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## Carcinoma of Mouth: The Retrospective Analysis of 598 Brazilian Patients



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### ABSTRACT

**Introduction:** Mouth cancer is a term that means cancers of the lip and oral cavity. Oral cancer is more common in some developing countries because it is related to the population lifestyle, particularly with the risk factors contact due to cultural issues and the difficulty accessing treatment. **Purpose:** The aim of this study is to present occurrence demographic data of patients diagnosed with squamous cell carcinoma in UFMG's Dentistry School. **Patients and Methods:** It was analyzed 598 diagnosed clinical charts. Histopathological reports of all patients with diagnosed oral cancer from 1956 to 2010 were analyzed, following inclusion and exclusion criteria. Information about genre, age, skin color, disease time report and injury site were collected and statistical analysis was done in the software Microsoft Excel 2013. **Results:** The sample consisted of 24,75% women and 74,75% men. Regarding skin color, 41,64% were leukoderma, 32,94% were afro Caucasian and 17,89% were melanoderma. The patient's majority was in sixth (28,93%) and seventh (20,74%) decades of life. About the injury location, the main sites were the tongue (165), the floor of mouth (123) and alveolar mucosa (117) cases. The injury time ranged from less than one month to 11 years. Reported time disease had up to 3 months. Oral cancer affected more Caucasians women who were in the 70th and more Caucasian men in 60th decade of life. **Conclusion:** Epidemiological studies were so much important to contribute to the database on the Minas Gerais State and Brazil cancer occurrence which may help prevention strategies.

## INTRODUCTION

Mouth cancer is a term that means cancers of the lip and oral cavity (oral mucosa, gingiva, hard palate, oral tongue and floor of the mouth). The disease has a global estimate of 300,000 new cases per year, 80% of this 1 in developing countries. The highest incidence rates were observed in populations from Central-South Asia, Malaysia, Africa and Central America. In Brazil, 15,290 new cases are estimated for 2014.<sup>1</sup>

Mouth cancer is the sixth most common cancer in the world, and squamous cell carcinoma accounts for 95%. Oral cancer is more common in some developing countries because it is related to the population lifestyle, particularly with the risk factors contact due to cultural issues and the difficulty accessing treatment.<sup>2</sup>

Squamous cell carcinoma derived from the stratified squamous epithelium of the oral mucosa and presents clinical and histological manifestations. The lesion, histologically, causes changes in the epithelium such as acanthosis, hyperkeratosis, hyperplasia and moderate to severe dysplasia in the cells and may be clinically associated with leukoplakia and erytroleukoplakia.<sup>3</sup>

The major predisposing factors to the disease are mainly smoking, alcohol consumption and ultraviolet radiation, but other factors such as HPV (human papillomavirus), *Candida sp* infections, nutritional deficiencies and genetic predispositions are associated.<sup>4</sup>

Although recent advances have been made in the diagnosis and treatment of malignant neoplasms, oral cancer appears to be a public health problem, once epidemiological data do not show improvement over time. One of the factors of this problem is the difficulty of the success of public policies that are directed to the main risk factors related to this neoplasia.<sup>5</sup>

Mouth cancers are malignant neoplasms that affect mouth's structures or tissues of the that may present lesions originating from that site, or maybe a distant site metastasis or an extension of an adjacent site. More than 90% of oral cavity neoplasm are squamous cell carcinomas that arise on the mucous membranes of the mouth and oropharynx.<sup>6</sup>

Mouth cancer is a disease that severely debilitates the patient and many cases are associated with extensive destruction of oral and orofacial structures and may result in resection of affected tissues. Treatments with radiotherapy and chemotherapy also have serious side effects. These factors generally contribute to worsening quality of life and health.<sup>7</sup>

From an epidemiological and clinical-pathological viewpoint, oral cancer can be divided into categories: oral cavity carcinomas proper, lip vermilion carcinoma and carcinoma of the oropharynx.<sup>8</sup>

The oral cavity itself extends from the lips to the palatoglossal folds, is limited below by the buccal floor and tongue and above by the hard palate and is limited laterally by jugal mucosa, teeth, and gingiva. The oropharynx is located behind the oral cavity, is limited superiorly by the soft palate, inferiorly by an imaginary line that passes in the tip of the epiglottis, previously by the posterior third of the tongue. The palatopharyngeal arches form the lateral wall and the posterior wall contains the palatine tonsils.<sup>9</sup>

Squamous cell carcinoma of the oral cavity is an invasive epithelial neoplasm that presents different degrees of cell differentiation and propensity for early and extensive lymph node nodal metastases, which mainly affects individuals who drink alcohol and cigarettes between the fifth and sixth decade of life.<sup>10</sup>

It is important to identify the biological aggressiveness of the tumors to provide the patient with an appropriate specific treatment for each type of tumor. Regional lymph node metastases, anatomic site, histological classification system, tumor malignancy classification (TNM) and depth of invasion are also indicators of prognosis.<sup>11</sup>

People who are not exposed to the tobacco's toxins present carcinogenic mechanisms different from those presented by smokers, possibly related to susceptibility to genetic mutation and viral pathogens; the latter is not yet well delimited. Prolonged exposure to carcinogens can lead to DNA damage and genetic changes in the oral epithelium leading to cancer.<sup>12</sup>

The cigarette smoke is made up of approximately 4000 substances, 81 of which are considered carcinogenic by the International Agency for Research on Cancer. Prolonged exposure to carcinogens can lead to DNA damage and genetic changes in the oral epithelium leading to cancer.<sup>12,13</sup>

In some populations, due to cultural habits, it is common for people to chew tobacco leaves, increasing the exposure time of the mucosa to the causative factor. On the other hand, populations with diets high in carotene, containing vegetables and citrus fruits, may have a greater protective effect<sup>14</sup>.

Patients diagnosed with squamous cell carcinoma who are on treatment and remain with the habit during treatment have a lower response to chemotherapy and radiotherapy and increase the invasive and metastatic power of tumor cells.<sup>13</sup>

Tobacco and alcohol are listed as the major risk factors for the disease. Tobacco ingested, chewed, inhaled or smoked in association with alcohol further increases the risk of cancer. Several mechanisms of action of alcohol were suggested: alcohol acting as a solvent, facilitating the passage of carcinogens through cell membranes; as a local irritant; improving liver metabolism and activating carcinogenic substances and may alter the intracellular metabolism of epithelial cells.<sup>15</sup>

Those patients who stop smoking are at risk of having the disease lessened over time and may approach the risk of nonsmoking patients after 10 years or more from the time they quit smoking<sup>16</sup>.

The relationship of HPV, especially HPV-16 type, between squamous cell carcinoma, has been implicated in young patients who have not been exposed to major risk factors such as tobacco and alcohol. In addition, HPV may result in a worse prognosis for tumors of the oral cavity. However, the role of HPV in oral lesions has not been fully elucidated yet.<sup>17</sup>

Recently biological markers have been linked to the disease, mainly the tumor suppressor gene p53. On the other hand, this same gene is considered the most frequently altered in cancer lesions in humans. The percentage of p53 immunoexpression found in the study was 50%, and it can not be related to worsening of the patient's prognosis.<sup>18</sup>

Squamous cell carcinoma may also be related to polymorphisms in cytochrome P-450 and glutathione-S-transferase, which decrease the detoxification of cancer cells and the number of reactive oxygen species.<sup>19</sup>

The aim of this study is to present demographic data on patients diagnosed with squamous cell carcinoma by the Faculty of Dentistry of the Federal University of Minas Gerais, Belo Horizonte, Brazil.

## **MATERIALS AND METHODS**

### **Clinical Records and Ethics**

The study analyzed data in the histopathological reports of diagnosed patients with epithelial lining cells carcinoma in the Laboratory of Anatomopathology, Dentistry School, University Federal of Minas Gerais(UFMG) from 1956 to 2010.

The project supervisor and the coordinator of the Department of Clinical, Pathology, and Surgery (DCPC), ensuring that the patients' identity should be preserved and highlight the objectives and methods of the study, authorized the histopathological reports access. The Research Ethics Committee of the Federal University of Minas Gerais under the number COEP / UFMG 33895414.4.0000.5149 approved the study.

All the patients who participated in the study signed a Free Informed Consent (FIC) form when they began their treatment at the Dentistry School of UFMG.

## 2.2 Studied population

Histopathological reports of all patients diagnosed in pathology clinics from 1956 to 2010, in a total of 598 files, were analyzed, following the criteria of inclusion and exclusion.

2.2.1 Inclusion criteria: epithelial lining cells carcinoma diagnosed patients, patients attended at the Clinic of Stomatology in UFMG Dentistry School, and correctly completed clinical records.

2.2.2 Exclusion Criteria: patients diagnosed differently than desired, patients who do not have correct.

### 2.2.3 Instrument for research and analysis of data

Data on age, gender, color, reported time of injury and site of injury were collected on all records (Table 1). The collection was done in the Dentistry School and statistical analysis was done in the software Microsoft Excel 2013. The data collected were grouped in some items for statistical analysis.

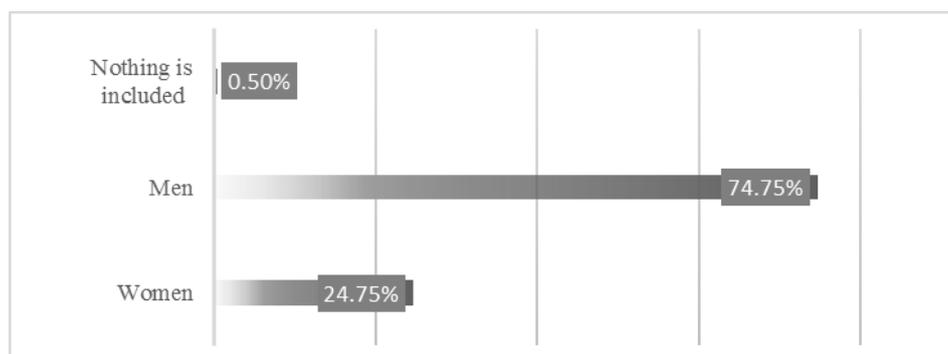
**Table 1- Demographic aspects of the studied population.**

Age (decade)	Gender	Skin color	Reported Time	Mouth localization
1 <sup>a</sup>	Man	Melanoderm	Up to 3 months	Floor
2 <sup>a</sup>	Woman	Pheoderm	From 4 to 6 months	Lip
3 <sup>a</sup>		Leukoderma	From 7 to 9 months	Language
4 <sup>a</sup>			10 to 12 months	Alveolar ridge
5 <sup>a</sup>			From 12 to 24 months	Palate
6 <sup>a</sup>			From 24 to 36 months	Mucosa Jugal
7 <sup>a</sup>			More than 3 years	Oropharynx/ retromolar
8 <sup>a</sup>				Others
9 <sup>a</sup>				
10 <sup>a</sup>				

## RESULTS

### Demographic Aspects

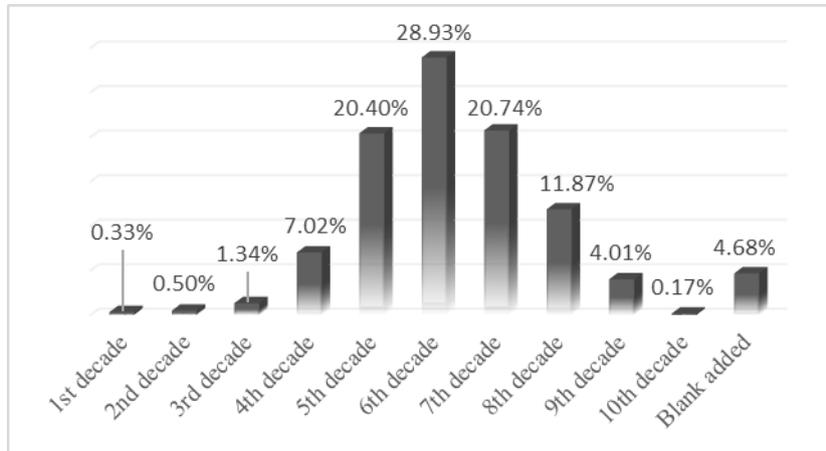
The research group had a higher percentage of male patients (74.75%) than women (24.75%)(Figure 1). Some records did not present any data regarding the gender, being allocated to the item nothing is included(0.5%).



**Figure 1 –Women and men percentage distribution in accessed records.**

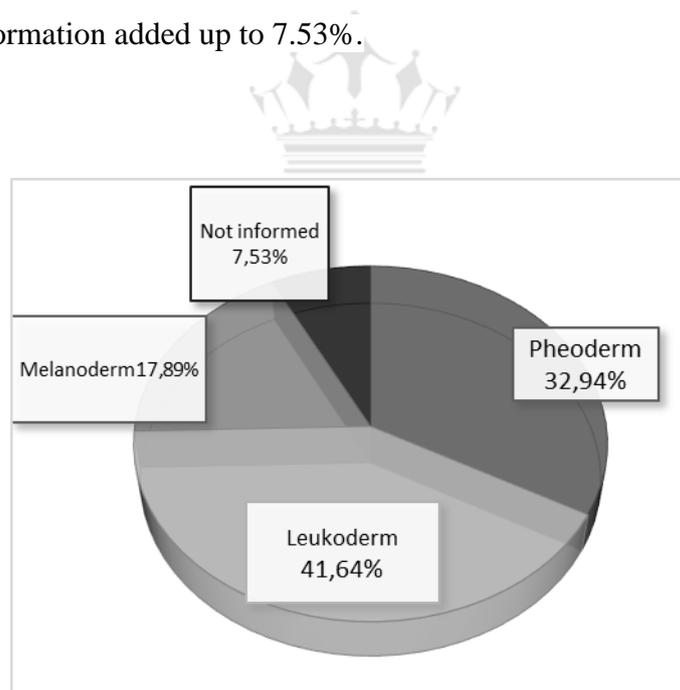
The 6th decade of life there was a higher prevalence (28.93%), followed by the 7th decade (20.74%) people and then in the 5th decade (20,40% ). After these came, in descending order,

people from the 8th decade, 4th decade, 9th decade, 3rd decade, 2nd decade, the 1st decade and 10th decade. The chips that went blank added 4.68%.



**Figure 2 –Age distribution of people with Clinical records.**

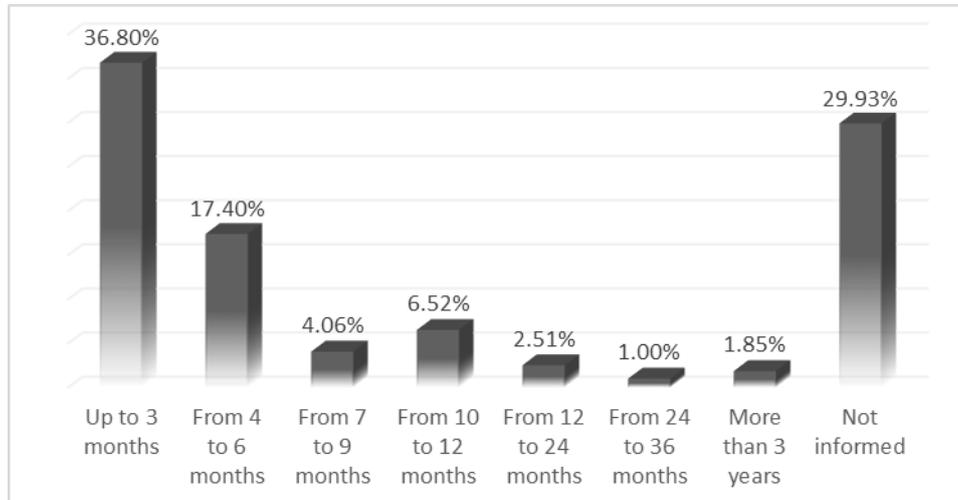
Among the study sample, leukoderma patients were the majority (41.64%) and melanoderma was the smallest percentage (17.89%). Pyoderma patients represented 32.94%. Chips that did not contain this information added up to 7.53%.



**Figure 3 - Distribution of skin color patients.**

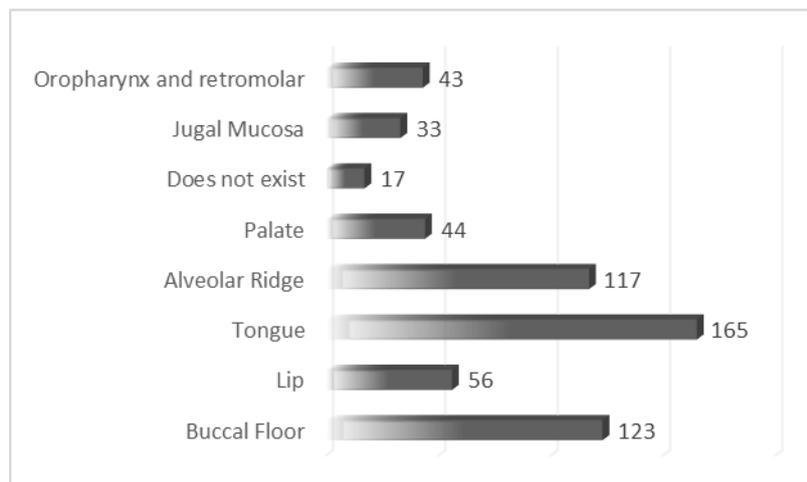
Regarding the reported time of injury by the patients, most of the files had a reported time of up to 3 months (36.80%). The second highest percentage of the reported time was in the files that did not include any written data, accounting for 29.93%, followed by the time sheets of 4

to 6 months (17.4%). Then came the chips with time from 10 to 12 months, 7 to 9 months, 12 to 24 months, more than 3 years and 24 to 36 months.



**Figure 4 –Patients distribution according to the lesions reported time.**

In the study, the site of the lesions that were most present in the files was the tongue, was located in 165 cases. The region of the buccal floor was the second most affected with 123 cases, followed by the alveolar ridge with 117 cases. The order of the other affected sites was: lip, palate, oropharynx and retromolar, jugal mucosa and tokens without data named as 'does not exist'.

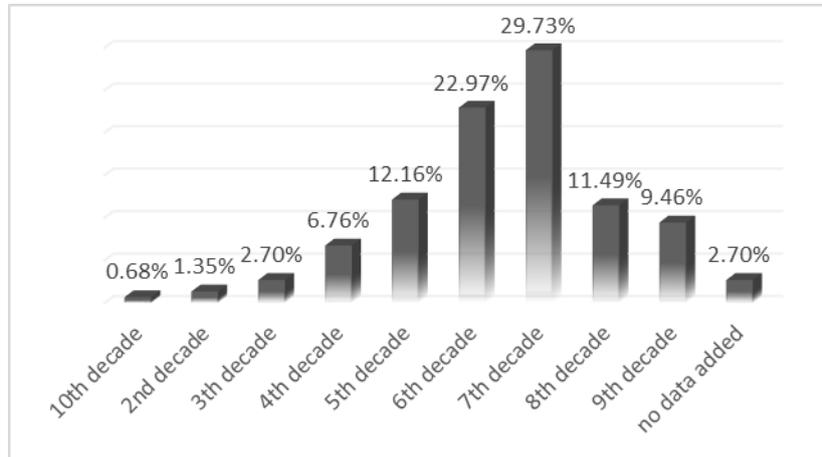


**Figure 5 - Distribution of the location of the lesion according to the clinical records.**

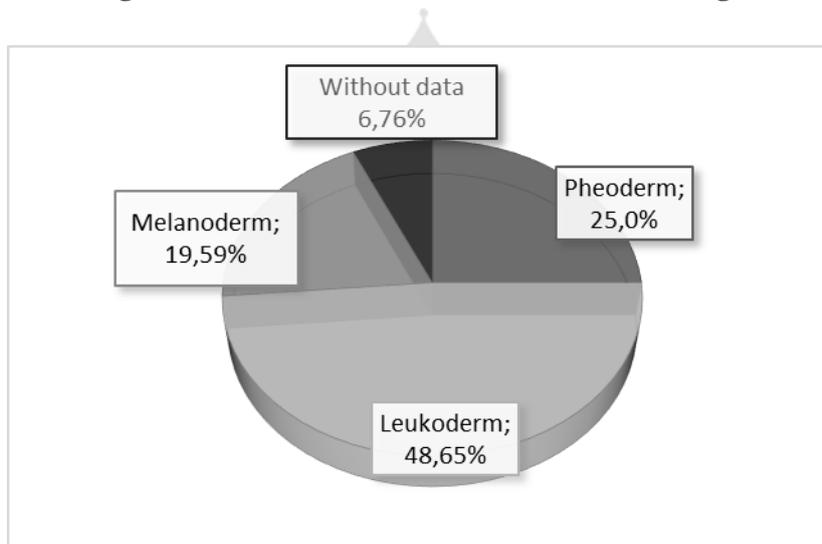
Among the analyzed data of female patients, a higher prevalence of lesions is observed in patients who are in the seventh decade of life (29.73%). Then come the ones that are in the

6th decade, 5th decade, 8th decade, 9th decade, 4th decade, 3rd decade and tokens that do not include data with the same percentage, 2nd decade and 10th decade.

There was also a higher prevalence of white women (48.65%) compared to pyoderma (25%) and melanoderma (19.59%). Chips that did not include data added 6.76%.

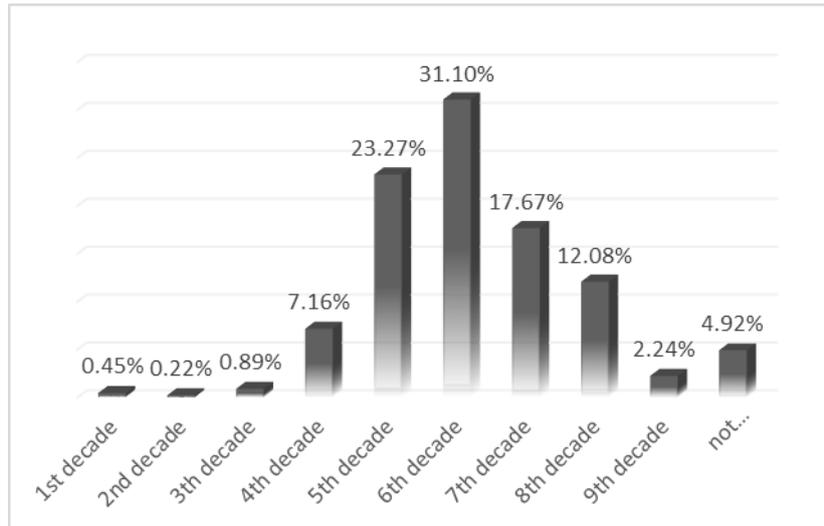


**Figure 6 –Women distribution in relation to age.**

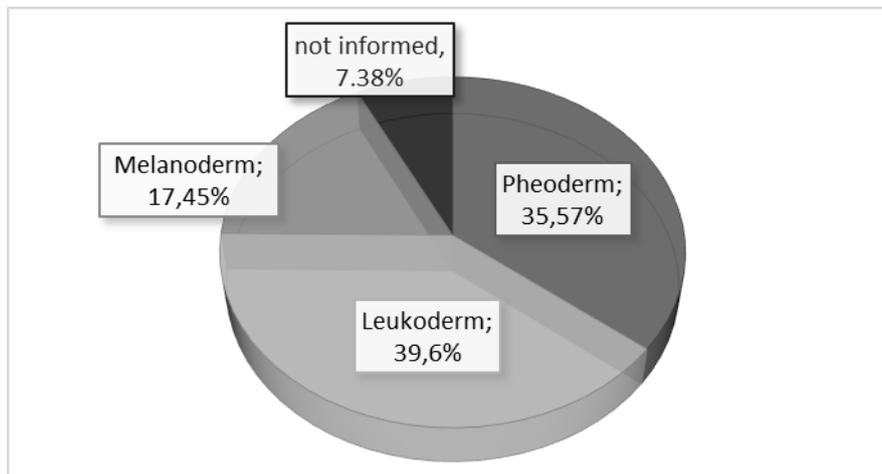


**Figure 7 - Women distribution in relation to skin color.**

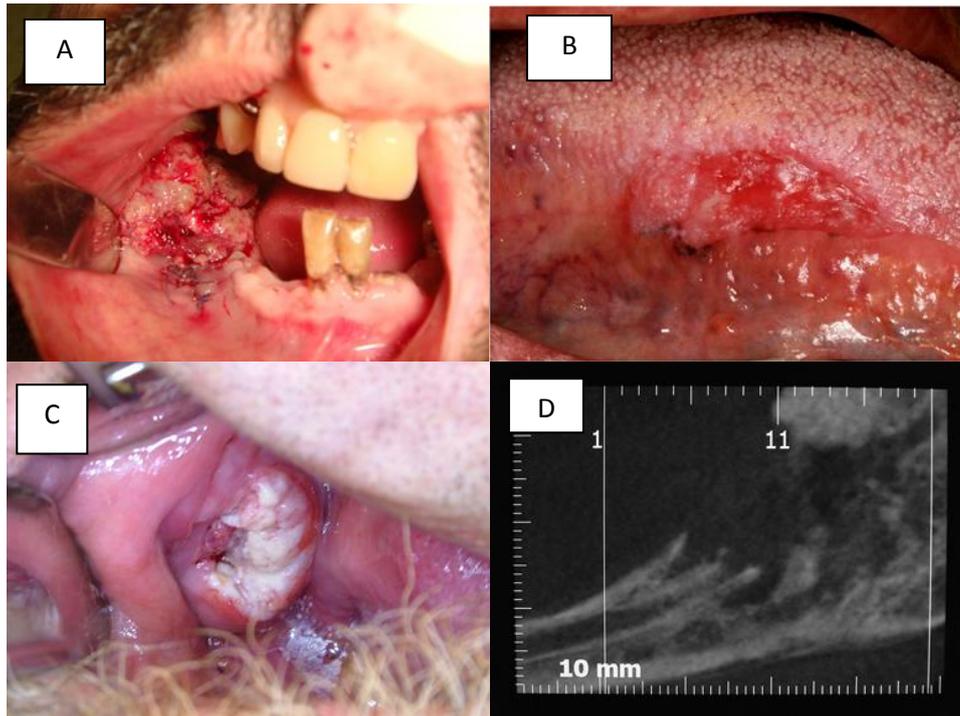
Analyzing the data of the male patients, there is a higher disease prevalence in men who are in the 6th decade of life (31.10%), then those in the 5th decade of life (23.27%). Followed by patients from the 7th decade, 8th decade, 4th decade, records that do not include data, 9th decade, 3rd decade, a 1st decade and 2nd decade in descending order. The prevalence of skin color in men was also similar to that of women, in which leukoderma had a higher percentage with 39.6%, followed by pyoderma (35.57%), melanoderma (17.45%) and chips without data (7.38%).



**Figure 8 - Men distribution in relation to the age.**



**Figure 9 - Men distribution in relation to skin color.**



**Figure 10 - Clinical and tomography aspects of oral carcinoma: A- Tongue; B- Jugal Mucosa; C- alveolar ridge; D- tomography showing invasion of the alveolar bone. (Kindly provided by Prof. Dr. Marcelo Drummond Naves).**

## DISCUSSION

In the present study, the charts used for the analysis presented a large information gap due to incomplete fillings by the students who sent the specimens to the laboratory for histopathological analysis. At the time of data collection, an important criterion had to be adopted: only those that had each item of analysis correctly filled out would be analyzed, evidencing the precariousness of the information collected during the anamnesis of the patients of the pathology clinic. For an epidemiological survey that can contribute to the database on the disease, correct registration is an essential factor for the adequate quantification of patient data.

The percentage of men affected in the study (74.75%) was higher than that of women (24.75%), as the study of Johnson et al.<sup>6</sup> that men are more affected by the disease than women[6]. However, in recent studies demonstrated by Arduino et al.<sup>20</sup> and El-Husseiny et al.<sup>21</sup> show that this discrepancy between men and women affected by carcinoma has been decreasing especially in recent years.<sup>20,21</sup> Probably due to the number of women exposed to risk factors, especially cigarette smoking, has been increasing. Brandizziet al.<sup>22</sup>, in a study in

Buenos Aires, showed that in the period between 1950 and 1970 the proportion of men/women affected by cancer in the oral cavity was 7.1: 1 and in the period from 1992 to 2000 the proportion was already 1.24: 1.<sup>22</sup> It is also important to emphasize that women visit dentists more frequently than men, a fact that generates more opportunities to make a diagnosis of precancerous lesions and lesions at an early stage, improving the patient's prognosis.<sup>23</sup>

The study reported a higher prevalence of the disease in patients who were in the 6th decade of life, followed by 7th and 5th decade of life, which coincided with previous studies by Arduino et al.<sup>20</sup> who observed that the peak of the disease in his study is in patients of the 6th and 7th decade of life.<sup>20</sup> Older adults were exposed to risk factors longer, the risk factors associated with cigarette smoking, for example, are dose-dependent in relation to daily consumption, therefore, the prevalence in patients of this age group.<sup>16</sup>

It was also observed in the study that in the present sample there was a higher prevalence of leukoderma patients (41.64%). This data coincides with the data of Weatherspoon et al.<sup>24</sup> who found a higher prevalence of the disease in white people in a study in the United States between 2000 and 2010.<sup>22</sup> However, the prevalence of leukoderma patients contrasts with other well documented previous studies including that of Neville and Day,<sup>8</sup> which shows that the percentage of cases by the population was higher among black individuals than among whites.<sup>8</sup>

Among the analyzed data, more than half of the files had the reported time of the lesion up to 6 months, which may be related to the degree of injury invasiveness, since the patients seek guidance from a professional usually when they present pain and loss of function<sup>25</sup>.

Regarding the location of the lesions, the tongue was the most affected in the files, in 165 cases of the total of the study. Note that it is very complicated to group data when it comes to lesion location data, because depending on the severity of the case and the aggressiveness of the lesion several sites may be affected. They were grouped as lesions on the tongue, which included places such as the lateral border of the tongue, the back of the tongue and the lingual belly. In some files that had lesion location in the lingual belly, they were also associated with the buccal floor (Figure 10). According to Orbak et al.<sup>25</sup>, the sites most affected by the disease were the lateral border and the belly of the tongue followed by oropharynx, floor, gingiva, buccal mucosa, lip, and palate.<sup>25</sup> In the study, the second site most affected was the alveolar ridge, which refers to the entire alveolar region, covering all the mucosa supported

on alveolar bone. The third most affected site was the lip, especially the lower lip, because in the study there was only one case in the upper lip. Lip lesions are closely linked to exposure to ultraviolet rays, especially in people who work under sunlight.<sup>6</sup>

In the study, it was also observed that in female patients, the prevalence of the disease was in women of the seventh decade of life and in white women. In male patients, the prevalence of the disease was in men of the sixth decade of life and in the white men. The fact that the prevalence of the disease occurs in men younger than women may be related to the fact that men are more exposed to risk factors and longer than women.<sup>8</sup>

## CONCLUSION

In the present study sample there was a prevalence of the disease in male patients, who were in the sixth decade of life, who reported a lesion time of fewer than three months and with a main localization in the language, coinciding with existing studies. It was also noticed that the non-completion of the records by the students of the Faculty of Dentistry of the Federal University of Minas Gerais is a relevant issue for data collection studies, especially when analyzing records of certain populations aiming at the possibility of improving the quality of diagnosis and treatment success.

## Declaration of interests

The authors confirm no conflict of interest in this work.

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