of the annual incidence of pharyngeal and oral cancers among males and females

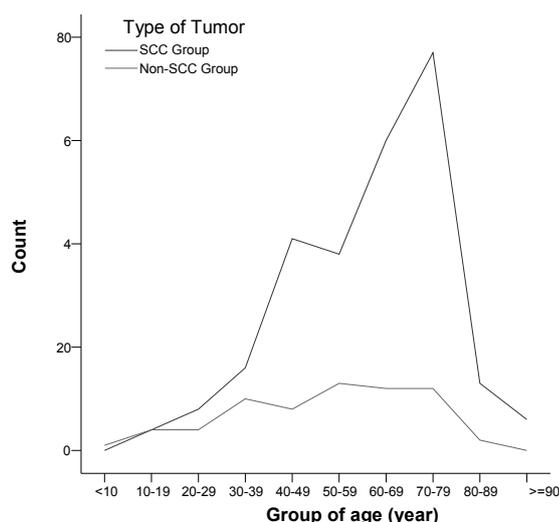


**Figure 2.** Age distribution of oral and pharyngeal cancers divided by category

It is necessary to highlight OPCs were the 12<sup>th</sup> common cancers of the body (the 9<sup>th</sup> in the male and the 13<sup>th</sup> in females). After age and sex adjustment, the incidence increased in both genders types and location (Figures 3 and 4). The increasing risks affected male population more than the double. The most common type of OPCs was SCC [80.9% (n = 283)]. SCC of the oral cavity and pharynx occurred in patient between 15 and 96 years of age. The mean age of oral and pharyngeal cases was 60.34 (SD = 16); although the age of 20 cases was not recorded. Of the 263 remaining patients, 38 cases (14.5%) were young adults (< 40 years of age) (Table 4). Considering the annual incidence, overall, average annual incidence rate for 1993-2006 was 1.2 cases per 100000 persons.



**Figure 3.** The temporal variation of the annual incidence of pharyngeal and oral cancers divided by place



**Figure 4.** Age distribution of oral and pharyngeal cancers divided by type of tumor

There was no regular pattern in the incidence rate of oral and pharyngeal SCC during this period.

The incidence of oral SCC was 0.9 per 100000 populations. Considering population, the highest incidence rate was recorded in 2000 (1.51 per 100000) and the lowest

incidence rate in the years 1995 and 1997 (0.33 per 100000). In this study, the most common site of oral SCC was a lip (in 166 patients), representing 78.0% of all oral SCC of these. 135 cases (81.32%) were found among males and 31 cases (18.7%) in females. Lower lip was affected in 120 cases (72.3%) and upper lip in 14 cases (8.4%), the exact site of 32 (19.0%) cases of lip cancer was unspecified. It was observed that the upper lip was more frequently affected among women than among men (19.6 vs. 2.4%), while lesions of the lower lip predominated among men (63.0 vs. 35.2%). All new lip cancers diagnosed in the period 1993-2006 were considered that lower lip cancer was almost 8.06 times than the upper lip cancers. The overall male to female ratio was 4.3:1. However, when specific subsite data were analyzed by gender, the male to female ratio was 0.5:1 for the upper lip and 5.7:1 for the lower lip. Considering the age factor, the patient's age at the time of diagnosis ranged from 22 to 96 years.

**Table 4.** Crude and relative frequency of oropharyngeal from March 1993 to March 2006

Group of age	Sex	Oral	Pharynx	Salivary gland	Total
		Count [n(%)]	Count [n(%)]	Count [n(%)]	Count
< 10 years	Female	1 (100)	-	-	1
10-19 years	Male	1 (17)	5 (83)	-	6
	Female	-	1 (50)	1 (50)	2
20-29 years	Male	2 (29)	4 (57)	1 (14)	7
	Female	3 (60)	1 (20)	1 (20)	5
30-39 years	Male	6 (50)	5 (42)	1 (8)	12
	Female	7 (50)	2 (14)	5 (36)	14
40-49 years	Male	23 (72)	6 (19)	3 (9)	32
	Female	10 (59)	3 (18)	4 (24)	17
50-59 years	Male	14 (41)	16 (47)	4 (12)	34
	Female	7 (41)	7 (41)	3 (18)	17
60-69 years	Male	40 (80)	7 (14)	3 (6)	50
	Female	16 (73)	3 (14)	3 (14)	22
70-79 years	Male	61 (81)	7 (9)	7 (9)	75
	Female	8 (57)	4 (29)	2 (14)	14
80-89 years	Male	9 (82)	1 (9)	1 (9)	11
	Female	3 (75)	1 (25)	-	4
90-99 years	Male	4 (100)	-	-	4
	Female	2 (100)	-	-	2
Unknown	Male	13 (81)	2 (13)	1 (6)	16
	Female	3 (60)	2 (40)	-	5
Total	Male	173 (70)	53 (21)	21 (8)	247
	Female	60 (58)	24 (23)	19 (18)	103

SCC of the tongue was next to that of the lip. 25 patients suffered from tongue SCC represented 7.7% of all oral SCC cases. The male to female ratio was 1.25:1 (Table 5).

**Table 5.** Distribution of location of oropharyngeal cancers (OPCs) classified by sex

Site	Male	Female
Upper lip	5	10
Lower lip	103	18
Lip unspecified	29	3
Tongue	14	11
Gum	5	2
Floor of the mouth	2	3
Palate	7	6
Buccal mucosa and vestibule	2	-
Parotid gland	13	9
Submandibular gland	5	1
Sublingual gland	-	3
Unspecified major salivary gland	3	4
Tonsil	9	3
Oropharynx	1	3
Nasopharynx	23	8
Piriform sinus	5	1
Hypopharynx	9	6
Oral unspecified	4	5
Pharynx unspecified	5	5
Total	247	103

In this study, cancer of gingiva represented 2.0% of all oral cancers. The male to female ratio was 2.5:1. The total number of OPC and oral SCC in the other sites show on tables 3 and 5, respectively.

## Discussion

In this study, skin cancer was the most common form (16.7%) of all cancers. The male to female ratio was 1.48:1. As a comparison, an epidemiological study in Kerman, Iran, showed that skin cancer had been the most common form (19.1%) of all cases.<sup>16</sup> In another study in Tehran, Iran, skin cancer was the most common form, 23.0% of all cases. The male to female ratio was 2:1.<sup>17</sup>

Other geographic areas with high incidences are eastern, Western and Southern Europe, Australia, New Zealand, and Malaysia.<sup>9</sup> In this study, the incidence of oral and pharyngeal cancers in Kermanshah province was 1.47/100000. The annual incidence of oral and

pharyngeal cancers showed a little change during the period of study.

The highest incidence was in the year 2000 (2.22/100000, M = 1.51, F = 0.71) and the lowest incidence in the year 1995 (0.56/100000, M = 0.45, F = 0.11). Overall, the incidence rate was low compared to other countries in the world, such as France (12.4 per 100000),<sup>18</sup> Finland (M = 12.5, F = 3.9 per 100000),<sup>19</sup> United States (8.3 per 100000),<sup>3</sup> and Australian (Men = 17.5/100000).<sup>20</sup>

Among eastern European countries, the highest combined rates among males were observed in Slovakia (19.7/100000) and Slovenia (18.9/100000).<sup>18</sup> Asia showed the broadest range in incidence rates of OPCs compared to this study. Some countries, such as India (20 per 100000) and Philippines (7.1 per 100000), were the highest recorded countries.<sup>18</sup> In Iran, the incidence of OPCs was found to be 1.13/100000 in Shiraz, Iran,<sup>21</sup> 1.19/100000 in Kerman.<sup>22</sup>

In Iran, 9% of the patients had a history of opium abuse, but more than half of the patients did not have any recognized risk factors. The incidence and stage of cancer had a significant relationship with cigarette smoking ( $P = 0.013$ ).<sup>23</sup> The highest incidence is observed in India and Philippines, with a clear predominance of the oral cavity. Therein, the habit of chewing betel quid is equally common among the two sexes. In India, Bengaluru, the incidence rate of oral cancer among women exceeded that of males.<sup>18</sup> Similar to other studies, this series showed men preponderance with male to female ratio of 2.39:1. In this study, there was male predominance in some age groups (60-69, 70-79 years). In 30-39 age groups, females were more predominated. As with malignant tumors in other parts of the body, OPC is a disease that is more common with advancing age, usually showing a sharply rising incidence after the age of 40 or 50.<sup>24</sup>

This study showed that OPC was more common in the age groups of 60-69 and 70-79. The mean age of oral and pharyngeal cases in Kermanshah province was 57

(SD = 17.09). The mean age of patients suffering from OPCs in other studies was as follows: Iran (Kerman 55.36, Fars 55, and Khuzestan province  $55 \pm 16$  years),<sup>25</sup> Basque country (60.5 years),<sup>26</sup> and Jordan (62.5 years).<sup>24</sup>

The finding also showed the most common OPC was SCC (80%). This finding was in agreement with the report of the amount of this cancer in South America, Europe, Asia and especially in Iran.<sup>2,3,4,7,13,20-23,25,27,28</sup> Other cancers of the oral and pharyngeal were as follows: Malignant salivary gland tumors (10.6%), lymphoma (7.4%), sarcoma (1.1%), and malignant melanoma (0.3%). These findings are in agreement with other studies. Elter et al.<sup>29</sup> analyzed a group of 7422 North Carolina patients with OPCs and observed the vast majority (93.0%) of cases were SCC and salivary gland tumor, including adenocarcinomas, accounted for 6.2% of all oral cancers. Canto and Devesa<sup>3</sup> reviewed, 65130 cases of oral and pharyngeal cancers in the United States and found that the majority (83.0%) were SCC. Adenocarcinomas accounted for 9% of all oral and pharyngeal cancers; they occurred mainly in the major salivary glands. In an epidemiological study of oral and pharyngeal cancers in Kerman, SCC was the most frequent histological type (78.9%), followed by malignant salivary gland tumors (4.9%), lymphoma (3.4%), melanoma (3.4%), and sarcoma (3.0%).<sup>27</sup> Another study conducted in Iran showed that 97% of all types of oral cancers were SCC in Fars<sup>21</sup> and this percent was about 75.0% in Khuzestan,<sup>25</sup> which is similar to the present results.

SCCs, accounting for an average of 70.0%, were the most common among all types of oral cancer and the epidemiological pattern of oral cancer in Iran is somewhat similar to that of other countries.<sup>13</sup> Lip cancer has a variable incidence worldwide, with the highest rates reported in the south of Australia and in some regions of Canada and Spain.<sup>30</sup> In North America, the incidence recorded in the USA for men varies from 0.4 to 4.4 per 100000 inhabitants per year,

whereas in the Newfoundland region of Canada it ranges from 12.7 to 27.1 cases per 100000. The literature reviews also point out that the vast majority of lip cancer cases occur in the lower lip.<sup>31</sup>

In this study, it was found that lips were the most common site of OPCs with a male to female ratio of 4.3:1. Lips SCC occurred in 166 patients, representing 78% of all SCCs. This finding was comparable to other reports from UK, India, Fars, Kerman, and Khuzestan province in Iran.<sup>13,23,22,25,27,28,32</sup> In this study, lower lip was affected in 120 cases (72%) and upper lip in 14 cases (9%). The exact sites of 32 (19%) cases of lip cancer were unspecified. Likewise, it was observed that upper lip was more frequently affected among women than among men (19.6 vs. 2.4%). These results are comparable to other retrospective study of cancer of the lip in the Mexico where lower lip was mostly common affected site in both sexes, but the upper lip was affected more frequently among women than among men (50.0 vs. 25.8%).<sup>31</sup>

In another study conducted in Iran, it was found that lower lip was the most frequently involved site cases 90%.<sup>21,27</sup> Compared to SCC of the oral cavity, lip cancer has a distinct analytical epidemiology. Potential etiological agents or carcinogens that might contribute to the onset of lip cancer may be independent or multifactorial and require a number of exposures before manifestation.<sup>33</sup> Since particularly the lower lip is involved in lip cancer, which receives considerably more direct sunlight than the upper lip, this observation has also been used as support for the actinic radiation-lip cancer association. The markedly lower incidence of lower lip cancer among women has been attributed to the more frequent use of protective sun screening agents, such as lipstick and shading devices and less outdoor activity.<sup>24,33</sup>

Since lip cancer is the most common in fair-skinned men with an outdoor employment and rural residence, occupational factor has been linked to the elevated risk of lip cancer. The higher risk of

developing lip cancer in rural compared to urban areas holds true for both sexes. Fishing, farming, forestry, agriculture, works involving exposure to creosote and work in greenhouses are strongly associated with lip cancer as compared to typical indoor occupations and urban dwelling. Despite the overwhelming number of data, the definitive pathogenic pathway remains unclear.<sup>33</sup> The cases of the high incidence rate of lower lip cancer in Kermanshah are probably from outdoor exposure because most people in the province are farmers.

The tongue has been the most common site of oral SCC in USA, Australia, Brazil, France, UK and Denmark.<sup>24,34</sup> Tongue cancer among males is most common in India (9.4:100000 in Bombay), Brazil (7.4:100000 in Sao Paulo), and France (7.9:100000 in Doubs) and in females (although rates are much lower) the rate in Bombay (3.4:100000), and among Indians in Singapore (3.3:100000) are considerably higher than those reported from cancer registries in other countries.<sup>35</sup> In Iran, studies showed that OSCC was the most common malignancy in the tongue and buccal mucosa.<sup>23,28</sup>

In our study, the tongue was the second most common site affected. The male to female ratio was 1.3:1 with a mean age of 65 years). Tongue SCC occurred in 25 patients, representing 12% of all oral SCC cases. This figure is low, compared to other countries, such as USA, Brazil, France, UK, and Denmark.<sup>24,34</sup> Of all 67 cases of oropharyngeal non-squamous cell malignant tumor (excluding metastatic tumors), giving an

incidence of 2.7 per million populations.

The other most common tumors cancer was salivary gland tumor (n = 36), followed by lymphoma (n = 26), sarcoma (n = 4) and melanoma (n = 1). These findings are in accordance with those reported by others.<sup>22,36</sup> There were 36 new cases of salivary gland tumor in this study population resulted in an incidence rate of 1.9 per million populations. Mucoepidermoid carcinoma was the most common malignant tumor of salivary glands in our series accounted for 36.1% of cases. Palate and parotid were the most common sites of involvement. This finding is in agreement with some other reports.<sup>37,38</sup> There were 26 cases of oral lymphoma in our series accounted for 7.4 of all oral and pharyngeal cancers. This is higher compared to the figure of 3.5-4% reported from other countries.<sup>24,39</sup>

### Conclusions

In summary, the incidence risk OPCs in the people of Kermanshah province are similar to the other reports from Iran. However, the study showed that the frequency of OPCs among males (9<sup>th</sup> most common cancer) is higher compared to other investigation from other regions of Iran.

### Conflict of Interests

Authors have no conflict of interest.

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