

# Oral cancer: potentially malignant lesions and statistics of diagnosed cases in the municipality of Santo André-SP

*Câncer bucal: lesões potencialmente malignas e estatística dos casos diagnosticados no município de Santo André-SP*

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## Abstract

**Objective** – The purpose of the study was to review the literature and to determine the incidence of potential malignant lesions and oral cancer according to gender, ethnicity, age and anatomical site, diagnostic hypothesis and final diagnosis. **Methods** – A total of 252 patients were evaluated at the Municipal Center Hospital of Santo André, Center for Dental Specialties and to the Campaigns for Oral Cancer Prevention promoted by the Paulista Association of Dentist Surgeons (APCD) from Santo André municipality (São Paulo- Brazil). Information about ethnicity, age, gender, anatomical location of injury, possible diagnosis and final diagnosis were analyzed. **Results** – It was observed a predominance of males, age between 5<sup>th</sup> and 6<sup>th</sup> decades of life and Caucasian ethnicity, respective with the potentially malignant lesions in the oral cavity. The lower lip, tongue and floor of mouth were the most affected anatomical sites. **Conclusions** – The oral cancer in the present study presented: higher prevalence in Caucasians, higher prevalence in males, predominance in the 5<sup>th</sup> and 6<sup>th</sup> decade of life with average age of 57.98 years old, predominant anatomical site was the lower lip followed by tongue, floor of the mouth, alveolar border and retromolar trigone.

**Descriptors:** Precancerous conditions/diagnosis; Carcinoma, squamous cell; Mouth neoplasms/epidemiology

## Resumo

**Objetivo** – O trabalho apresentado tem como objetivo realizar revisão de literatura e quantificar estatisticamente a incidência das lesões potencialmente malignas e do câncer bucal, sua incidência quanto a etnia, faixa etária, gênero, localização anatômica, hipótese de diagnóstico e diagnóstico final. **Métodos** – Foram estudados 252 pacientes, atendidos no Centro Hospitalar Municipal de Santo André, Centro de Especialidades Odontológicas e 1<sup>a</sup> a 8<sup>a</sup> Campanhas de Prevenção do Câncer Bucal – APCD Santo André. Informações sobre etnia, faixa etária, gênero, localização anatômica das lesões, hipóteses de diagnóstico e diagnóstico final, foram analisados estatisticamente. **Resultados** – Houve predomínio do gênero masculino, faixa etária entre a 5<sup>a</sup> e a 6<sup>a</sup> décadas de vida, etnia branca, o lábio inferior, língua a assoalho bucal foram os locais anatômicos mais acometidos. **Conclusões** – Diante do presente estudo concluiu-se que o câncer bucal apresentou: maior prevalência pela etnia branca, maior prevalência no gênero masculino, tendência ao predomínio pelas 5<sup>a</sup> e 6<sup>a</sup> décadas de vida e a média de idade foi de 57,98 anos, quanto à localização anatômica, predomínio no lábio inferior, seguido da língua, assoalho bucal, rebordo alveolar e trígono retromolar.

**Descritores:** Lesões pré-cancerosas/diagnóstico; Carcinoma de células escamosas; Neoplasias bucais/epidemiologia

## Introduction

Nowadays, dentistry and other health sciences play an important role in the prevention and early diagnosis of mouth diseases. Among these disorders, there are lesions defined as potentially malignant such as leukoplakia, proliferative verrucous leukoplakia, lichen planus, erythroplakia and actinic cheilitis. In America, the number of new cases has been decreasing by 1% a year in the last 20 years. However, the estimative pointed 20,180 new cases among men and 10,810 among women in 2009 while in Brazil the estimative was 10,000 for males and 3,400 for females, being the epidermoid carcinoma the 5<sup>th</sup> most common disorder<sup>1</sup>.

Epidemiologic evidences show that sun exposure, alcoholism, tabagism, HPV infection, vitamin deficiency, gender, inheritance, age and ethnicity are all risk factors for this type of neoplasia<sup>2-3</sup>. The most common signs and symptoms of the disease are: non-healing lesions at the mouth and lips, painless ulcers measuring less than 2 cm of diameter that can bleed or not, white and red patches, pain or discomfort when eating or swallowing, difficulty to speak and fast weight loss<sup>4</sup>.

Oral cancer is more frequent in men than women at a proportion of 2:1. A higher incidence on the 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> decade of life<sup>5</sup>, affecting more Caucasians than Asians and black people in a proportion of 3:1 is generally observed in studies worldwide<sup>6</sup>.

## Literature review

The term leukoplakia was first used in 1877 by Schwimmer and the World Health Organization (WHO) defines the disorder as “a white patch or plaque of the buccal mucosa which can not be rubbed off or characterized clinically or clinically or histopathologically as any other disease”<sup>7</sup>. Despite its unknown etiology, the exposure to some exogenous carcinogens as tobacco, alcohol, sun radiation and oral infection can predispose to leukoplakia<sup>8</sup>. Prevalence rates are 10 times higher among men between the 3<sup>rd</sup> and the 8<sup>th</sup> decade of life and 2 times higher in women between the 4<sup>th</sup> and 7<sup>th</sup> decade of life<sup>9</sup>. The most affected anatomic areas are the oral and alveolar mucosa and lower lip but lesions of the floor of the mouth, lateral border of the tongue and also lower lip are more prone to show dysplasia<sup>1</sup>.

Oral leukoplakias can be divided into 3 categories according with the degree of dysplasia: light, moderate and severe<sup>8</sup>. Because of the difficult diagnosis, risk factors should be eliminated and biopsy is needed if signs and symptoms persist. Treatment options are the conventional surgical excision, identification and removal of risk factors, laser surgery and the use of retinoid derivatives<sup>10</sup>.

Verrucous proliferative leukoplakia, first described by Hansen *et al.*<sup>11</sup> (1985) and Greer *et al.*<sup>12</sup> (1999), is a slow-growing, persistent,

and irreversible mucosal disease that can present exophytic areas. According to Ghazali *et al.*<sup>13</sup> (2003) and Bagan *et al.*<sup>14</sup> (2003) report no association of risk factors such as tabagism and alcoholism with this type of lesion. Higher prevalence is found in females (ratio of 4:1) with an average age of 62 years old, being gingiva and alveolar mucosa the most affected areas<sup>14-15</sup>. The malignization process of verrucous proliferative leukoplakia is higher than leukoplakia. According with some authors<sup>14,16-17</sup>, 60% to 100% became malignant. Despite it should be treated aggressively, the complete excision is almost impossible by the extension and disposition on the oral cavity, and radiotherapy or chemotherapy seems to have no effect<sup>18</sup>.

The term erythroplakia, first described by Queyrat in 1911, is still modern and largely used according with WHO, being a flat red patch or lesion in the mouth that cannot be attributed clinically or histopathologically to any other pathology<sup>7</sup>. The etiology is associated with alcohol and tobacco abuse, vitamin C, E and beta-carotene deficiency, exposure to carcinogens, viral infections, genetic and hereditary factors<sup>19</sup>. It affects more men than women in a ratio of 3.3:1, especially during the 6<sup>th</sup> and 8<sup>th</sup> decade of life<sup>20</sup> and appears preferentially on palate, floor of the mouth and oral mucosa<sup>21</sup>. The treatment is guided by the biopsy but if the inflammation cause is known and removed, biopsy should be performed in 2 weeks only if the lesion persists. In this case, lesions showing moderate to severe degree of dysplasia should be entirely removed and a long term follow up is needed as recurrence is common<sup>1</sup>.

Lichen planus was first described in 1869. It is an autoimmune disease of skin and mucosa, and is the most common dermatologic anomaly with oral manifestation, showing prevalence around 0.02 to 1.2% in general population<sup>22</sup>. Risk factors such as stress, consume of citric fruits and spices, dental procedures, systemic diseases, abuse of alcohol and tobacco have been related with the disease exacerbation<sup>23</sup>.

Lichen planus is more prevalent in Caucasian women between the 4<sup>th</sup> and 5<sup>th</sup> decade of life, affecting the jugal mucosa, in particular<sup>23</sup>. Among the several types described in the oral cavity, the reticular form is the most common presentation and manifests as white lacy streaks on the mucosa (known as Wickham's striae). The lesions tend to be bilateral and affect mostly the jugal mucosa. Other presentations of lichen planus are the plaque (slightly elevated and flat) and bullous forms (the rarest form). The treatment includes to inform the patient about the disease, the removal of local irritants, clinical follow-up and the use of topical corticosteroids at the site of the inflammatory reaction<sup>22</sup>.

Actinic cheilitis is a lesion affecting the vermilion border of the lower lip caused by excessive exposure to ultraviolet radiation in sunlight without protection<sup>1,24</sup>. It affects mainly Caucasian men with light complexion who tan easily. The men to women ratio is 10:1. This condition may leads to squamous cell carcinoma (SCC) and immunocompromised people are more susceptible to the malignant form<sup>1</sup>. Individuals under 45 years old are rarely affected. Clinically there is atrophy of the vermilion border of the lower lip characterized by a flat surface with pale areas and eruptions. Patients normally report that the squamous material can be removed but is redone in few days<sup>1</sup>. Malignant transformation can reach 6% to 10% of the cases and diagnosis needs biopsy to define the lesion's degree of dysplasia. The treatment involves orientation about the need of sun protection including lips. Vermillionectomy is performed in severe but non-malignant cases<sup>24</sup>.

There are some variants of the squamous cell carcinoma (SCC). Verrucous carcinoma spindle cell carcinoma, adenosquamous carcinoma and basaloid squamous cell carcinoma are rare forms and the most aggressive form is the epidermoid carcinoma<sup>1</sup>. The etiology of the epidermoid carcinoma is multifactorial. Alcohol and tobacco abuse, HPV infection, vitamin deficiency, excessive exposure to ultraviolet radiation, genetic and hereditary factors are common causes<sup>25</sup>.

According with some authors<sup>23</sup>, the higher incidence of epidermoid carcinoma on males has been decreasing since the late 60's because of the increased consumption of alcohol and tobacco among women. However, the prevalence of males is still high as demonstrated in an epidemiological study conducted in southern

Brazil between 2002 and 2006 when the oral cancer was diagnosed in 88.8% of men and in only 11.1% of women<sup>23</sup>.

Oral cancer has been observed in patients who underwent renal transplantation, in those treated with immunosuppressive drugs and in young HIV positive patients<sup>1,3-4</sup> confirming the susceptibility of immunosuppressed individuals to this condition. The main signs and symptoms related to oral cancer are non-healing lesions of the mouth and lips, painless superficial ulcerations less than 2 cm in diameter which may bleed or not, red or white patches on the gums, tongue or oral mucosa, pain or discomfort to eat and swallow, speaking difficulty, severe weight loss, painful and enlarged cervical lymph nodes<sup>4</sup>. The major complain of patients during diagnosis were odynophagia (48.4%), neck lumps (19.3%), dysphagia (12.9%) and sore tongue (6.4%).

A high incidence of oral cancer by the 5<sup>th</sup>, 6<sup>th</sup> and 7<sup>th</sup> decade of life is pointed out in the literature which includes the study of 58 patients with oral cancer, being 46.6% of them over 60 years old<sup>5</sup>.

With regard to ethnicity, there is predominance of Caucasians in relation to Asians and black people in a ratio of 3:1 which is corroborated by several studies around the world. Black people suffer social exclusion and have no access to prevention programs while Asians are less affected for genetic factors<sup>3,19</sup>.

The tongue is the anatomical area most affected by oral cancer, followed by the lip. An epidemiological study of the incidence of oral cancer in different regions of Brazil confirms the tongue as the most frequently affected area by tumors and emphasizes that this site of mouth has the worst prognosis<sup>2</sup>.

The treatment of patients with oral cancer depends on its location, extension of primary tumor, lymph node involvement and age of the individual<sup>26</sup>. Surgery, radiotherapy, chemotherapy or a combination of them are possible choices of treatment. Radiotherapy has been increasingly used as a treatment of oral cancers, forcing the dentists to improve their knowledge about the methods, principles and side effects of this treatment such as dry mouth, rampant caries, mucositis, taste loss, infections and the most important complication after irradiation which is the osteoradionecrosis<sup>1,27</sup>.

## Methods

This study was approved by the Ethics and Research Committee of Santo André municipality (São Paulo- Brazil) in accordance with the Resolution 196/96 of the National Health Service (CEPSSA 079/2009).

A total of 252 patients were evaluated at the Municipal Center Hospital of Santo André, Center for Dental Specialties and during the 1<sup>st</sup> to 8<sup>th</sup> Campaigns for Oral Cancer Prevention accomplished by the Paulista Association of Dentist Surgeons – (APCD) of Santo André from July 2002 to July 2009. The oral exam was performed followed by incisional biopsy on patients who presented oral lesions. The specimen was stored in tubes with 10% formalin and sent to the Department of Buccal Pathology from the University of São Paulo, for histopathology, along with the standard form.

The diagnostic hypothesis was based on the clinical and macroscopic examination of the lesion. It was registered in the form the gender, age and ethnicity of the patient, the anatomical site of injury, the diagnostic hypothesis and the final diagnosis.

First, all variables were analyzed descriptively. For quantitative variables, the minimum and maximum values, and the calculation of averages, standard deviations and medians were calculated. For qualitative variables, absolute and relative frequencies were determined.

## Results

A total of 252 patients presenting some kind of potentially malignant lesions in the oral cavity were studied. The age range was from 19 to 86 years old (mean 57.8 years with SD  $\pm$  12.45 and median of 59 years) with 68 patients (27%) between 5<sup>th</sup> and 6<sup>th</sup> decades of life. It was observed that only 6 patients (2.4%) were 30 years old or younger. The male gender predominated (174/252 or 69%) compared to female (78/252 or 31%). Regarding ethnicity, 206 (82%) were white followed by 43 (17%) blacks and 3 (0.4%) Asians.

The anatomical site with higher incidence of potentially malignant lesions and/or squamous cell carcinoma was the lower lip with 69 occurrences (27.4%) followed by the tongue with 57 (22.6%), floor of the mouth with 49 (19.4%), alveolar border with 22 (8.7%) and retromolar trigone with 18 (7.1%).

Table 1 shows the diagnostic hypothesis. There was a higher incidence of suspected squamous cell carcinoma with 110 cases (43.7%), followed by 39 of leukoplakia (15.5%) and 37 of actinic cheilitis (15.5%).

Table 2 shows the final diagnosis: 125 (49.6%) cases of squamous cell carcinoma, 23 (9.1%) of hyperkeratosis, 7 (2.8%) of hyperkeratosis with mild atypia, 15 (6%) with moderate atypia and 4 (1.6%) with severe atypia.

**Table 1. Patients distribution according with the hypothetical diagnosis**

Hypothetical diagnosis	n	%
SCC (Squamous cell carcinoma)	110	43.7
Leukoplakia	39	15.5
Actinic cheilitis	37	14.7
Leukoplakia X SCC	8	3.2
Lichen planus	6	2.4
Actinic cheilitis X SCC	5	2.0
Erythroplakia	4	1.6
SCC X Actinic cheilitis	3	1.2
Paracoccidioidomycosis X SCC	3	1.2
Pleomorphic adenoma	2	0.8
Pyogenic granuloma	2	0.8
Hyperkeratose	2	0.8
Adenoid carcinoma	1	0.4
Basal cell carcinoma	1	0.4
Salivary glands carcinoma	1	0.4
Salivary glands carcinoma X Adenoid carcinoma	1	0.4
Epidermoid carcinoma	1	0.4
Carcinoma <i>in situ</i>	1	0.4
Mucoepidermoid carcinoma	1	0.4
Verrucous carcinoma	1	0.4
SCC X Verrucous carcinoma	1	0.4
SCC X Hyperkeratosis	1	0.4
SCC X Leukoplakia	1	0.4
SCC X Paracoccidioidomycosis	1	0.4
Haemangioma	1	0.4
Leuko-erythroplakia	1	0.4
Leukoplakia X Hyperkeratosis	1	0.4
Lipoma X Whartin's tumour	1	0.4
Lichen planus X Hyperkeratosis	1	0.4
Macular melanocytic	1	0.4
Mucocele	1	0.4
Salivary glands neoplasia	1	0.4
Neurofibrosarcoma	1	0.4
Nevus	1	0.4
Paracoccidioidomycosis	1	0.4
Pemphigus vulgaris	1	0.4
Actinic cheilitis X Epidermoid carcinoma	1	0.4
Keratosi X Leukoplakia	1	0.4
Rhabdomyosarcoma	1	0.4
Sarcoma	1	0.4
Non healing ulcers X SCC	1	0.4
No information	2	0.8
Total	252	100.0

Nine cases were diagnosed as actinic cheilitis, 9 (3.6%) with mild atypia, (3.6%) 15 (6%) with moderate atypia and 11 (4.4%) with severe atypia. The proliferative verrucous leukoplakia was diagnosed in 2 cases (0.8%), lichen planus in 2 (0.8%) and leukoplakia in only 1 case of (0.4%).

After checking data of diagnostic hypothesis and final diagnosis the results were: 31 (83.8%) confirmed cases of actinic cheilitis from

37 cases with probable diagnosis. From 8 cases with hypothetical diagnosis of actinic cheilitis versus squamous cell carcinoma, 4 (50%) were confirmed as actinic cheilitis and 4 (50%) as squamous cell carcinoma. The 3 (8.18%) confirmed cases of epidermoid carcinoma from 37 suspected cases of actinic cheilitis show its potential malignization.

There were 114 (88.4%) confirmed cases of epidermoid carcinoma against 129 suspected. From 42 hypothetical diagnoses of leukoplakia, 32 (76.19%) were confirmed as hyperkeratosis and 3 (7.14%) cases as epidermoid carcinoma. Three (33.3%) of nine suspected cases of erythroplakia were confirmed as squamous cell carcinoma.

After comparing data between hypothetical diagnosis and final diagnosis, 151 (60.4%) hypothetical diagnoses matched with the anatomopathological results.

**Table 2. Patients distribution according with the final diagnosis**

Final diagnosis	n	%
Epidermoid carcinoma	125	49.6
Hyperkeratosis	23	9.1
Hyperkeratosis with mild atypia	7	2.8
Hyperkeratosis with moderate atypia	15	6.0
Hyperkeratosis with severe atypia	4	1.6
Actinic cheilitis	9	3.6
Actinic cheilitis with mild atypia	9	3.6
Actinic cheilitis with moderate atypia	15	6.0
Actinic cheilitis with severe atypia	11	4.4
Adenocarcinoma	2	0.8
Acinic cell adenocarcinoma	2	0.8
Basal cell carcinoma	2	0.8
Verrucous carcinoma	2	0.8
Proliferative verrucous leukoplakia	2	0.8
Lichen planus	2	0.8
Pleomorphic adenoma	1	0.4
Candidiasis	1	0.4
Adenoid cystic carcinoma	1	0.4
Acinic cell carcinoma	1	0.4
Mucoepidermoid carcinoma	1	0.4
Leukoplakia	1	0.4
Non-specific chronic inflammatory process	15	6.0
Myoepithelioma	1	0.4
Total	252	100.0

## Discussion

The present study showed a prevalence of male in 174 (69%) and 78 (31%) of female from 252 patients examined.

According to Dedivitis *et al.*<sup>25</sup> (2004) 77% of the patients who presented epidermoid carcinoma were men and 23% women. Amorim *et al.*<sup>26</sup> (2003), found similar percentage between males (51.7 %) and females (48.2%). This prevalence tends to decrease because some of the male habits related to the etiology have been adopted by women which could partially justify the relatively homogeneous distribution among men and women<sup>27</sup>.

The prevalence of the disease on the 5<sup>th</sup> and 6<sup>th</sup> decade of life in this study is in accordance with Amorim Filho *et al.*<sup>6</sup> (2003) as 38.9 % of the patients with oral cancer were in the 6<sup>th</sup> decade of life. In contrast, Chen and Chen *et al.*<sup>28</sup> (1995) observed higher incidence in the 5<sup>th</sup> decade of life and Rosa *et al.*<sup>29</sup> (1997) in the 7<sup>th</sup> decade of life.

According to Neville and Day<sup>1</sup> (2002), the annual rate of oral cancer in black Americans is 12.4 cases /100,000 inhabitants and 9.7 cases /100,000 inhabitants for Caucasian Americans. The incidence rate among black American male is 20.5 cases/100,000 inhabitants. Regarding the anatomical site, the lower lip is the most affected (27.4%) followed by the tongue (22.6%), floor of the mouth (19.4%) and alveolar border (8.7%). Dedivitis *et al.*<sup>25</sup> (2004) showed higher incidence of oral cancer in tongue followed by floor of the mouth.

Many studies evaluated the percentage of malignancy of oral le-

sions. The present study showed 7.14% of dysplasia. Dunsche and Harle<sup>30</sup> (2000) reported 45% of dysplasia in the leukoplakia of the oral cavity. According with the present study, there was no malignant transformation in proliferative verrucous leukoplakia but Bagan *et al.*<sup>14</sup> (2003) reported 63.3% of malignant transformation in this type of lesion.

This present study detected 33.3% of dysplasia in erythroplakia.

According to Wanakulasuriya *et al.*<sup>26</sup> (2007), 19% of dysplasia was found in lesions diagnosed as erythroplakia and Hosni *et al.*<sup>20</sup> (2009) encountered 50% of malignant transformation in 13 cases studied.

The lichen planus lesions diagnosed in this study did not show any type of dysplasia. Bouquot *et al.*<sup>9</sup> (1986), after a study conducted in China with 2,119 patients with lichen planus lesions, verified malignant transformation in 1.1% of the cases.

Actinic cheilitis in this study presented 3.6 % of light dysplasia, 6% of moderate dysplasia and 4% of severe dysplasia, in contrast with Fernandes *et al.*<sup>3</sup> (2008) that detected light dysplasia in 10.34% of the cases, moderate in 27.59%, and severe in 62.07%.

## Conclusions

Dentists and other health care professionals play an important role in the early diagnosis of oral cancer and potential malignant lesions as it can prevent the development of severe dysplasia of potential malignant lesions or provide a better prognosis for patients affected by oral cancer through an immediate treatment.

Within the conditions of this study, it can be concluded that:

1. Higher prevalence in Caucasians.
2. Higher prevalence in males.
3. Predominance in the 5<sup>th</sup> and 6<sup>th</sup> decade of life with average age of 57.98 years old.
4. Predominant anatomical site was the lower lip followed by tongue, floor of the mouth, alveolar border and retromolar trigone.

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