



# Epidemiological study of lip cancer between 2004 and 2016 in public hospitals of Tehran, Iran: Squamous cell carcinoma as the most common cancer

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## Abstract

**Background:** The majority of oral cancers, which make up 25% to 30% of all malignancies in the oral area, are lip cancers (LCs). As far as we are aware, there haven't been any thorough epidemiologic research on LC. This study's objective is to look at the trend of tumor prevalence across the whole lip area in Iranians between 2004 and 2016 (Tehran, Iran).

**Methods:** This retrospective cross-sectional study, which examined tumor location, age, gender distribution, histological tumor type, metastasis, clinical diagnosis, and recurrence of the lesion, was carried out on the pathology records of patients admitted to the Department of Pathology at the Cancer Institutes of Imam Khomeini hospital and Tajrish hospital between 2004 and 2016. The data was analyzed using the chi-square test and Fisher's exact test.

**Results:** Out of a total of 237392 biopsy reports filed with the Department of Pathology, 512 instances (0.21%, 92% malignant, and 8% premalignant) involving 385 (75.2%) males and 127 (24.8%) females were discovered to be lip-related. A statistically significant difference between sex and the site of the lesion was found using the chi-square test ( $P=0.032$ ). Lower lip and squamous cell carcinomas (SCC) were the most typical locations and types, respectively. Recurrence and metastasis were noted in 7.8% and 25.84% of cases, respectively, with males more likely than women to experience these outcomes. Moreover, there was a significant ( $P=0.025$ ) correlation between gender and histological tumor type.

**Conclusion:** The chance of developing LC was greater in men over the age of 54. The most typical location for SCC involvement is the lower lip. We discovered that women had an increased frequency of upper lip lesions. These disparities might be the result of gender-specific professional and behavioral differences. Hence, as possible contributors to the occurrence of LCs, variables including occupational and behavioral variations and public knowledge of sun exposure should be carefully evaluated.

**Keywords:** Lip cancer, Oral, Epidemiology, Squamous cell carcinoma, Iran

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## Introduction

The most common cancer in the oral and maxillofacial area, which accounts for 25–30% of all mouth malignancies, is cancer of the lip (5.2 per 100 000 people each year).<sup>1-3</sup> There are several varieties of lip cancer (LC). At this anatomical position, basal cell carcinoma (BCC) is rare (less than 10%), but squamous cell carcinomas (SCC) are the most prevalent histological type (more than 90%).<sup>4</sup> The second most frequent kind of skin cancer in the head and neck is SCC of the lip.<sup>5</sup> Additional malignant lesions include mesenchymal malignancies, hematologic tumors (such as angiosarcoma), melanomas, and lymphomas. Minor salivary gland cancers include

mucoepidermoid carcinomas, adenoid cystic carcinomas, and adenocarcinomas.<sup>6,7</sup> The lower lip vermilion is a typical site for LCs, which mostly affect males over the age of 65. The occurrence is more prevalent in certain regions of Australia, Canada, and Spain.<sup>8</sup> During the last 30 years, there has been a rise in the incidence of lip and oral cavity cancers globally, with Asia showing the biggest increase.<sup>9</sup> Sun exposure is the most common etiological cause of LC, according to research (UV, especially UVB, wavelengths of 320–900 nm). Less frequent factors include race (e.g., light complexion, eyes, and hair), smoking pipes or cigarettes, drunkenness, viral infections, immunosuppression, and immunodeficiency.<sup>3,10</sup> Radiation therapy or surgery are



used as treatments.<sup>11</sup> Surgery is the major form of therapy for lip tumors, and the recommended surgical technique is complete thickness resection. The rebuilding of the lip poses a substantial challenge to reconstructive surgeons even though malignant tumors are frequently identified and treated in their early stages. Early tumor stages, advanced tumors for palliative purposes, or the treatment of cervical lymph nodes, either as an alternative to surgery or after surgery, all call for the use of radiotherapy.<sup>4,11</sup> According to a World Health Organization (WHO) study from 2019, cancer was the third or fourth major cause of death before the age of 70 in 23 additional nations, placing it first or second in 112 out of 183 countries.<sup>12</sup> One in four Iranians may acquire cancer before the age of 74, and the prevalence of cancer rose by 20% between 2008 and 2012 in Iran, according to a research by Mohebbi et al<sup>13</sup> published in 2017. Moreover, as LCs are sometimes lumped in with oral and pharyngeal cancers, there is a lack of information on the epidemiology and histology of LCs in Iran. The two most frequent locations of lip, oral, and oropharyngeal involvement in Iran, according to a comprehensive study of the epidemiology of oral cancer, are the tongue with an average prevalence of 29.9% and the lip with an average prevalence of 25.5%.<sup>14</sup> This study's objective is to examine the patterns of tumor prevalence in the entire lip region between 2004 and 2016 in a population of Iranians (Tehran, Iran), taking into account the lesion's location, age at diagnosis, gender distribution, histological tumor type, metastasis, and recurrence of the lesion. Findings might provide information for better understanding and locating high-risk populations.

## Methods

### Study Subjects and Case Selection

In this retrospective cross-sectional study, every biopsy report that had been registered over a 13-year period from the pathology department archives of the cancer institutes at Tajrish hospital and the Imam Hospital in Tehran, Iran, totaled 237392 cases. These reports were retrieved, and they were analyzed by age, location, clinical and histopathological findings, recurrence, and metastasis. The International Classification of Diseases (ICD) 10th version was used to recode all cases throughout the research period (2004–2016).<sup>15</sup> The ICD-10 code for LC is C:00, and its precise sub sites (C00.0–00.9) are as follows: C00.0 (external upper lip), C00.1 (external lower lip), C00.2 (external lip, *not otherwise specified* [NOS]), C00.3 (mucosa of upper lip), C00.4 (mucosa of lower lip), C00.5 (mucosa of lip, NOS), C00.6 (commissure of lip), C00.8 (overlapping sites of lip), and C00.9 (lip, NOS).

### Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 16 was used to assess descriptive statistics to determine the prevalence and characteristics of lip lesions in terms

of sex, kind, and location. Descriptive epidemiology was done applying frequencies, percentages, means, and standard deviation. The data were analyzed applying  $\chi^2$  test and Fisher's exact test.

A value of  $P \leq 0.05$  was considered significant.

## Results

In this research, out of a total of 237392 biopsy reports, 512 cases (0.21%, 92% malignant and 8% premalignant) were found in the lip, 385 (75.2%) of whom were males and 127 (24.8%) females. The mean age of patients was  $63.71 \pm 14.11$  years (ranging from 3 to 92 years). The mean age of female and male patients was  $66.19 \pm 12.47$  years and  $63.14 \pm 12.77$  years, respectively. A 3-year-old girl with rhabdomyosarcoma was the youngest patient, while a 92-year-old man with lip squamous cell carcinoma was the oldest. Among the total lesions, 288 (0.12%) were in the lower lip [237 (82.3%) male, 51 (17.7%) female], and 122 (0.05%) were in the upper lip [75 (61.5%) male, 47 (38.5%) female]. The chi-square statistic test resulted in a statistically significant difference between the sex and location of the lesion ( $P=0.032$ ). Based on this statistical test, it was shown that women are substantially more likely than males to have lesions on their upper lip ( $P<0.05$ ). No particular place is mentioned in Table 1, which just shows the association between gender and geography. Men experienced all lesions at a higher rate than women. 350 cases (68.3%) of SCC were found, with 79.4% of the patients being male. BCC was the second most frequent lip lesion, with 74 instances (14.5%), mostly in men. Actinic keratosis and actinic cheilosis, which are mostly seen in men (70% of the time), make up 8% of all lip pathology biopsies. Malignant neoplasms of the lip are distributed by gender and histologic subtypes in Table 2 ( $P=0.025$ ). Fisher's exact test is used to this table to analyze the connection. More than 20% of the lesions (exactly 68.2%) had an anticipated frequency of less than 5, while the lowest predicted frequency was 0.25, which was less than 1. The pathological grade of SCC, (Table 3, Figure 1) was:

1. Well differentiated in 172 cases (49.15%)
2. Moderately differentiated in 95 cases (27.15%)
3. Poorly differentiated in 19 cases (5.42%)
4. In 64 cases (18.28%), grade was not mentioned

**Table 1.** Frequency distribution of location of the lesion and sex ( $P=0.032$ )

Location	Female No. (%)	Male No. (%)	Total No. (%)
Upper lip	47 (38.5)	75 (61.5)	122 (23.8)
Lower lip	51 (17.7)	237 (82.3)	288 (56.3)
Commissure	6 (40)	9 (60)	15 (2.9)
Lip (NOS)	23 (26.4)	64 (73.6)	87 (17)
Total	127 (24.8)	385 (75.2)	512 (100)

NOS, not otherwise specified.

**Table 2.** Histologic subtypes/gender distribution of malignant neoplasms of lip ( $P=0.025$ )

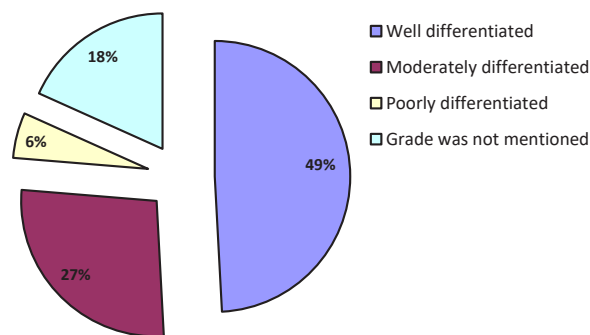
Pathologic type	Female No. (%)	Male No. (%)	Total No. (%)
SCC	276 (78.9)	74 (21.1)	350 (100)
BCC	47 (63.5)	27 (36.5)	74 (100)
Verrucous carcinoma	6 (75)	2 (25)	8 (100)
Adenoid cystic carcinoma	4 (4.44)	5 (55.6)	9 (100)
Adenocarcinoma NOS	1 (100)	0	1 (100)
Carcinoma in situ	5 (83.3)	1 (16.7)	6 (100)
Basosquamous cell carcinoma	9 (64.3)	5 (35.7)	14 (100)
Rhabdomyosarcoma	0	1 (100)	1 (100)
Melanoma	3 (75)	1 (25)	4 (100)
Spindle cell carcinoma	3 (100)	0	3 (100)
Mucoepidermoid carcinoma	1 (50)	1 (50)	2 (100)
Total	355	117	472 (100)

BCC, basal cell carcinoma; SCC, squamous cell carcinomas; NOS, not otherwise specified.

**Table 3.** Frequency distribution of SCC based on pathological grade

Pathologic diagnosis SCC	Number	Percent
Well differentiated	172	49.15
Moderately differentiated	95	27.15
Poorly differentiated	19	5.42
Grade was not mentioned	64	18.28
Total	350	100

SCC, squamous cell carcinomas.

**Figure 1.** Frequency distribution of SCC based on pathological grade

Forty cases (7.8%) had metastatic disease, of which 30 cases (75%) were male and 10 cases (25%) female. The chi-square statistic test revealed no statistically significant association between location or gender and metastasis ( $P=0.526$ ) or gender with metastasis ( $P=0.976$ ). The greatest rate of metastasis was seen in SCC (36 cases). The link between metastasis and histological tumor type was statistically significant, according to the Chi-square test ( $P=0.038$ ). The site of the metastasis, however, was not noted in the archive data. The recurrence rate was 23.8% (122 cases), of which 23% (28 cases) were women and 77% (94 cases) were men.

## Discussion

In the research on global oral cancer epidemiology, LC and malignancies of the oral cavity are often combined.<sup>15,16</sup> A comprehensive study of the epidemiology of oral cancer conducted in Iran in 2015 revealed that the tongue (29.9%) and lip (25.5%) were the two most frequent sites of involvement.<sup>14</sup> Yet, according to Chamani et al<sup>17</sup> (Iran, 2009), the lip was the most common location for oral and pharyngeal cancer in Kerman. Yet, there are not many thorough epidemiologic research on LC in Iran. The present research looked at the trend of tumor occurrence in an Iranian population between 2004 and 2016 in the whole lip area. Throughout a 13-year period, patients who were sent to the Cancer Institute of Imam Khomeini Hospital and the Cancer Institute of Tajrish hospital were examined for the occurrence of malignant lesions of the lip. In Iran, there are 3.83 instances of lip/oral cavity cancer for every 100 000 people. In Iran, lip and oral cavity cancer is the 20th most prevalent cancer and has the 22nd highest fatality rate out of 35 malignancies.<sup>12</sup> In Iran, skin cancer is the most prevalent malignancy in both men and women, with a standard incidence rate of 18.93 for males and 13.09 for women.<sup>18</sup> The male-to-female ratio in this study was 3:1, which is higher than the average in Iran (2015)<sup>14</sup> and comparable to the studies of Alho et al<sup>19</sup> (Northern Finland, 2000) and Abreu et al.<sup>20</sup> Out of 512 cases of malignant lip lesions, 385 (75.2%) cases were reported in men and 127 (24.8%) cases in women (Western Australia, 2009). This study found that men made up the majority of those who developed LC, which is consistent with research from Maruccia et al<sup>4</sup> (Italy, 2012), Casal et al<sup>5</sup> (Portugal, 2010), Domínguez-Gordillo et al<sup>8</sup> (Spain, 2016), Czerninski et al<sup>21</sup> (Israel, 2006), Luna-Ortiz et al<sup>22</sup> (Mexico, 2004), McCartan et al<sup>23</sup> (Ireland, 2005), de Visscher et al<sup>24</sup> (Netherlands, 1998), and Géraud et al<sup>25</sup> (Germany, 2012).

The average age of males was  $63.14 \pm 12.77$  years and the average age of females was  $66.19 \pm 12.47$  years; also, the overall mean age was  $63.71 \pm 14.11$  years which is higher than the average in Iran (2015)<sup>14</sup> and similar to the studies of Casal et al,<sup>5</sup> Domínguez-Gordillo et al,<sup>8</sup> Maruccia et al,<sup>4</sup> and de Visscher et al.<sup>24</sup> This finding is inconsistent with the study of Géraud et al<sup>25</sup> which reported an average age of 71.1 years, this difference may be in terms of the larger sample size.

Out of 512 cases, 122 (23.8%) cases were reported in the upper lip, 288(56.3%) cases in the lower lip, and 15(2.9%) cases in the lip commissure. These findings are consistent to the studies of Czerninski et al,<sup>21</sup> Luna-Ortiz et al,<sup>22</sup> de Visscher et al,<sup>24</sup> Maruccia et al,<sup>4</sup> Casal et al,<sup>5</sup> and Domínguez-Gordillo et al<sup>8</sup> which is inconsistent with the study of Géraud et al.<sup>25</sup>

According to Luna-Ortiz et al research's women were substantially more likely than males to have lesions on their upper lips.<sup>22</sup> These disparities might be the result of

gender-specific professional and behavioral differences. SCC is the predominant histopathological type with 350 (68,3%) cases, this rate was similar to the results of studies of Maruccia et al,<sup>4</sup> Casal et al,<sup>5</sup> Domínguez-Gordillo et al<sup>8</sup> and Luna-Ortiz et al<sup>22</sup> which is inconsistent with study of Géraud et al.<sup>25</sup>

The metastasis was found in 40 (7.8%) cases, 10 cases (25%) in women and 30 cases (75%) in men. This finding is in contrast with the studies of Vartanian et al<sup>26</sup> (Brazil, 2004), and McGregor et al<sup>27</sup> (Canada, 1992). Gender and location had no statistically significant relationship with metastasis, but there was a statically significant relationship between the histopathological type of SCC and metastasis.

The recurrence rate was 23.8% (122 cases), 28 cases (23%) in women and 94 cases (77%) in men, which is contrary to the study of Luna-Ortiz et al,<sup>22</sup> and the reason maybe the smaller sample size in the latter study.

The inability to examine important risk variables for cancer and premalignant lesions, such as UV exposure, smoking, alcohol use, particular dietary practices, employment, and way of life, is one of this study's weaknesses. Unfortunately, there was no access to this data. Also, a lack of pertinent data prevented an investigation of the outcomes of patients with malignant lesions and effective variables.

## Conclusion

In this epidemiological research of LC, we found that males and persons over the age of 54 had greater rates of the disease. The most typical location for SCC involvement is the lower lip. We discovered that women had an increased frequency of upper lip lesions. These disparities might be the result of gender-specific professional and behavioral differences. In order to change the incidence of lip tumors, variables including occupational and behavioral variations and public awareness of sun exposure should be carefully studied.

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## Authors' Contribution

**Conceptualization:** Roohollah Safarpour, Nafiseh Shamloo.

**Data curation:** Roohollah Safarpour, Nafiseh Shamloo, Alireza Ghannadan.

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**Supervision:** Roohollah Safarpour, Nafiseh Shamloo.

**Software:** Roohollah Safarpour.

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**Validation:** Roohollah Safarpour, Nafiseh Shamloo, Alireza Ghannadan.

**Visualization:** Roohollah Safarpour, Nafiseh Shamloo.

**Writing - original draft:** Roohollah Safarpour.

**Writing - review & editing:** Roohollah Safarpour, Nafiseh Shamloo.

## Competing Interests

Authors have no conflict of interests.

## Ethical Approval

Prior to the research, the protocol was reviewed and approved by the National Ethics Committee for Biomedical Research (Meeting 32,2017-5-20) and received the ethics code IR.SBMU.RIDS.REC.1396.455.

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