

Epidemiological Pattern of Lip Premalignant Lesions in an Iranian population: A 13-Year Evaluation

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Objectives This study investigated the prevalence and pattern of lip premalignant lesions in patients referred to the Cancer Institute of Imam Khomeini and Shohada-E-Tajrish Hospitals between 2004 and 2016.

Methods This retrospective cross-sectional study was conducted on the pathology reports of patients retrieved from the archives of the Pathology Departments of the Cancer Institute of Imam Khomeini and Shohada-E-Tajrish Hospitals between 2004 and 2016. The gender, age, lesion location (upper lip, lower lip, commissure, lip in general, not stated), pathological type, and clinical diagnosis of the lesions were extracted from patient records. The Fisher's Exact test was used to analyze the data by SPSS version 16.

Results Of a total of 237,392 patients, 40 (0.02%) cases had lip premalignant lesions. The mean age of patients was 63.71±14.11 years (range 3 to 92 years). The prevalence of lip premalignant lesions was higher in males, with a male to female ratio of 4:1. The most common location and histopathological type of lesions were the lower lip, and actinic keratosis (60% of the cases), respectively.

Conclusion Lip premalignant lesions were observed in 0.02% of patients. Although this rate is lower than the global prevalence of precancerous lesions of the lip and oral cavity (4.47%), because of the high malignant transformation rate of lip premalignant lesions, every clinician must take part in early detection of these lesions by clinical examination. To confirm the diagnosis, biopsy may be requested for histopathological diagnosis.

Keywords Lip; Actinic cheilitis; Actinic keratosis; Keratoacanthoma

Introduction

Premalignant (precancerous) lesions can bring about serious consequences if not detected and treated early.¹ The lips share common characteristics with the oral mucosa and skin.² Squamous cell carcinoma (SCC) is the most common type of lip cancer (>90% of lip cancers), and is the second most common type of skin cancer in the head and neck region.^{3, 4} SCC frequently develops from a premalignant lesion, such as actinic cheilitis, actinic keratosis, leukoplakia, keratoacanthoma and xeroderma pigmentosum originating from the lower lip mucosa in 90% of the cases.³ The most common cause of actinic keratosis and actinic cheilitis is excessive exposure to ultraviolet (UV) rays of the sun. Therefore, early diagnosis and treatment of premalignant lesions are extremely important to avoid their malignant transformation.^{3, 5} Premalignant lesions of the lip and oral cavity occur in about 1.5% to 4.5% of the world's population, 6 with a relatively higher prevalence among men, older people (>80% between 41 and 80 years), and people with a low literacy level and low income.^{6, 7} Cases of premalignant lesions of the lips are more likely to be related to patients' occupation and exposure to sunlight, which justifies the male predilection. The male/female ratio is changing because of increased incidence of tobacco and alcohol use by women.⁸ Predisposing factors for the lip premalignant lesions include exposure to sunlight (UV especially UVB), pipe or cigarette smoking, chronic trauma, preexisting lesions with malignant transformation potential, viruses (human papillomavirus, retroviruses), immunosuppression, and immunodeficiency.⁵ The

treatment is surgical excision with safety margins followed by reconstruction of the lip.⁹

The current study is the first to evaluate the prevalence of lip premalignant lesions in an Iranian population.

Methods and Materials

Study subjects and case selection:

This retrospective cross-sectional study was conducted on the pathology reports of 237,392 patients retrieved from the archives of the Pathology Departments of Cancer Institute of Imam Khomeini and Shohada-E-Tajrish Hospitals. All lip premalignant lesions diagnosed between 2004 and 2016 occurring in males and females of any age were considered for analysis.

Statistical analysis:

Data were analyzed using SPSS version 16. All data obtained from patient records were entered in the software, and the gender, age, lesion location (upper lip, lower lip, commissure, lip in general, not stated), pathological type, and clinical diagnosis of the lesion were extracted from patient records and reported in number and percentage values. Data regarding the location and size of lesions and etiological factors (e.g., sunlight, tobacco use, alcohol consumption, etc.) were not available. The results were analyzed by the Fisher's Exact test. In this test, p-value <0.05 was considered to be statistically significant.

Ethical considerations:

The study protocol was reviewed and approved by the National Ethics Committee for Biomedical Research (Meeting 32, 2017-5-20) and received an ethical approval

code (IR.SBMU.RIDS.REC.1396.455).

Results

The present study was performed on 237,392 records. Forty cases (0.02%) were diagnosed with premalignant lesions of the lip; among them, 4 cases (10%) were detected in Shohada-E-Tajrish Hospital, and 36 cases (90%) were detected in the Cancer Institute of Imam Khomeini Hospital. The mean age of patients was found to be 63.71 ± 14.11 years (range 3 to 92 years). The mean age of female and male patients was 66.19 ± 12.47 years and 63.14 ± 12.77 years, respectively. The age range of female patients was 3 to 91 years, and the age range of male patients was 16 to 92 years. Males were more affected (33 out of 40, 82.5%) with a male to female ratio of 4:1. The lip premalignant lesions were 3 to 4 times more prevalent in males than females (Table 1). The Chi-square test showed that the correlation of gender and lesion location was statistically significant ($p=0.032$).

Table 1- Frequency distribution of location of precancerous lesions of the lip in males and females

Location	Female N (%)	Male N (%)	Total N (%)
Upper lip	1(16.6)	5(83.4)	6(15)
Lower lip	4(13.79)	25(86.21)	29(72.5)
Commissure	1(33.7)	2(66.7)	3(7.5)
Lip in general (not mentioning the exact location)	1(50)	1(50)	2(5)
Total n (%)	7(17.5)	33(82.5)	40(100)

In general, six histopathological types of premalignant lesions had been reported in the pathological reports. Actinic keratosis was the most common (60% cases), followed by actinic cheilosis, leukoplakia, lichen planus, erythroplakia, and keratoacanthoma (Figure 1). Table 2 shows the incidence of lesions based on gender.

Clinical diagnosis of lesions had been correctly made in 7 cases (17.5%), all of which were present in males. Among them, actinic keratosis, cutaneous lichen planus, eratoacanthoma, nevus, and melanoma were observed.

Table 2- Incidence of premalignant lesions of the lip based on gender

Pathologic type	Male N (%)	Female N (%)	Total N (%)
Actinic keratosis	22(91.6)	2(8.4)	24(60)
Actinic cheilosis	6(85.8)	1(14.2)	7(17.5)
Leukoplakia	2(75)	1(25)	3(7.5)
Cutaneous lichen planus	1(25)	2(75)	3(7.5)
Erythroplakia	1(50)	1(50)	2(5)
Keratoacanthoma	1(100)	0	1(2.5)
Total	33(82.5)	7(17.5)	40(100)

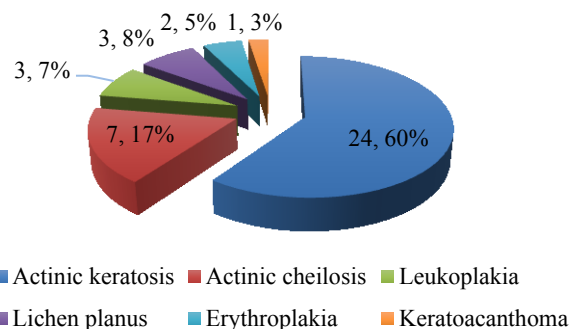


Figure 1: Incidence of premalignant lesions of the lip in the study population

Discussion

The current study was the first to assess the lip premalignant lesions in an Iranian population. The prevalence of lip premalignant lesions was evaluated over a period of 13 years in patients referred to the Cancer Institute of Imam Khomeini and Shohada-E-Tajrish Hospitals. The prevalence of lip/oral cancer in Iran is 3.83/100,000 cases per year. Lip and oral cancer is the 20th most common cancer in Iran and ranks 22nd in mortality among 35 cancers.¹⁰ Skin cancer is the first most common cancer in males (standard incidence rate = 18.93) and the second most common cancer in females (standard incidence rate = 13.09) in Iran.¹¹ In the current study, the most common precancerous lesions of the lip were found to be actinic keratosis followed by actinic cheilosis. Unlike the present study, Calcaianu et al,⁵ in their study conducted from 2012 to 2014 described keratoacanthoma as the most common precancerous lesion of the lip, followed by actinic keratosis and actinic cheilitis. The difference between their results and the present study can be attributed to differences in study group definitions and differences in lifestyles in various communities. Saghravanian et al,¹² and Sousa et al.¹³ reported lichen planus followed by leukoplakia to be the most prevalent among premalignant lesions. In the current study, an increase in the incidence of lip premalignant lesions over a 13-year period (2004–2016) was observed in both sexes in the study population in Iran. This finding may be related to the population increase during these years in Iran. Also, in the current study, men were more predominantly affected than women. The results of other studies are consistent with those of the present study in this regard.^{1, 5, 7, 12} The mean age of patients in the current study was 63.71 ± 14.11 years, while the mean age of patients with oral premalignant lesions in studies conducted by Saghravanian et al,¹² and Maia et al.¹⁴ were 47.52 ± 15.63 years and 56.09 ± 21.89 years, respectively (slightly lower than the value in the current study). In the current study, lip premalignant lesions were observed predominantly on the lower lip, which is consistent with

the results of Calcaianu et al.⁵ and Reinehr and Bakos.¹⁵ The rate of malignant transformation of premalignant lesions is 33.3% for keratoacanthoma,¹⁶ 10% to 30% for actinic cheilitis,¹⁷ and 0.1% to 16% for actinic keratosis.¹⁶ SCC is the most common histopathological type of the malignancies of the lip, oral cavity, and head and neck region.¹⁸ In the lips, this type of malignancy commonly begins with a premalignant ulcerative lesion, known as actinic cheilosis.¹⁹ Early diagnosis of malignancy, especially in the precancerous stage, significantly decreases complications, problems, and mortality rate from cancer. Since the clinical appearance of precancerous lesions is often similar to that of SCC, histopathological examination is the gold standard to confirm the diagnosis. Because of the high potential for malignant transformation of precancerous lesions, especially to SCC, treatment in many cases should be surgical excision with safety margins, followed by reconstruction of the lip.^{5, 9} In general, the recurrence rate of these lesions varies in different treatment methods but is minimal after surgery.^{5, 6, 8} The limitations of this study included inability to investigate the major risk factors associated with

premalignant lesions and cancer, such as smoking, alcohol consumption, and dietary habits due to retrospective design of the study. Moreover, the outcome of patients with premalignant lesions and effective factors could not be investigated due to the lack of relevant data in patient records.

Conclusion

In the present study, lip premalignant lesions were observed in 0.02% of patients. Although this rate is lower than the global prevalence of precancerous lesions of the lip and oral cavity (4.47%), because of the high malignant transformation rate of common precancerous lesions of the lip, every clinician must take part in early detection of these lesions by clinical examination. To confirm the diagnosis, biopsy may be requested for histopathological diagnosis.

Conflict of Interest

No Conflict of Interest Declared ■

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