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Epidemiology and association of risk factors with molecular data of oral cancer in Senegal sub-Sahara region

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Oral cavity cancers appear to be more common among head and neck cancers (HNCs). Its incidence and etiology vary from country to country. In this study, the aim is to describe the epidemiological profile and emerge the risk factors for oral cancer in Senegal and their association with genetic alterations. The study is prospective and was conducted on 54 patients and 54 controls. Epidemiological and clinicopathological data were entered into Microsoft Excel. Descriptive and association analyses were determined using R software. Differentiation and genetic distance factors were performed with the Arlequin software. The results showed a female predominance, with a sex ratio of 0.86 and a mean age of 57.11 years. Age between 50 and 70 years, poor oral hygiene, smoking and cola consumption are risk factors for OCCs. Gum and cheek cancers as well as smokers and nonsmokers are genetically different. In view of these results, it seems that Senegalese patients have epidemiological profiles different to those of patients from other countries. The *TP53* variants found in this study could be used as a biomarker in at-risk populations.

Key words: Epidemiology, risk factors, *TP53*, mutations, cancer, oral cavity.

INTRODUCTION

Oral cavity cancers (OCCs) are the 16th most common malignancy and the 15th leading cause of death worldwide. In 2020, these cancers accounted for 377,713 cancer cases and 177,757 deaths (Sung et al., 2021). The incidence varies by country, sex, age group, ethnicity, and socioeconomic status (World Health Organisation, 2018). Most of the differences between developing and Western countries are due to differences in habits, life expectancy, preventive education, and quality of medical records (Inchingolo et al., 2020). Globally, its prevalence is reportedly higher in men than in women (5.8 versus 2.3 per 100,000) (Nocini et al., 2020). Between 1990 and 2011, the five-year overall survival rate increased from 59 to 70% (Amit et al., 2013).

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However, the survival rate may vary according to different subsites, stages and grades, age at diagnosis, treatment, and comorbidities. The percentages of diagnosed and mortality cases also vary according to geographic location (Chamoli et al., 2021). Thus, the mortality rate remains high and mainly depends on the stage of the disease at the time of diagnosis, which is often advanced. Thus, the prognosis of these cancers is sometimes poor in developing countries (Miranda-Filho and Bray, 2020). Furthermore, the overall increase in oral cancers has been widely attributed to modern lifestyles and carcinogenic environmental factors such as smoking, alcoholism, diet, and pollution (Inchingolo et al., 2020). Alcohol and tobacco use are known risk factors for OCCs, and incidence rates are higher in regions with high rates of alcohol and tobacco use. Several countries have experienced a decline in the incidence of oral cavity cancer in correlation with a decline in tobacco use.

In contrast, other countries, notably Senegal, have experienced an increase in the rate of OCCs despite declining smoking rates (GLOBOCAN, 2020). This has led to the theory that other environmental factors can increase the risk of developing oral cancer. Oral tumors may also arise because of family antecedents of certain genetic alterations in the genome, such as Fraumeni syndrome, Fanconi anemia, and dyskeratosis congenital (Venugopal et al., 2017). Moreover, there may be a strong link between prognostic and environmental factors and the accumulation of genetic alterations (Chamoli et al., 2021). Furthermore, prevention and early detection are the fundamental elements of cancer control programs (LeHew et al., 2017). Therefore, the reducing cancer morbidity and mortality rate in the most affected developing countries remains a priority (Miranda-Filho and Bray, 2020). In general, the methods available for preventing, detecting and treating of these cancers are ineffective in reducing their high incidence and mortality rates (Kakande and Kamulegeya, 2010). This justifies the need for the study to better understand the epidemiological profiles of OCCs in Senegal. This study aimed to describe the epidemiological profile and emerge risk factors for oral cancer in Senegal and their association with genetic alterations.

METHODOLOGY

Samples

This study was conducted between February 2021 and January 2023, in patients with OCCs and controls, from the Stomatology and Maxillofacial Surgery Department of the Aristide le Dantec Hospital and University Center in Dakar. The study is prospective and was conducted on 54 patients and 54 controls. After obtaining approval from the UCAD Research Ethics Committee, all patients were informed of the study to obtain their consent before recruitment. Epidemiological and clinicopathological data were obtained from patients' medical records. Data related to patient identification, environmental factors, and clinical and histopathological characteristics were collected using a data collection form.

Statistical analysis

The collected data were entered into Microsoft Excel spreadsheet software to perform the statistical analyses and then exported to R software version 4.2.2 (R Core Team, 2022). The epidemiological profile of patients with oral cancer was determined by determining the distribution of demographic characteristics between patients and controls. The distribution of environmental and clinicopathological factors was also determined globally and according to sex in patients. Quantitative parameters such as weight, height, and age were expressed as mean ± standard deviation, and qualitative parameters were expressed as percentages. Although the literature suggests that most patients are diagnosed between 50 and 70 years of age (Hashim et al., 2019), we defined our age groups as follows: less than 50 years (]50), (50-70) years ([50-70]), and older than 70 years (70[).

Parameters that showed a significant difference in distribution between patients and controls were evaluated by estimating the odds ratios (OR). Logistic regression was used with a 95% confidence interval (CI).

If the OR was greater than 1, the parameter in question was considered a risk factor for the disease.

If the OR was less than 1, the parameter in question was considered a protective factor against the disease.

If the OR was 1, the parameter in question was not related to the disease.

The *TP53* mutations previously identified in our study (Samb et al., 2023) were used to determine whether if there was a link between these genetic alterations and risk and clinicopathological factors. Fisher's exact test was used to determine associations.

The differentiation factors (F*st*) and genetic distance (D) of the tumors according to the risk and clinicopathological factors were tested using analysis of molecular variance (AMOVA). AMOVA estimates genetic structuring indices using information regarding the allelic content of haplotypes, such as allelic frequencies (Excoffier et al., 1992), using molecular data based on number of substitutions between haplotypes (or alleles). These tests were performed using Arlequin version 3.5.1.3 (Excoffier and Lischer, 2010).

The significance level was set at 5% (*P*-value = 0.05) for all the tests.

RESULTS

Demographic characteristics

Quantitative data

Boxplot analysis (Figure 1) shows that the mean age of the patients was 57.11±13.73 ranging from 25 to 83 years, in contrast to the controls who had a mean age of 42.41±15.57, with extremes of 14 and 75 years. In patients, the mean weight and height are 61.68±18.04 and 1.70±0.08 m, respectively; in contrast, in controls, these were 67.59±13.11 and 1.70±0.09 m, respectively.

Qualitative data

Parameters such as age class, ethnicity, sex, marital status, oral hygiene, cola, smoking, hot drinks, family

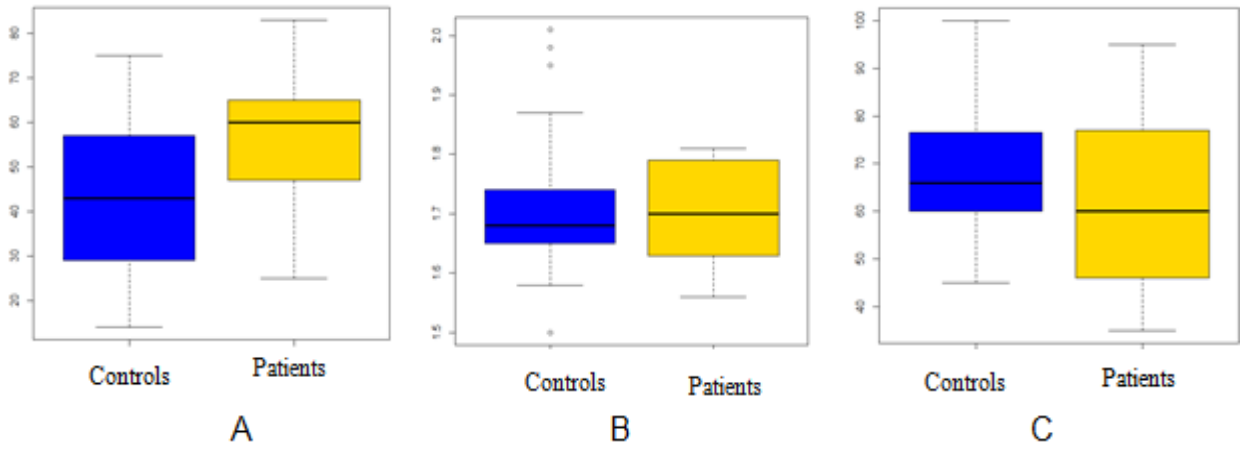

Figure 1. Boxplots the comparison between controls and patients (A: according to age, B: according to weight and C: according to height).

antecedents of cancer, and other environmental factors, showed a statistically significant difference in distribution between patients and controls. However, no differences were found between controls and patients according to locality, alcohol consumption, or body mass index (BMI). Although the BMI distribution was not statistically significant, 36.36% of the patients were underweight compared to only 13.73% of controls (Table 1).

Demographic and clinico-pathological characteristics

Overall, 53.70% of the patients were women and 57.7% were between [50-70] years of age. Only 25.93 and 5.66% of participants used tobacco and alcohol, respectively. In contrast, 89.1% consumed hot beverages, with 58.34% consumed them at least twice a day, and 33.33% consumed them once a day. In addition, 68% had poor oral hygiene and 37.2% consumed cola. Of all the subsites, the gum and cheek were the most frequent (40.74 and 27.77%, respectively). More than half of the patients were at advanced stages with 80% at stage T3-T4, 96% with lymphadenopathy, and 55% with Grade 3 disease. The most common histological type is squamous cell carcinoma with 88.90 and 22.44% of patients having a family antecedent of cancer.

According to sex, only oral hygiene and tobacco use showed a statistically significant difference. This analysis shows that poor oral hygiene was more common in women (81.48%) than in men (60%). However, men consumed more tobacco (52%) than did women (3.44%). Although not statistically significant, cola consumption is much more frequent in women (48%) than in men (28.57%). These results are shown in Table 2.

Risk factors

Overall, oral hygiene and age were identified as risk factors for OCCs (Table 3). Those with poor oral hygiene are 27.52 times more at risk than those with good oral hygiene. People aged between [50-70] had a 5.28 times higher risk, which is multiplied by 4 for people aged over 70. We found that cola and tobacco caused different risks according to sex.

Thus, women who consumed cola were 13.76 times more at risk and men who consumed tobacco were 5.53 times more at risk of developing the disease. Moreover, although not statistically significant, those who consumed 5 mega/days were 3 times more at risk than those who consumed less than 5 mega/days. Therefore, smokers for a period of 25 to 50 years were 4.2 times more at risk than smokers for a period of less than 25 years.

Factor of differentiation and genetic distance

The results show that gum cancers were genetically different from cheek cancers. Furthermore, patients that smoked were genetically different from those who did not (Table 4).

Association of *TP53* mutations with risk and clinicopathological factors

The results revealed a statistically significant association between *TP53* pathogenic mutations, risk factors, and clinicopathological factors (Table 5). Thus,

(1) c.640C>G p.214His>Asp and c.662A>T p.221Glu>Val were associated with lymphadenopathy;
(2) c.638G>A p.213Arg>Gln was associated with FAC;
(3) c.640C>G p.214His>Asp was associated with cola consumption;
(4) c.653T>G p.218Val>Gly; c.661G>A p.221Glu>Lys, and c.662A>T p.221Glu>Val were associated with

Table 1. Distribution of demographic characteristics according to patients and controls.

Parameter	Patients	Controls
	Number (frequency (%))	Number (frequency (%))
Age class		**1.307e-05***
]50	14 (25.92)	37 (69.81)
[50-70]	32 (59.25)	16 (30.19)
70[	8 (14.83)	1 (-)
Sex		**0.02602***
Men	25 (46.30)	13 (24.08)
Woman	29 (53.70)	41 (75.92)
Locality		**0.09577**
Dakar	28 (51.85)	40 (74.07)
Others	26 (48.15)	14 (25.92)
Ethnicity		**0.02348***
Diola	1 (2.04)	-
Lebou	5 (10.20)	3 (5.55)
Mandingue	5 (10.20)	1 (1.85)
Maures	1 (2.04)	2 (3.70)
Peulh	13 (26.53)	21 (38.88)
Serere	10 (20.41)	8 (14.81)
Wolof	14 (28.57.)	19 (35.18)
NA	5 (-)	
Status		**0.05483***
Single	6 (12)	11 (20.75)
Divorced	2 (4)	4 (7.55)
Marred	34 (68)	37 (69.81)
Widower	8(16)	1 (1.89)
NA	4 (-)	1 (-)
Oral hygiene		**2.095e-05***
Good	1 (1.92)	12 (22.22)
Poor	37 (71.15)	17 (31.48)
Mean	14 (26.93)	25 (46.30)
NA	2 (-)	-
Hot drinks		**1.266e-05***
At least 1 time	16 (33.33)	21 (38.89)
At least 2 time	28 (58.34)	16 (29.63)
No	4 (8.33)	17 (31.48)
NA	6 (-)	-
Cola		**2.092e-07***
Yes	18 (39.13)	2 (3.70)
No	28 (60.87)	52 (96.30)
NA	8 (-)	-
Tobacco		**0.002017***
Yes	14 (25.93)	2 (3.70)
No	40 (74.07)	52 (96.30)

Table 1. Cont'd.

Alcohol		**1**
Yes	3 (5.66)	3 (5.56)
No	50 (94.34)	51 (94.44)
NA	1 (-)	-
Others		**3.07e-08***
Yes	37(72.55)	15 (27.78)
No	14 (27.45)	39 (72.22)
NA	3 (-)	-
FAC	**0.03409***	
Yes	11 (22.45)	7 (12.96)
No	38 (77.55)	47 (87.04)
NA	5 (-)	-
BMI	**0.1559**	
Insufficiency	8 (36.36)	7 (13.73)
Normal	8 (36.36)	30 (58.81)
Obesity	3 (13.65)	7 (13.73)
Overweight	3 (13.65)	7 (13.73)
NA	32 (-)	3

FAC = Familial antecedent of cancer; BMI = body mass index; NA = non-answer; ***= s**ignificance.

Table 2. Distribution of demographic and clinicopathological characteristics according to sex.

Parameter	**Total**		**Women**		**Men**	
	Number	**Frequency (%)**	**Number**	**Frequency (%)**	**Number**	**Frequency (%)**
Age class				**1**		
]50	14	25.92	8	27.58	6	16
[50-70]	32	59.25	17	58.62	15	60
70[	8	14.83	4	13.8	4	16
Oral hygiene				**0.049***		
Good	1	1.92	1	3.70	0	0
Poor	37	71.53	22	81.48	15	60
Mean	14	26.55	4	14.82	10	40
NA		2		2		
Cola				**0.424**		
Yes	18	39.13	12	48	6	28.57
No	28	60.87	13	52	15	71.43
NA		8		4		4
Hot drinks				**0.262**		
No	4	8.33	3	12	1	4.34
At least 1 time	16	33.33	7	28	9	39.13
At least 2 time	28	58.34	15	60	13	56.53
NA		6		4		2
Tabacco				**0.0002***		
Yes	14	25.93	1	3.44	13	52

Table 2. Cont'd.

No	40	74.07	28	96.56	12	48
Alcohol				**0.092**		
Yes	3	5.66	0	0	3	5.56
No	50	94.34	28	100	22	94.44
NA	1		1		-	
Others				**0.911**		
Yes	37	72.55	19	70.38	18	76
No	14	27.45	8	29.62	6	24
NA	3		2		1	
FAC				**0.0616**		
Yes	11	22.44	4	16.66	7	28
No	38	77.56	20	83.34	18	72
NA	5		5		-	
Subsite				**0.909**		
Gum	22	40.74	12	41.37	10	40
Cheek	15	27.77	9	31.03	6	24
Tongue	8	14.81	4	13.80	4	16
Lip	5	9.25	2	6.90	3	12
Palate	3	5.55	2	6.90	1	4
Floor	1	1.85	-	-	1	4
Tumor size				**0.52**		
T ≤ 2	2	4.08	2	8	0	0
2 < T ≤ 4	7	14.28	4	16	3	12.5
4< T ≤ 6	21	42.85	11	44	10	41.66
T ≤ 6	19	38.79	8	32	11	45.84
NA	5		4		1	
Lymphadenopathy				**0.534**		
Yes	48	96	24	92.30	24	100
No	2	4	2	7.70	0	0
NA	4		3		1	
Tumor grade				**0.514**		
Grade 1	3	7.5	2	10	1	5
Grade 2	15	37.5	9	45	6	30
Grade 3	22	55	9	45	13	65
NA	14		9		5	
Stage				**0.534**		
T1-T2	10	20	7	26.92	3	12.5
T3-T4	40	80	19	73.8	21	87.5
NA	4		3		1	
Histology				**0.294**		
Squameus cell carcinoma	40	88.90	21	95.45	19	82.60
adenocarcinoma	3	6.66	1	4.55	2	8.70
Verrucous carcinoma	1	2.22	0	0	1	4.35
Lymphoma	1	2.22	0	0	1	4.35
NA	9		7		2	

FAC = Familial antecedent of cancer; NA = non-answer; ***=** significance.

Table 3. Risk factors.

Risk factor	OR	Confidence interval		*P*-value
		2.5%	97.5%	
FAC				
Yes	1.004^{e-07}	5.982^{e-42}	7.594^{e+40}	0.988
No	5.165^{e-08}	5.982^{e-42}	1.151^{e+41}	0.987
Alcohol				
Yes	1.736^{e-07}	8.647^{e-123}	5.158^{e+121}	0.991
No	1.702^{e-07}	8.647^{e-123}	1.083^{e+122}	0.991
Hot drinks				
At least 1 time	7.661^{e-02}	6.7891^{e-21}	8.646^{e+25}	0.806
At least 2 time	1.365^{e+03}	1.2095^{e-20}	1.541^{e+26}	0.789
No	1.720^{e+02}	1.5123^{e-21}	1.956^{e+25}	0.849
Oral hygiene				
Poor	27.52	3.311	228.850	0.002**
Mean	6.71	0.788	57.226	0.081
Age calss				
]50	0.189	0.077	0.437	0.0001***
[50-70]	5.285	2.238	12.481	0.0001***
70[	21.142	2.419	184.792	0.0058**
Cola				
Yes	2.115^{e-07}	1.410^{e-44}	1.717^{e+88}	0.991
No	1.265^{e-08}	1.410^{e-44}	2.862^{e+43}	0.989
Tobacco				
Yes	1.336^{e-07}	8.647^{e-123}	8.456^{e+121}	0.991
No	1.128^{e-06}	8.647^{e-123}	2.864^{e+122}	0.992
According to sex				
Cola	13.764	3.304	94.900	0.001**
Tobacco	5.538	1.187	40.538	0.047*
At least 5mega/day	4.272^{e+08}	0.000^{e00}	14.428	0.997
[25-50]	3	0.097	94.484	0.482

OR= Odds ratio; FAC = familial antecedent of cancer; * = significance.

tobacco consumption;
(5) c.640C>G p.214His>Asp and c.662A>T p.221Glu>Val were associated with tumor stage.

DISCUSSION

To the best of our knowledge, this is the first study to evaluate the epidemiological characteristics of elderly patients with OCCs. This study included 54 patients and 54 controls recruited at the Aristide le Dantec Hospital in Dakar. Patients differed significantly from controls regarding age, ethnicity, sex, marital status, oral hygiene, cola, smoking, hot beverages, FAC, and other risk factors. Of the 54 patients, 53.70% were female and 46.30% were men, with a sex ratio of 0.86. This sex ratio was slightly higher than the 0.8 found by Dieng et al. (2012) and Mbaye et al. (2021). In Benin, Hounkpatin et al. (2020) found a sex ratio of 0.90, similar to the present results. These data indicate a progressive female predominance in the incidence of oral cancer in West Africa, and particularly in Senegal. In Western countries such as Germany, the Netherlands, and Norway, the incidence in women has increased slightly in recent years

Table 4. Factor of differentiation and genetic distance.

Factor	Fst (*P*-value)	Distance (Sd)
FAC		
Yes -No	0.10 (0.74)	0.129 (0.016)
Alcohol		
Yes -No	0.127 (0.14)	0.158 (0.019)
Age class		
]50-[50-70]	0.006 (0.41)	0.137 (0.016)
]50-70[	0.06 (0.80)	0.166 (0.018)
70[-[50-70]	0.009 (0.33)	0.182 (0.02)
Hot drinks		
No -At least 1	0.14 (0.10)	0.190 (0.023)
No -At least 2	0.09 (0.26)	0.156 (0.019)
At least 1-At least 2	0.01 (0.44)	0.150 (0.017)
Cola		
Yes-No	0.01 (0.54)	0.152 (0.017)
Lymphadenopathy		
N1-N2	0.07 (0.90)	0.158 (0.018)
N1-N3	0.01 (0.37)	0.115 (0.015)
N2-N3	0.01 (0.46)	0.130 (0.015)
Tumor grade		
Grade 1-grade 2	0.18 (0.55)	0.171 (0.023)
Grade 1-grade 3	0.07 (0.65)	0.169 (0.021)
Grade 2-grade 3	0.05 (0.75)	0.159 (0.017)
Oral hygiene		
Moyenne-mauvaise	0.01 (0.43)	157 (0.017)
Subsites		
Gum -tongue	0.07 (0.14)	0,174 (0.02)
Gum -lip	0.08 (0.15)	0.122 (0.01)
Gum -cheek	0.15 (0.05*)	0.188 (0.023)
Gum -palate	0.06 (0.57)	0.158 (0.02)
Tongue- lip	0.11 (0.13)	0.120 (0.01)
Tongue -cheek	0.02 (0.33)	0.159 (0.019)
Tongue -palate	0.15 (0.70)	0.148 (0.019)
Cheek -lip	0.12 (0.17)	0.115 (0.01)
Cheek -palate	0.10 (0.61)	0.147 (0.019)
Lip -palate	0.06 (0.41)	0.099 (0.014)
Tumor stage		
T2 -T3	0.07 (0.83)	0.161 (0.019)
T2 -T4	0.05 (0.65)	0.126 (0.017)
T3 -T4	0.04 (0.86)	0.146 (0.016)
Tobacco		
Yes -no	0.10 (0.03*)	0.158 (0.02)

FAC = Familial antecedent of cancer; * = significance.

Table 5. Association of *TP53* mutations with risk and clinicopathological factors.

Parameter	c.638G>A p.213Arg>Gln	c.640C>G p.214His>Asp	c.643A>G p.215Ser>Gly	c.644G>A p.215Ser>Asn	c.647T>G p.216Val>Gly	c.653T>G p.218Val>Gly	c.655C>G p.219Pro>Ala	c.661G>A p.221Glu>Lys	c.662A>T p.221Glu>Val
Lymphadenopathy	0.08048	**0.05926***	0.09614	0.2756	0.1334	0.09614	0.1732	0.3019	**0.0072***
FAC	**0.0303***	0.1785	0.344	0.06092	0.3674	0.344	0.344	0.1701	0.344
Alcohol	1	0.4955	0.4865	1	0.5315	0.4865	0.4865	0.4865	0.4865
Hot drinks	1	0.8499	1	1	0.955	0.6734	0.955	0.5722	1
Age class	0.598	0.5653	1	1	0.1943	1	1	0.565	1
Cola	0.3793	**0.03094***	0.1546	0.7472	0.1704	0.4538	0.4011	0.3517	0.4011
Tumor grade	0.6402	1	0.9078	0.5964	0.909	0.9515	0.6933	0.9515	0.7419
Hygiene	0.1077	0.2744	0.4756	0.09426	0.2749	1	1	1	0.4756
Sex	1	1	1	0.714	0.7374	0.1939	1	0.1939	0.5171
Tobacco	0.5431	0.2479	0.1245	0.3932	0.4463	**0.01875***	0.1245	**0.01875***	**0.01875***
Stage	0.3921	**0.03574***	0.08158	0.4009	0.211	0.2743	0.312	0.4866	**0.01693***

(Miranda-Filho and Bray, 2020). Mbaye et al. (2021) suggested that aesthetic concerns lead women in our societies to seek medical advice more often than men when a significant anomaly is observed in the oromaxillofacial sphere. However, other studies consider OCCs as a male pathology (Gallì et al., 2009; Diaz et al., 2016; Borchiellini et al., 2017; Manoharan et al., 2019).

The mean age of diagnosis was 57.11±13.73 years, with 57.7% between 50 and 70 years. These results corroborate those of Touré et al. (2005), Dieng et al. (2012) and recently Mbaye et al. (2021) who found mean ages of 52.6, 52.9, and 53.2 years, respectively. Moreover, in the study by Borchiellini et al. (2017), the mean patient age was 60 years. Indeed, in the present study, the minimum age was 25 years and the maximum age was 83 years, reflecting the youth of the population affected by this oral pathology in Senegal. In addition, patients with head and neck cancers are generally younger than those with other types of cancer (Chen et al., 2007).

In the present study, the gums and cheeks were the most frequent sites (40.74 and 27.77%, respectively). These results are consistent with the trends found by Mbaye et al. (2021) with 30.5% gum tumors. In contrast, in India and Taiwan, the tongue and cheeks were the most frequently affected sites (Nagpal et al., 2002; Chen et al., 2007). Non-healing after dental extraction could explain why the gum was the most affected site. The lack of adequate materials and insufficiently of qualified health personnel in sub-Saharan countries sometimes lead to dental extractions, the need for extensive radiological and clinical examinations (World Health Organisation, 2012). Therefore, if dental extraction is poorly performed and especially on tumoral grounds, repercussions on the patient's life can even lead death (Mfutu et al., 2020).

Independent of the accessibility of the oral cavity on clinical examination, oral cancer remains a fatal disease in more than 50% of cases diagnosed annually (Warnakulasuriya, 2009). This largely reflects the fact that most patients were in advanced stages at the time of detection. Thus, 80% of our patients were in the advanced stages (T3-T4), 96% had lymphadenopathies, and 55% are high grade disease. The ignorance of insignificant ulcerations, the use of prolonged traditional treatments, the poor socioeconomic status, the cost of care, and the high illiteracy rate in developing countries could be factors in the diagnosis delay. In parallel, the lack of awareness in the general population as well as widespread cultural beliefs, lead to delayed diagnosis and, consequently, advanced presentation of the disease. Furthermore, treating oral cancers at early stages results in higher survival rates and less associated morbidity (Warnakulasuriya, 2009).

A unifying characteristic of the present study with that of Mbaye et al. (2021), in addition to location and stage, was that 88.99% of cases were cell carcinomas. It was also the most common histological type reported in several studies in Africa, such as those by Toure et al. (2005) from Dieng et al. (2012) and Hounkpatin et al. (2020), and in Europe such as those by Hayes

et al. (2018) and Azulay et al. (2020). According to Mfutu et al. (2020), this is due to the squamous nature of the oral mucosa. These differences between developed and developing countries reflect differences in age, habits, lifestyles and environmental exposure between populations.

Tobacco consumption, alcohol consumption, hot drinks, kola nuts, and poor oral hygiene accounted for 25.93, 5.66, 89.1, 37.2 and 68%, respectively. This low frequency of tobacco and alcohol consumption confirms the findings of Mbaye et al. (2021) who reported tobacco and alcohol consumption in 16.2 and 4.8% of their patients, respectively. This small minority who claimed to have consumed alcohol could be because Senegal is a Muslim majority country with 95% of the population practicing this religion. Nevertheless, tobacco use was more frequent and preferred by men. This confirms that smoking was a risk factor in men in the present study (OR = 5.53; *P*-value = 0.04; and 95% CI = 1.18 - 40.53). Several studies have considered tobacco consumption as a risk factor for OCCs (Aupérin and Hill, 2005; Gallì et al., 2009; Rivera, 2015). In 2007, tobacco smoke was found to be carcinogenic and cause oral cancer (Rivera, 2015). In addition, people who have never smoked, but have been exposed to cigarette smoke, have an 87% risk compared to those who have never smoked or have not been exposed (Lee et al., 2009). Therefore, the risk of developing OCCs increases with smoking quantity and duration. In our cohort, men who smoked at least 5 mega/days for at least 25 years had a 3 times and 4.272^{e+08} times higher risk, respectively. In fact, the risk of this disease is 35% lower in people who stopped smoking four years ago than in those who continued to smoke (Marron et al., 2010).

Among women in the present study, the proportions attributable to tobacco and alcohol consumption were 3.44 and 0%, respectively. This difference was due to the different smoking and drinking habits of men and women in Senegal. However, 48% of women consume cola, making it a risk factor specifically for women (OR = 13.7; *P*-value = 0.001 and 95% IC = 3.3 – 94.9). Cola nut consumption is widespread in Senegal, especially in older women. In Nigeria, Otoh et al. (2004) reported that 38.2% of their cohort consumed cola nuts, which is consistent with the present results. The authors suggested that this factor was most strongly associated with oral cancer. Habitual cola chewing has been reported to be an important factor for oral cancer, especially in the northwestern and northeastern parts of Nigeria (Otoh et al., 2004). Cola nut contains tannins capable of inducing palatal keratinization and their chewing has a carcinogenic potential (Salami et al., 2021). Thus, smoking and cola consumption can directly have effect on oral health and are strongly correlated with poor oral hygiene.

The present study's results showed that those with poor oral hygiene have a 27.52 times greater risk (*P*-value = 0.002 and 95% IC = 4.85 – 521.89) than those with good oral hygiene. In 2021, Mbaye et al. (2021) found that 21.9% of their cohort had poor oral hygiene, which is lower than our results (71.15%). This difference may be due to the confusion between poor and average oral hygiene. Oral bacteria associated with conditions such as caries, gingivitis and periodontics, may be caused by poor oral hygiene. According to Hayes et al. (2018), these conditions are risk factors for OCCs. For example, the evolution of caries can lead to infection, sepsis, and eventually tooth loss. This may explain why there are more gum tumors in Senegal, which may be due to non-healing tooth loss.

Another potential risk factor may be the consumption of hot beverages with a frequency of consumption of 91.67% among our patients. Indeed, tea and coffee consumption is frequent in Senegal. Drinking mate or "yerba mate", which is comparable to tea has been associated with an increased risk of developing OCCs in South America (Dasanayake et al., 2010). According to Gillison (2007), coffee intake is independently associated with oral cancer risk. In addition, the consumption of coffee and tea are drunk at high temperature and frequencies, may play a significant role in the occurrence of this oral pathology. The lack of a significant association between these hot beverages and cancer in the present study may be due to the sample size and the imprecision of the frequency of consumption.

Another aim of this study was to determine the association between *TP53* mutations and these different risk factors, and clinicopathological factors. The results of the present study showed genetic structuring according to gum and cheek tumors. Indeed, the gum and cheek were the most affected sites; however, they may be associated with different exposures. Therefore, the genetic mutations that induce cheek cancer may differ from those that induce gum cancer. We also found that smokers are genetically different from nonsmokers. Tobacco, a risk factor for cancer may play a role in modifying the DNA of smokers, which is not evident in nonsmokers. Furthermore, cancers occurring in smokers may be distinct from those occurring in nonsmokers (Le Guevelou et al., 2019). Therefore, the smoking population appears to have a different genetic profile from that of the non-smoking population. This may explain the association of mutations such as p.218Val>Gly p.221Glu>Lys and p.221Glu>Val with smoking.

In addition, we found an association of p.214His>Asp mutations, p.214His>Asp and p.221Glu>Val, p.214His>Asp and p.221Glu>Val, and p.213Arg>Gln with cola consumption, lymphadenopathy, tumor stage, and FAC, respectively. We previously showed that cola nut contains tannins that induce carcinogenesis. This could indicate that "tannins" would have a detrimental effect on the DNA molecule and thus lead to the mutation p.214His>Asp. The fact that the p.214His>Asp and

p.221Glu>Val as well as p.214His>Asp and p.221Glu>Val are associated with the presence of lymphadenopathy and tumor stage reflects the genetic differences that may exist between early and late stage tumors. This can be explained by the fact that diseases diagnosed at an early stage are easier to treat than those diagnosed at a later stage. Although OCCs occur sporadically, *TP53* mutations can be inherited resulting in Li-Fraumeni syndrome. Thus, the p.213Arg>Gln mutation was associated with FAC in the present study. Therefore, this mutation can be defined as predisposing mutation for cancer. In addition, the risk of cancer has been shown to increase in individuals with cancer predisposition syndromes such as hereditary non-polyposis colorectal cancer and Li-Fraumeni syndrome (Argiris et al., 2008).

All of these alterations would not only indicate the interaction of a carcinogen with cellular DNA but also the selection of these mutations could confer a clonal growth advantage to premalignant and malignant cells. This means that all these variants can be used as biomarkers in at-risk populations.

Conclusion

OCCs are cancers with an increasing incidence worldwide. The relatively high female predominance and proportion of subjects younger than 50 years suggest particular trends and risk factors. Although this study is limited by a large amount of missing data due to incomplete medical records and patients lost to follow-up, it reflects the epidemiological profile of Senegalese patients with OCCs. However, the results of the present study need to be further validated by additional studies including larger case series and the assessment of other region-specific factors. In addition, the existence of a register or database of oral cancers, that compiles data from all hospital services that receive patients with this pathology, would make it possible to know more about this disease and its incidence in Senegal. Additional data will help bridge the knowledge gap between Western and sub-Saharan African countries and assist health authorities in implementing public health strategies.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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