

# Original Article

## Epithelial Precursor Lesions and Squamous Cell Carcinoma Prevalence for a Period of 10-years in the Anatomic Pathology Service of the Antonio Pedro University Hospital, Fluminense Federal University

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### Abstract

Oral squamous cell carcinoma represents approximately 90% of all oral malignancies and in some cases can be preceded by lesions considered epithelial precursor lesions. Early diagnosis of these lesions and intervention at an early stage constitute keys to reduce mortality, morbidity and expenses with oral cancer treatment. The objective of this paper is to present the prevalence of epithelial precursor lesions and oral squamous cell carcinoma at the Anatomic Pathology Service of Antônio Pedro University Hospital, Fluminense Federal University in the last ten years. Considered data were sex, age, race, location, addictions, clinical and histological aspects. A total of 3,752 oral lesions were found and evaluated. The epithelial precursor lesions represented 4.23% of the oral biopsies, while the squamous cell carcinoma represented 4.21%. Leukoplakia was the most prevalent clinical aspect among the epithelial precursor lesions. The white women in their sixties were the most affected and the buccal mucosa was the most common anatomic localization. The most frequent histological finding was the epithelial hyperplasia without dysplasia. The squamous cell carcinoma showed up clinically as an ulceration in 80.3% of the cases. The white men in their sixties were the most affected. The tongue was the most affected area. In relation to the histological classification, the most frequent type was the moderately differentiated squamous cell carcinoma. The patients with epithelial precursor lesions and with squamous cell carcinoma were smokers in its majority.

**Keywords:** Prevalence. Carcinoma squamous cell. Oral Mucosa. Precancerous Conditions.

### Introduction

Oral cancer represents the 4<sup>th</sup> most common malignant neoplasm among men and the 7<sup>th</sup> most common among women.<sup>1</sup> The squamous cell carcinoma comprehends about 90% of the mouth malignancies and some cases can be preceded by lesions considered premalignants.<sup>2-6</sup>

The term premalignant lesion was defined by the World Health Organization (WHO) in 1997 as a morphologically altered tissue in which cancer is more likely to occur than in its apparently normal counterpart<sup>7</sup> and in 2005 the WHO altered this term to “epithelial

precursor lesions”.<sup>4</sup>

The main epithelial precursor lesions are: leukoplakia, erythroplakia and actinic cheilitis.<sup>4,7</sup>

Leukoplakia is defined as a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion.<sup>7</sup> The erythroplakia is defined as a fiery red patch that cannot be characterized clinically

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or pathologically as any other definable disease. On the other hand, the actinic cheilitis is a premalignant alteration of the vermilion border of the lip that is clinically characterized as an atrophy of the vermilion border of the lip, characterized by a smooth and pale surface with eruptions, with the possibility of developing into leukoplakic lesions.<sup>5,8</sup>

Histologically, the epithelium of a precursor lesion may appear thick or atrophic and, mild, moderate or severe epithelial dysplasia, or even a carcinoma *in situ* may develop. In the actinic cheilitis, the underlying connective tissue shows an acellular and amorphous basophilic degeneration, named solar elastosis, an alteration of the collagen and elastic fibers induced by sunlight.<sup>4,8</sup>

Squamous cell carcinoma (SCC) is shown histologically as islands and invasive cords of malignant squamous epithelial cells, with variable formation of keratin pearls. The invasion appears through the destruction of the basal membrane and the progression of the tumor to the underlying connective tissue, followed by the stromal reaction. The tumor traditionally graduates into well, moderately or poorly differentiated carcinoma.<sup>4,8</sup>

The risk factors related to the epithelial precursor lesions and to the SCC are mainly the use of tobacco and alcohol. Other factors such as virus infections considered oncongenic, such as the human papilloma virus (HPV), mainly the subtypes 16 and 18, a diet poor in fruit and vegetables and immunosuppression seem to predispose to a higher risk of developing oral cancer. Anaemia due to iron deficiency, specially the severe and chronic form known as the Plummer-Vinson or Paterson-Kelly syndrome, is also associated to a high risk of carcinoma of the oral cavity, oropharynx and esophagus.<sup>2-10</sup> The carcinomas of the lower lip show a strong association with the chronic exposure to ultraviolet solar radiation, though some cases have been related to the area of contact with cigarettes, pipes and cigarillos.<sup>3,6,8,11</sup>

The importance of recognizing of the epithelial precursor lesions and the SCC in early stages by health professionals, along with the prevention focused mainly on the risk group are currently the most effective measures available to improve the prognostic of oral cancer.

The objective of this paper is to present the prevalence of the epithelial precursor lesions and the squamous cell carcinoma in the Anatomic Pathology Service of the Antônio Pedro University Hospital, Fluminense Federal University for a period of 10 years, along with the analysis of data related to sex, age, race, anatomic localization, addictions, histological and clinical aspects.

## Material and Methods

The material analyzed was the histological results of oral lesions during the period of 1996 to 2005 by the Anatomic Pathology Service of the Antônio Pedro University Hospital, Fluminense Federal University.

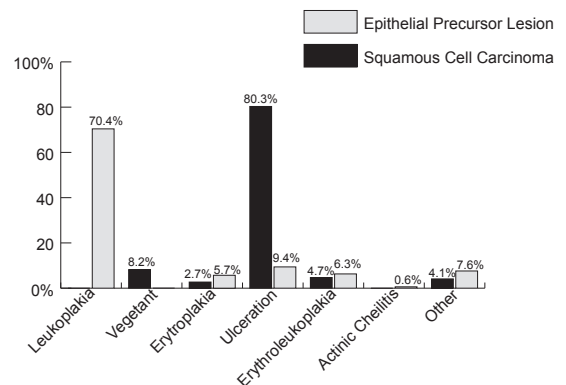
The histological conclusions of epithelial hyperplasia with or without dysplasia (mild, moderate or severe), carcinoma *in situ*, well, moderately or poorly differentiated squamous cell carcinoma, actinic cheilitis with or without dysplasia and lichenoid dysplasia were selected.

The histological requirements of each case were analyzed by sex, race, age, anatomic localization of the lesion, clinical aspect, addictions and histological description.

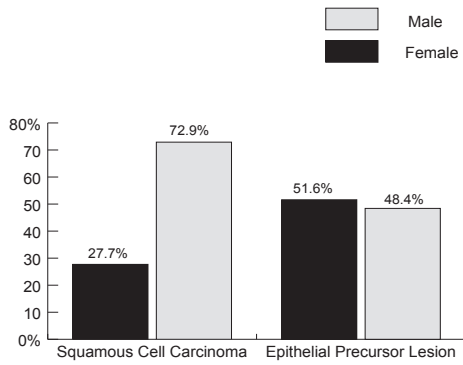
## Results

During the period of 1996 to 2005, 3,752 oral lesions were evaluated. The epithelial precursor lesions represented 4.23% (159) of the oral biopsies, while the squamous cell carcinoma represented 4.21% (158).

The leukoplakia was the most prevalent clinical aspect among the epithelial precursor lesions (70.4%), followed by the ulcerated lesion (9.4%), erythroleukoplakia (6.3%), erythroplakia (5.7%) and actinic cheilitis (0.6%) (Figure 1). The white patients (72%) female gender (51.6%) in their sixties (28.8%) were the most affected (Figure 2).



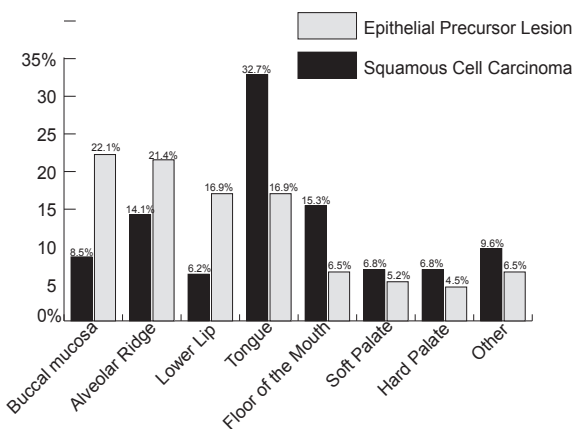
**Figure 1** – Most frequent clinical aspects of the epithelial precursor lesions and squamous cell carcinoma.



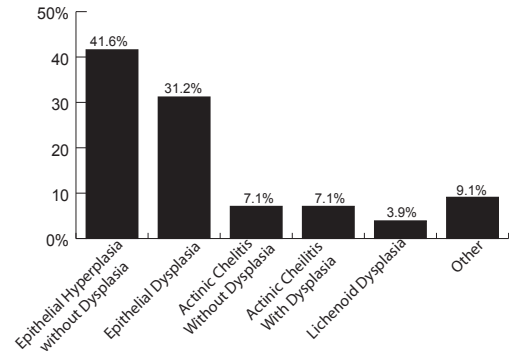
**Figure 2** - Epithelial precursor lesions and squamous cell carcinoma according to gender

The buccal mucosa was the most common anatomic localization (22.1%), followed by the alveolar ridge (21.4%), lower lip (16.9%), tongue (16.9%), floor of the mouth (6.5%), soft palate (5.2%) and hard palate (4.5%) (Figure 3). Other localizations amounted to 6.5%. The most frequent histological finding was the epithelial hyperplasia without dysplasia (41.6%) compatible with the leukoplakia clinical diagnosis (Figure 4). Other findings were epithelial dysplasia (31.2%), actinic cheilitis with dysplasia (7.1%), actinic cheilitis without dysplasia (7.1%) and lichenoid dysplasia (3.9%). Other histological aspects amounted to 9.1%. In relation to the addictions 61.5% were smokers, 13.5% smokers and drinkers, 11.5% were only drinkers, 3.9% reported other addictions and 9.6% denied addictions (Figure 5).

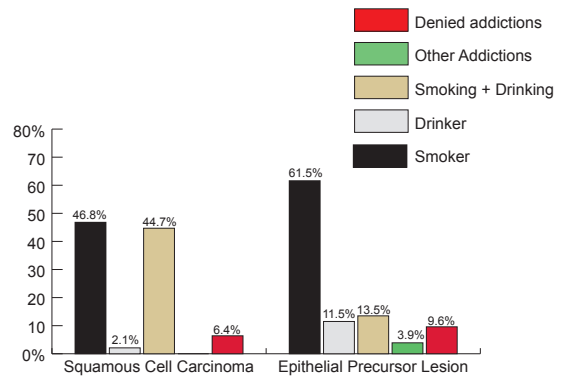
The squamous cell carcinoma showed up clinically



**Figure 3** - Most frequent locations of the epithelial precursor lesions and squamous cell carcinoma



**Figure 4** - Histological aspects of the epithelial precursor lesions



**Figure 5** - Addictions relation to epithelial precursor lesions and squamous cell carcinoma

as an ulceration in most of the cases (80.3%) (Figure 1). Other aspects found were vegetant lesion (8.2%), erythroleukoplakia (4.7%) and erythroplakia (2.7%). Further clinical aspects amounted to 4.1%. The white patients (59%) male gender (72.9%) in their fifties (27%) were the most affected (Figure 2). The tongue was the most affected area (32.7%), followed by the floor of the mouth (15.3%), the alveolar ridge (14.1%), buccal mucosa (8.5%), soft palate (6.8%), hard palate (6.8%) and lower lip (6.2%). Other areas amounted to 9.6% (Figure 3).

In relation to the histological classification, the moderately differentiated squamous cell carcinoma accounted 73.6%, the well differentiated type accounted 20.9% and the poorly differentiated, 5.5%. The patients with squamous cells carcinoma were smokers in its majority (46.8%). The smoking and drinking patients amounted to 44.7%, 2.1% were only drinkers and 6.4% denied any vicious (Figure 5).

## Discussion

During the data collection it was verified that many professionals do not perform an adequate filling of the histological requirements, what may make the anatomic-pathological examination and the collection of information for epidemiologic studies difficult. The information filled out the least was about the vicious of the patients (66.5%), followed by race (23.6%), age (6.6%), clinical aspect of the lesion (4.4%), location (0.9%) and sex (0.6%).

Most of the epithelial precursor lesions showed up in the histological examination as epithelial hyperplasia without dysplasia (41.6%), due probably to the fact that most of the lesions are leukoplakias (69.8%). The leukoplakia final diagnosis depends predominantly on the evaluation and correlation of clinical data. The literature shows the percentage of just 5% to 25% of risk of presence of the epithelial dysplasia or carcinoma.<sup>3,8-9,12-13</sup> However, the performance of biopsies and the periodical accompaniment of epithelial precursor lesions with or without epithelial dysplasia are justifiable for the fact that the development to cancer may occur in any degree of epithelial dysplasia or yet originate from a morphologically normal epithelium.<sup>4</sup>

The white patients who are over sixty years old were the most affected, as much by the epithelial precursor lesions as the squamous cells carcinoma, matching the literature records.<sup>5</sup>

The women were the most affected by the epithelial precursor lesions (51.6%), while the SCC was the most prevalent among men (72.9%). This fact may suggest that some factor may interfere avoiding the progression of the epithelial precursor lesions to the SCC in the female gender, or yet be justified by the fact that the female patients show more care concerning the self-examination and returning to the dentist for periodic appointments. In spite of these findings, there are reports in the literature that the leukoplakias are more common among men than women.<sup>8,11</sup>

The major prevalence of the SCC among men is due mainly to a higher exposure by men to oral carcinogens, such as tobacco and alcohol.

According to what has been related by other authors, although the epithelial precursor lesions have a higher incidence on the buccal mucosa and alveolar ridge, these lesions found on the tongue and mouth floor are more preoccupying, for they are the areas that are most frequently affected by the SCC.<sup>8,12</sup> These zones of increasing susceptibility for the development of the oral cancer have been called "drainage areas" where the

carcinogens accumulate before being swallowed. Thus, any precursor lesion in this area must be considered highly suspicious.<sup>4</sup>

The patients with epithelial precursor lesions as well as the ones with the SCC in their majority were only smokers or smokers and drinkers, reinforcing the role of those agents in the etiology of the oral cancer and turning these individuals into the main risk group. Around 45% of the patients with SCC were related both to smoking and drinking while only 13.5% of the cases of epithelial precursor lesions showed this association, this fact reinforces the strong synergetic effect of alcohol with tobacco in the development of oral cancer, the same not being associated to leukoplakia, a fact which has already been described in the literature.<sup>4,8</sup>

Though most of the SCC cases show clinically as an ulcer (80.3%) other aspects were found (vegetant lesion, erythroleukoplakia and erythroplakia). Amidst the lesions considered as epithelial precursor lesions the erythroplakia and the erythroleukoplakia were associated with the histological results of the SCC, which justifies a higher preoccupation with lesions that show this aspect. These findings corroborate the reports of the literature that red or erythroleukoplakia lesions show up more often in the histology severe epithelial dysplasia or carcinoma.<sup>4,8,11</sup>

Most of the SCC consists of the moderately differentiated grade. Our findings match the literature, for this histological type represented 73.6% of the cases. However the grade by the histological differentiation criterion shows limited prognostic value, when compared to the pattern of invasion. Currently new proposals of histological classification of risk have been spread, besides essays that evaluate the epithelial molecular changes in an attempt to predict the clinical behavior of epithelial precursor lesions and malignant lesions, guiding its treatment and prognostic.<sup>4</sup>

In spite of the advancements in the oral cancer treatment, the rate of five years of survival has not undergone significant improvement in the last decades.<sup>4,11</sup> Preventive measures for the oral cancer comprehend the self-examination for the detection of precursor lesions, care with the oral hygiene, healthy diet, rich in fresh vegetables and mainly the abandonment of vicious addictions such as smoking and drinking. Furthermore, periodical medical appointments for early diagnosis of malignant or epithelial precursor lesions also constitute one of the keys to the decrease in mortality, in the morbidity and in the costs with the treatment of the oral cancer.

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