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**Research Article**

# Oral Cavity Cancers : Epidemiology and Risk Factors

**Jaoudy H<sup>2\*</sup>, Ilhami O<sup>1</sup>, Oukerroum A<sup>1,2</sup> and Slimani F<sup>1,2</sup>**

1.Faculty of Medicine and Pharmacy, Hassan II University of Casablanca, B.P 5696, Casablanca, Morocco

2.Oral and Maxillofacial Surgery Department, CHU Ibn Rochd, B.P 2698, Casablanca, Morocco

**\*Corresponding Author:** Hiba Jaoudy, Oral and Maxillofacial Surgery Department, CHU Ibn Rochd, B.P 2698, Casablanca, Morocco, Email: hibatj7@gmail.com

## 1. Abstract

**1.1. Background:** The oral cavity is the most common site for cancers of the upper aerodigestive tract. Although the oral cavity is easily accessible to clinical examination, oral cancers are diagnosed at advanced stages. Their prognosis remains unfavourable despite advances in imaging and treatment in recent years, with a relatively high mortality rate.

**1.2. Materials and methods:** This is a retrospective study with descriptive and analytical aims carried out at the Ibn Rochd Hospital in Casablanca. This study was spread over a 5-year period. A sample of 45 cases was collected from the stomatology and maxillofacial surgery department admitted for cancer of the oral cavity and who benefited or not from tumor excision with immediate or deferred reconstruction

**1.3. Discussion:** Oral cavity cancer represents a major public health challenge. The fact that it occurs in elderly, multi-targeted subjects and is diagnosed at an advanced stage explains the complexity of management and the severity of the prognosis. Despite the identification of new risk factors, alcohol and tobacco intoxication remain the main etiological factor in the development of this cancer. Diagnosis is radio-clinical, as the oral cavity is accessible to inspection. This clinical examination should be systematic in our context. Biopsy of any suspicious oral lesion, at the slightest doubt, can either confirm or rule out the diagnosis. The most frequent histological type is squamous cell carcinoma.

## 2. Keywords

Oral cavity ; Squamous cell carcinoma ; Oral cancer; Mouth cancer ; Malignant tumors of the oral mucosa

## 3. Introduction

Cancers of the lip, oral cavity, hypopharynx, oropharynx and larynx are collectively known as cancers of the mouth and oral cavity. Cancers of the lip and oral cavity are the 16th most common in the world in 2022, and the 3rd most common in countries with a medium development index, including Morocco. Squamous cell carcinomas of the oral cavity appear to be a multifactorial disease, involving tobacco and alcohol consumption, as well as dietary, infectious and genetic factors. The location of the tumor and the after-effects of various treatments (surgery, radiotherapy or chemotherapy) lead to significant impairment of essential functions such as chewing, swallowing and speech, and thus to a significant deterioration in the patient's general and oral quality of life.

## 4. Results

### 4.1. Age

The mean age at diagnosis was 63 years, with extremes ranging from 30 to 89 years (Figure1).

For men, the mean age was 60, with extremes ranging from 36 to 85.

For women, the mean age was 66.5, with extremes ranging from 30 to 89.

The most representative age group was 60-79 (Figure 2).

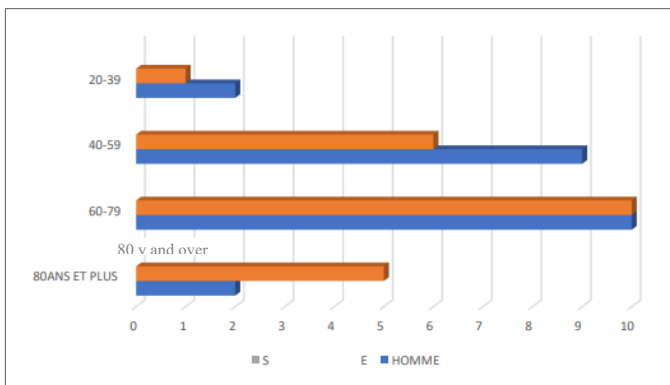


Figure 1: Patient distribution by age group

#### 4.2. Gender

24 were male, i.e. 53.34%, and 21 were female, i.e. 46.66%.

The sex ratio was 1.14.

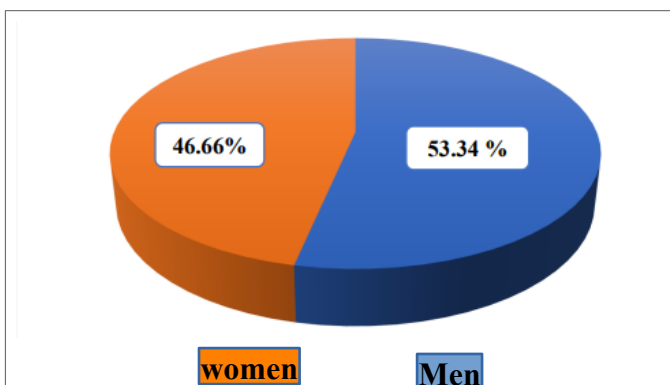


Figure 2: Patient distribution by gender

#### 4.3. Past history

**4.3.1. Comorbidities:** In our series, 12 patients, or 26.7% of cases, had a medical history: type II diabetes was found in 3 patients; 5 patients had hypertension, 2 patients had heart disease, 1 patient had chronic obstructive pulmonary disease and the last patient had hypothyroidism following thyroidectomy. No personal history of cervico-facial cancer was reported.

**4.3.2. Risk factors:** Smoking was reported by 10 patients (22.22% of cases). Tobacco-alcohol association was noted in 11.12% of cases. Cannabism was found in 8.89% of cases. 55.56% had poor oral hygiene at the time of diagnosis. 11.12% were chronically irritated by ill-fitting removable denture.

**4.3.3. Family history:** No family history of head and neck cancer was found. At least one familial cancer (digestive, gynaecological, urological) was found in 7 patients (Figure 3).

#### 4.4. Time to consultation

The time between onset of symptomatology and consultation ranged from 1 month to 3 years, with an average

of 8 months. Only 7% of patients consulted within the first 3 months after the onset of clinical symptoms.

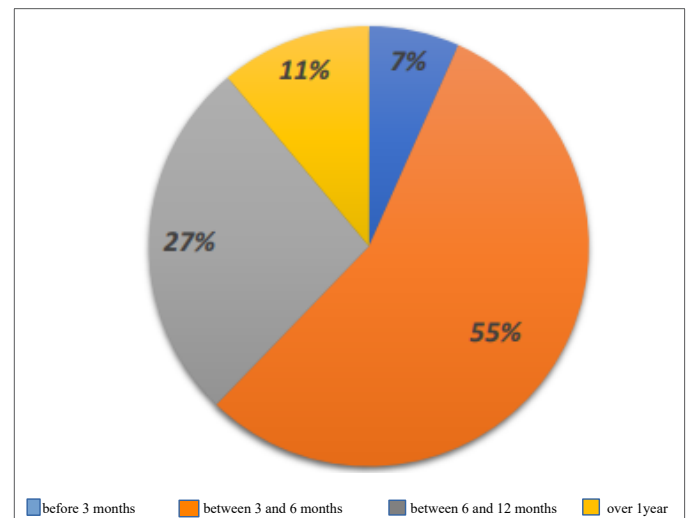


Figure 3: Distribution of patients by time to onset of symptoms

#### 4.5. Tumor site

In our series:

- 40% of lesions were located at the lingual level (of which the lateral border accounted for 88.89% of cases),
- 22.22% at gingival level,
- 13.34 % on the palate,
- 11.11% at internal jugal area,
- 6.67% at the retro-molar trigone level,
- 4.44% at floor level
- 2.22% at vestibular level.

#### 4.6. Loco-regional extension

We noted extension to adjacent structures in 8 cases (17.8%), of which 2 patients presented extension to the base of the tongue and one patient presented extension to the anterior part of the soft palate (Figure 4).

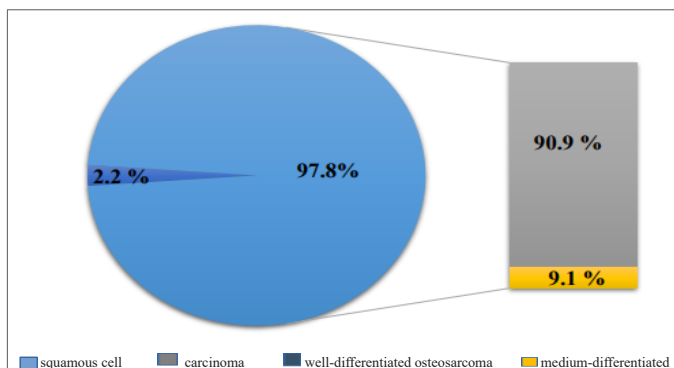


Figure 4: different locations of oral cavity cancer (1) lower gingival extended to vestibule (2) tongue (3) hard and soft palate

#### 4.7. Anatomopathological aspects

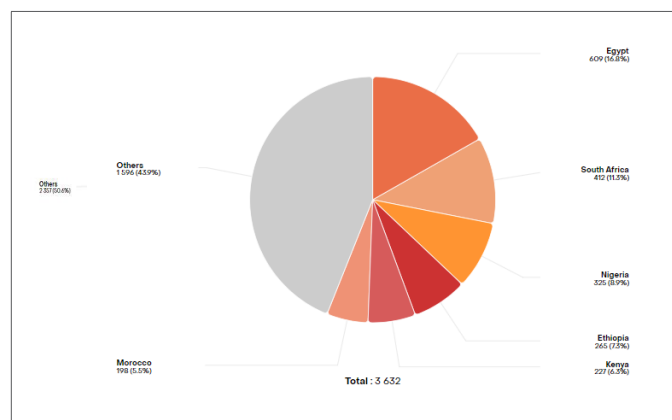
Anatomopathological confirmation was obtained in all our patients by histological examination of the

biopsy sample taken from the tumour (Figure 5). This revealed invasive squamous cell carcinoma in 44 patients (97.8%), having been well-differentiated in 90.9% of cases. A single case of intermediate-grade conventional osteosarcoma was observed in one patient (2.2%) (Figure 6).

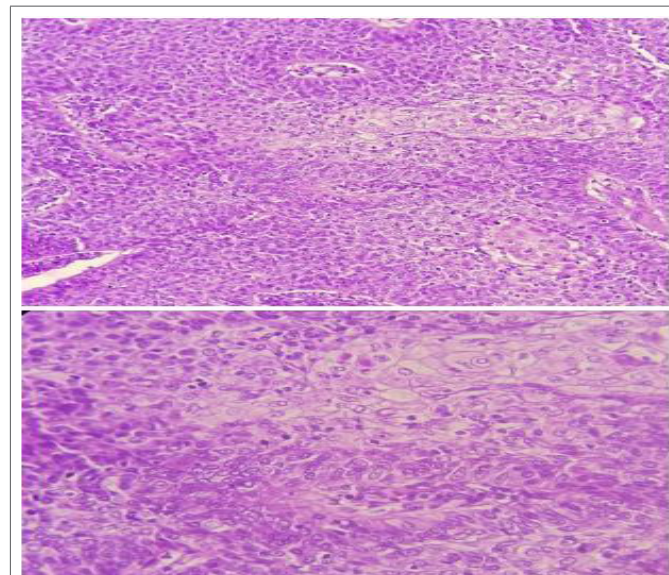


**Figure 5:** Distribution of our patients by histological type of cancer.

cancers of the lip and oral cavity are the most common upper aerodigestive tract cancers, and represent the 16th most frequent cancers overall with over 389 846 cases in 2022. In men, they rank as the 11th most common cancers in men, and 18th in women [1].



**Figure 7:** Estimated number of prevalent cases of lip and oral cavity cancers in Africa (1-year), in 2022 [1]



**Figure 6:** Histology revealing a poorly to moderately differentiated squamous cell carcinoma at two different microscopic magnifications [HE].

According to the International Agency for Research on Cancer (IARC), lip and oral cancer lip and oral cavity cancer were the 3rd most common cancer in 2020 in countries countries with an average human development index for all sexes with a percentage of 7.6%, and first in men in particular. Its incidence varies enormously from one country to another, and from one region of the same countries. By 2020, according to the Global Cancer Observatory, South Asian countries (India, Pakistan, Bangladesh) had the highest overall rates of cancer due to high consumption of betel quid (Noix d’Arec). These cancers represent a public health problem worldwide, with a death toll equivalent to 188438 for all ages and sexes combined in 2022. They rank 15th among causes of death by cancer [1].

In Africa, Morocco ranks 5th after South Africa, Egypt, Nigeria and Ethiopia, with a 5-year prevalence rate of 1,707 (4.6%). According to the Casablanca Cancer Registry 2013–2017, a total of 241 cases of oral cavity cancer C003–006, tongue cancer C001–002 and lip cancer C00 were recorded in the database over the period studied, representing 1% of all cancer locations.

### 5.1.Age and Gender distribution

**5.1.1.Age:** Cancers of the oral cavity are most common between the ages of 6th to 8th decade, with a mean age of 60 to 65 years, and are unusual in patients under 20 years of age [2]. Nevertheless, the incidence rate is beginning to rise in younger subjects [3]. The age group with the highest incidence during the period 2013–2017, according to the Registre des Cancers du Grand Casablanca, is between 60 and 64 in men. Among women, two modal modal classes are identified, the class going beyond 75 years of age followed by the one going from 50 to 59 years. The results of our study series concur with

## 5. Discussion

Because of the different physiological roles of the oral cavity, the terrain and the advanced stages at diagnosis, cancers of the oral cavity are associated with significant morbidity and mortality for the patient, and a high financial cost for the healthcare system and society.

Symptoms that are mostly latent, neglected by patients or sometimes underestimated by primary care teams, call for information, education and awareness campaigns. information, education and training campaigns. However, this cancer can now be diagnosed early, thanks to the refinement of imaging and the advent of new radiological techniques (Figure 7).

those found in the national and worldwide literature.

**5.1.2. Gender:** The latest WHO statistics show that the age-standardized incidence rate of cancer of the lip and oral cavity in medium-HDI countries, including Morocco, is 74.24% in men, with a sex ratio of 2.9 [4,5]. However, this ratio differs according to the age group studied. This high male predominance is also established by several studies carried out in different countries, with a sex ratio varying between 10.9 and 2.07 (Table 1).

A lower rate was observed in a retrospective study carried out between 2000 and 2015 in Brazil, with a sex ratio of 1.5. This is in line with the results reported in our sample, 53.34% of whom were men, i.e. a sex ratio of 1.14. Nevertheless, the studies carried out by G.Allaye, K.Dhanuthai, M. Dieng and Augustin showed a predominance of women, with a male-female ratio of 0.94, 0.86, 0.8 and 0.55 respectively. This discrepancy can be explained by the increasing exposure of women to tobacco, whereas it is decreasing in men [6,7].

Study	Sex-ratio ( M/F)
O.Elaiwy <sup>4</sup>	10,9
Delagranda <sup>5</sup>	7,77
L.Barthelemy <sup>6</sup>	5,41
R. Anis <sup>7</sup>	4,13
Bouzoubaa <sup>8</sup>	2,2
Slimani <sup>9</sup>	2,05
Al.Almeida.Leite <sup>10</sup>	1,5
G.allaye <sup>11</sup>	0,94
Dhanutai <sup>12</sup>	0,86
M.dieng <sup>13</sup>	0,8
Augustin <sup>14</sup>	0,55
Our study	1,14

## 6. THE MAIN RISK FACTORS

**6.1. Alcohol and tobacco intoxication:** Squamous cell carcinomas of the oral cavity appear to be a multifactorial disease. multifactorial disease involving tobacco and alcohol consumption, as well as dietary, infectious and genetic factors [15].

However, the risk factor found in 90 percent of cases remains chronic ethylo-tobacco intoxication, the effects of which are synergistic but not additive [15-19].

Oral carcinogenesis results from an accumulation of both genetic and epigenetic alterations in oncogenes and/or tumour suppressor genes. Chronic smoking, ethylism and human papilloma virus (HPV) induce these genetic alterations, triggering stromal cell transformation, immunosuppression and inflammation. This suggests that reducing tobacco and alcohol consumption can significantly help prevent oral cancer.

Chronic smoking is responsible for 71% of oral cancer deaths in high-income countries in high-income countries and 37% of deaths in low- and middle-income middle-

income countries [16]. At present, there is a new form of consumption called snus or snuff resulting from the cross between chewing and snuffing, which explains the different tumor localizations specific to the type of consumption. At the Joliot-Curie Institute in Dakar, based on a study of 70 cases, only 17% of cases of tobacco intoxication were diagnosed cases of tobacco intoxication were found [9,13]. In Morocco, in the study carried out at the CHU Mohammed VI de Marrakech, chronic smoking was found in 31% of cases [10,11] which is in line with the study by Erraisse [20] carried out at the Chu Hassan II de Fès in 2017 with tobacco intoxication found in 7 patients (31.81%), all male and varying between 20 and 50 packs/year. In our study, 10 patients were chronic smokers, i.e. 22.22% of cases, which is in line with the literature.

Ethyl smokers are 35 times more likely to develop oral cancer than those who don't drink or smoke. This is because alcohol is a solvent for the carcinogens contained in tobacco, which explains the synergistic effect responsible for the toxic multiplicative effect of the tobacco-alcohol combination. In M.M. Dieng's study, an alcoholic past was identified in only 7% of cases [16], which is in line with Augustin's study of 8.9% alcoholics and 7.6% chronic ethylo-tobacco addicts [14]. In Amanda Leite's series from Brazil, only 1 patient was a chronic alcoholic while 29 patients were alcohol-dependent [21]. In our country, this rate is unexpectedly higher. M. Ait Erraisse's study, carried out at the Hassan II University Hospital in Fez, found ethylism in 22.72% of patients, all of whom were male and smokers [20], which is in line with Bouzoubaa's study [8] with 21.70% alcoholics and 38.30% alcohol-smokers. In our series, ethylism alone was not found in any case, whereas the tobacco-alcohol association was noted in 5 patients (4 men and 1 woman), i.e. 11.12% of cases.

## 6.2. Consumption of Narcotics

Marijuana (USA), ganja (India), kif (Morocco and Algeria), Tekrouri (Tunisia), Hashish (Middle East), Gadda (South Africa, India and Bangladesh) and joints rolled up pure or mixed with tobacco represent the various forms of recreational cannabis use [10]. The correlation between cannabis consumption and the onset of cancer remains not yet clearly elucidated, despite the fact that it is composed of over 33 carcinogenic constituents identical to those found in tobacco smoke [10,22,23]. Because of the simultaneous consumption of alcohol and tobacco, it remains difficult to determine its effect [8]. In his study, Bouzoubaa found cannabism in 15.6% of patients [8]. This rate is much lower in our series, with only 8.89 %.

## 6.3. Oral condition

It is customary to emphasize the poor oral condition (caries, tooth decay, periodontal problems) of subjects undergoing treatment for VADS and/or ethylo-tobacco cancers [14]. According to the study by Rachit Marthur et al, poor oral hygiene is strongly associated with cancers of the oral cavity. This contributes to potentiating the effect

of other elucidated carcinogenic agents. Even taking into account known confounding factors such as tobacco and alcohol consumption, the presence of poor oral hygiene independently increases the risk of developing oral cancer [12,24-26].

In fact, many commensal or pathogenic bacterial species present in the oral cavity (*Porphyromonas gingivalis* and *Fusobacterium nucleatum*) are involved in chronic inflammation, inhibition of apoptosis cell invasion and genomic alterations in host cells leading to the development of oral carcinogenesis [3]. In addition, chronic irritation of the oral mucosa represents a potential cofactor to the development of oral cancer [27]. The oral and tongue; being highly susceptible to chronic irritation by ill-fitting dentures or decaying teeth; are common sites for this cancer [17,28,29].

In addition to being a breeding ground for oral cancers and infections, poor oral hygiene is a major morbidity factor, as it facilitates the onset of the dreaded complications associated with treatment.

In Morocco, F.Slimani noted this factor in 52% of patients [9], which is in line with the study by G.Allaye [11] with 58.5% of cases. In a retrospective study carried out at the Hassan II University Hospital in Fez on a series of 22 cases, 63.63% of patients had never received dental treatment, and three patients (13.63%) were totally edentulous, 2 of whom wore dental prostheses [20].

In our series, the oral condition was defective in 25 patients (55.6%). 48.9% of our patients were edentulous, including 6 with dentures. 11.12% presented chronic irritation due to ill fitting dentures.

#### 6.4. Other risk factors

Among the other risk factors for cancers of the oral cavity [9,16,26]

- Nutritional factors: Chronic undernutrition, hypoprotidemia, vitamin A and C deficiency (often found in alcoholics) and martial deficiency.
- Viral factors: Infection with the human papillomatosis virus (HPV) papilloma virus (HPV), in particular HPV16 and HPV18, associated with a mutation of P53, which regulates the cell cycle and maintains genome integrity in young subjects or those with no traditional risk factors.
- Pre-cancerous conditions (leukoplakia, erythroplakia, lichen planus, oral sub-mucosal fibrosis OSMF, etc.).

#### 7. Recommendation

In the light of our study, we have drawn up several recommendations concerning the multidisciplinary management of cancers of the oral cavity:

1. Conduct studies to determine the exact causes of the delay in diagnosis in this population (socioeconomic

disadvantage, self-medication and reliance on self-medication and traditional medicines, difficulty access to care), in order to improve diagnosis times, use less burdensome and less costly treatments, or even improve prognosis.

2. Educate the population at risk about the various prodromal stages of the disease to modulate the time elapsed between the 1st symptom and diagnosis.

3. Improve diagnostic conditions by training and informing front-line front-line healthcare professionals (general practitioners and dentists) to detect for early detection of malignant lesions, and thus shorten delays by referring them to specialized structures as quickly as possible (the only way to guarantee curative and functional treatment)

4. To increase the number of specialized maxillofacial surgery centers at health facilities in remote regions, to bring expertise closer to the skills closer to the population, so as to optimize referral paths with specific, adapted fast-track routes.

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