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ORIGINAL RESEARCH
Oral Pathology

Contribution of public oral pathology services to the diagnosis of oral and oropharyngeal cancer in Brazil

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Abstract: This study aimed to evaluate the contribution of oral and maxillofacial pathology laboratories (OMPLs) in Brazilian public universities to the diagnosis of lip, oral cavity, and oropharyngeal squamous cell carcinoma (SCC). A cross-sectional study was performed using biopsy records from a consortium of sixteen public OMPLs from all regions of Brazil (North, Northeast, Central-West, Southeast, and South). Clinical and demographic data of patients diagnosed with lip, oral cavity, and oropharyngeal SCC between 2010 and 2019 were collected from the patients' histopathological records. Of the 120,010 oral and maxillofacial biopsies (2010-2019), 6.9% (8,321 cases) were diagnosed as lip (0.8%, 951 cases), oral cavity (4.9%, 5,971 cases), and oropharyngeal (1.2%, 1,399 cases) SCCs. Most cases were from Brazil's Southeast (64.5%), where six of the OMPLs analyzed are located. The predominant profile of patients with lip and oral cavity SCC was Caucasian men, with a mean age over 60 years, low schooling level, and a previous history of heavy tobacco consumption. In the oropharyngeal group, the majority were non-Caucasian men, with a mean age under 60 years, had a low education level, and were former/current tobacco and alcohol users. According to data from the Brazilian National Cancer Institute, approximately 9.9% of the total lip, oral cavity, and oropharyngeal SCCs reported over the last decade in Brazil may have been diagnosed at the OMPLs included in the current study. Therefore, this data confirms the contribution of public OMPLs with respect to the important diagnostic support they provide to the oral healthcare services extended by the Brazilian Public Health System.

Keywords: Lip Neoplasms; Mouth Neoplasms; Oropharyngeal Neoplasms; Pathology, Oral; Public Health.

Introduction

Oral and oropharyngeal cancer are among the most common types of cancer worldwide, and accounted for an estimated 476,125 new cases and 225,900 deaths in 2020.[1] However, there are considerable global variations regarding the incidence rates of these lesions, with the highest rates of oral cancer occurring in India, France, Slovakia, and Brazil. Regarding oropharyngeal cancer, France, Slovakia, and Switzerland have the highest incidence rates.[2] Tobacco smoking and alcohol consumption

are well established as the main etiologic factors in the development of oral cavity and oropharyngeal cancer, while exposure to ultraviolet radiation from the sun is the main factor in lip cancer.[1] An increase in oral human papillomavirus (HPV) infection has been suggested as the main reason for the growth in the incidence of oropharyngeal cancer observed over recent decades.[2-4]

Worldwide, oral and maxillofacial pathology laboratories (OMPLs) have played a key role in the histopathological diagnosis of head and neck lesions, including lip, oral cavity, and oropharyngeal cancer[5-7], especially squamous cell carcinoma (SCC), which represents approximately 90% of cases.[8] In Brazil, most public universities maintain OMPLs that perform histopathological and cytological analyses on surgical specimens sent by the National Public Health System (SUS—its acronym in Portuguese) and from private clinics.[9-13] The Brazilian National Cancer Institute (INCA, its acronym in Portuguese) estimates that approximately 15,190 new cases of lip, oral cavity, and oropharyngeal SCC cases are expected by the end of 2022.[14] According to a previous report, most of these cases will be diagnosed by the SUS.[15] With this in mind, this multi-institutional collaborative study aimed to assess the role and contribution of Brazilian public university OMPLs to the diagnosis of lip, oral cavity, and oropharyngeal SCC between 2010 and 2019.

Methodology

Ethics

The study protocol was approved by the Research Ethics Committee of the Piracicaba Dental School, under protocol n. 37603420.0.0000.5418, and was conducted in agreement with the Declaration of Helsinki.

Study design

A cross-sectional study was performed using biopsy records from a consortium of sixteen public university OMPLs from all regions of Brazil: North, including the Federal University of Amazonas, Manaus, and the Federal University of Pará, Belém; Northeast, including the Federal University of Bahia, Salvador, the Federal University of Pernambuco, Recife, the Federal University of Paraíba, João Pessoa, and the Federal University of Rio Grande do Norte, Natal; Central-West, including the Federal University of Goiás, Goiânia, and the Federal University of Mato Grosso do Sul, Campo Grande; Southeast, including the University of Campinas, Piracicaba, the Federal University of Minas Gerais, Belo Horizonte, the University of São Paulo, São Paulo, the Federal University of Rio de Janeiro, Rio de Janeiro, the State University of São Paulo, São José dos Campos, and the State University of Rio de Janeiro, Rio de Janeiro; South, including the Federal University of Santa Catarina, Florianópolis, and the Federal University of Rio Grande do Sul, Porto Alegre. This study followed the recommendations of the *Strengthening the Reporting of Observational Studies in Epidemiology* (STROBE) statement.[16]

Samples

The histopathological records from patients diagnosed with primary lip (International Classification of Diseases for Oncology [ICD-O-03]: C00), oral cavity (ICD-O-3: C02, C03, C04, C05 [except C05.1 and C05.2], and C06), and oropharyngeal (ICD-O-3: C01, C05.1, C05.2, C09, and C10) SCC between January 2010 and December 2019 were retrieved.[17] In addition, the following morphological codes used for SCC and their variants were included in the analysis: 8051/3, 8052/3, 8070/3, 8071/3, 8072/3, 8073/3, 8074/3, 8075/3, 8076/3, 8078/3, 8082/3, 8083/3, and 8084/3.[17]

Sociodemographic data including the Brazilian region, year of diagnosis, age, gender, ethnicity/race, schooling level, alcohol consumption, smoking status, anatomical site, clinical aspect of the lesion, signs and symptoms, duration of signs and symptoms, clinical lesion size, color and consistency, biopsy type, clinical diagnosis, and histopathological variant were retrieved from the patients' histopathological records. All cases were revised by an experienced pathologist for confirming SCC diagnoses. Records lacking information regarding the histopathological diagnosis were excluded.

Data analysis

The data were collected in a Microsoft Excel® (Microsoft Corporation, Redmond, USA) spreadsheet.

Missing values were excluded from the analysis, and only valid percentages were considered. An analysis of the association between sociodemographic variables and tumor site was performed using the chi-squared test. Descriptive and inferential analyses were carried out using SPSS software version 21.0 (IBM Corporation, Armonk, USA), and a *p-value* ≤ 0.05 was considered statistically significant.

Results

A total of 120,010 oral and maxillofacial biopsies conducted within a 10-year period in 16 Brazilian university OMPLs were analyzed. Among them, 8,373 specimens were from patients diagnosed with lip, oral cavity, and oropharyngeal SCC. Fifty-two cases were excluded for the following reasons: unclear diagnosis, missing histopathological data, and multiple biopsies from the same tumor/patient. Therefore, a final sample of 8,321 cases (6.9%) of primary lip (0.8%, 951 cases), oral cavity (4.9%, 5,971 cases), and oropharyngeal (1.2%, 1,399 cases) SCC were included. Most cases were from the Southeast, where six of the OMPLs included in the study (64.5%, 5,364 cases) are located, followed by the Central-West (16.2%, 1,349 cases), where two of the included OMPLs are located. Figure 1 shows the distribution of all cases according to the five Brazilian geographic regions. The sociodemographic and clinical data from the 8,321 cases of lip, oral cavity, and oropharyngeal SCC are summarized in Table 1.

Lip squamous cell carcinoma

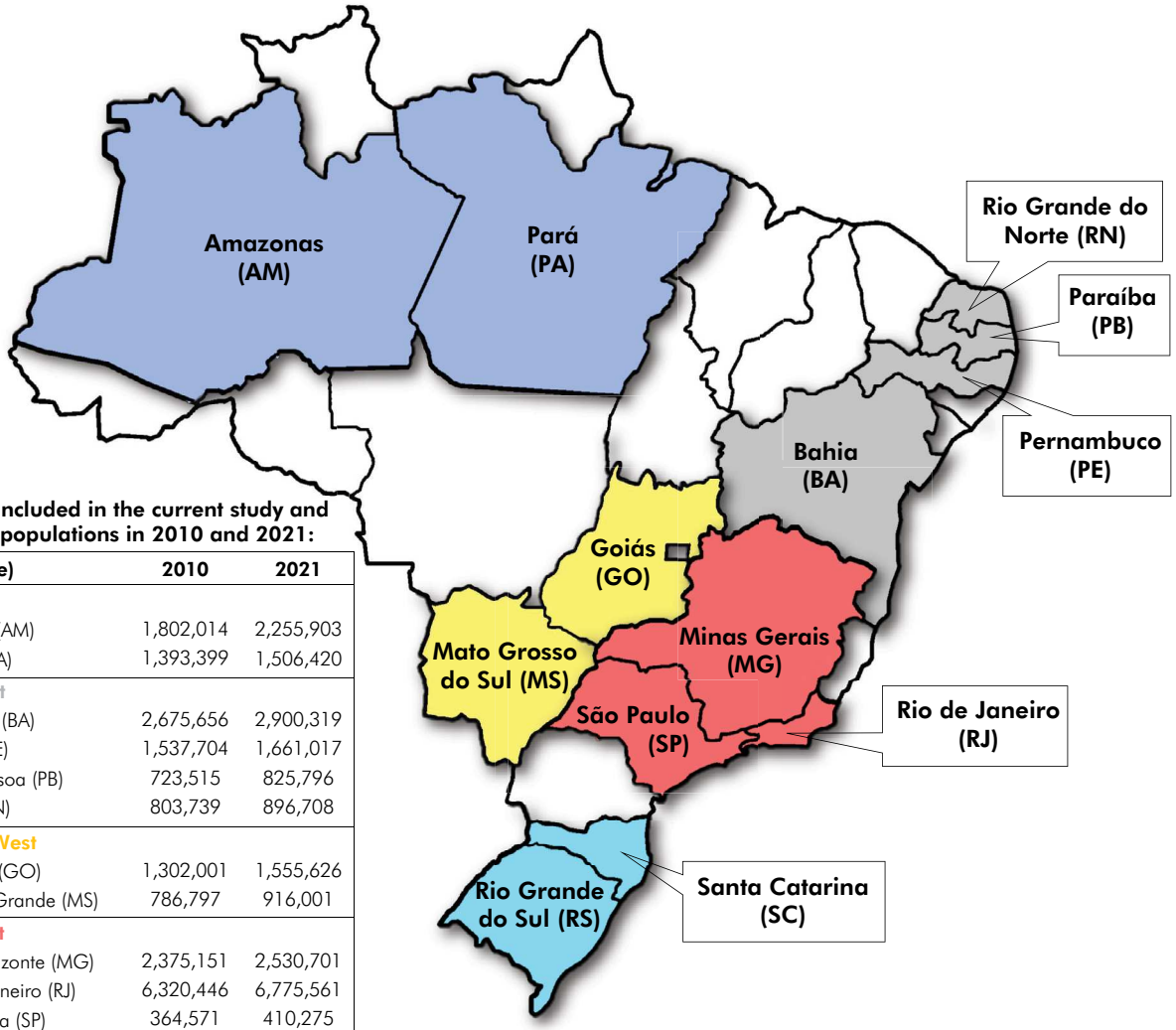
Among the 8,321 cases, approximately 11.4% (951 cases) were lip SCC (LSCC). Male and Caucasian patients comprised 75.5% (718/951 cases) and 85.3% (702/823 cases) of the sample analyzed, respectively, with a male-to-female ratio of 3.08:1. The patients' ages ranged from 17 to 99, with an average age of 63.7 ± 13.7 years. The most affected age group comprised patients over 71 (30.6%, 285/931 cases). With respect to educational level, 57.3% (228/398 cases) of the patients had 1–8 years of formal education. Concerning lifestyle behavior, 58.6% (276/471 cases) of the patients had never consumed alcohol; however, 51% (265/520 cases) reported being current tobacco smokers.

The lower lip was the subsite most commonly affected, comprising 86.1% (819/951 cases) of the lip cancer cases, followed by the upper lip (5.1%, 49/951 cases), and a site on the lip not otherwise specified (NOS, 5.1%, 49/951 cases; Table 2). With respect to clinical features (Figure 2A), most lesions were characterized by ulceration (64.3%, 562/874 cases), reddish coloration (46.9%, 338/720 cases), and hardened consistency (54.4%, 280/515 cases), and measured less than or equal to 2 centimeters (74.6%, 527/706 cases), ranging from 0.2 to 15 centimeters at their maximum diameter (median: 1.5 centimeters). Approximately 57.6% (377/654 cases) of the patients reported having an asymptomatic lesion at diagnosis, and a median time of 6 months between perceiving signs and/or symptoms and being diagnosed (range: 0.2–360 months). As expected, 80.6% (729/905 cases) of the specimens consisted of incisional biopsies, and the majority of the clinical professionals had sent the material obtained for the anatomopathological analysis indicating a clinical hypothesis of malignant tumor (67.2%, 607/903 cases) or potentially malignant lesion (23.9%, 216/903 cases).

Oral cavity squamous cell carcinoma

Approximately 71.8% (5,971/8,321 cases) of the total sample consisted of oral cavity SCCs (OSCCs). Of these, 69.3% (4,132/5,961 cases) and 58.2% (2,833/4,867 cases) were from male and Caucasian individuals, respectively, with a male-to-female ratio of 2.2:1. Patients in the sixth decade of life (30.6%, 1,783/5,822 cases) were the most affected, and the mean age of the total sample was 61.9 ± 13 years (range: 16–104 years). Regarding educational level, most individuals (60%, 1,290/2,150 cases) had 1–8 years of formal education (Elementary/Middle school). As to lifestyle behavior, 56.2% (2,029/3,610 cases) and 69.1% (2,699/3,905 cases) of the patients reported being current alcohol drinkers and tobacco smokers, respectively.

The oral tongue accounted for 39% (2,333/5,971 cases) of the oral cavity sample, followed by the floor of the mouth (21.7%, 1,297/5,971 cases),



Cities included in the current study and their populations in 2010 and 2021:

City (State)	2010	2021
North		
Manaus (AM)	1,802,014	2,255,903
Belém (PA)	1,393,399	1,506,420
Northeast		
Salvador (BA)	2,675,656	2,900,319
Recife (PE)	1,537,704	1,661,017
João Pessoa (PB)	723,515	825,796
Natal (RN)	803,739	896,708
Central-West		
Goiânia (GO)	1,302,001	1,555,626
Campo Grande (MS)	786,797	916,001
Southeast		
Belo Horizonte (MG)	2,375,151	2,530,701
Rio de Janeiro (RJ)	6,320,446	6,775,561
Piracicaba (SP)	364,571	410,275
São José dos Campos (SP)	629,921	737,310
São Paulo (SP)	11,253,503	12,396,372
South		
Florianópolis (SC)	421,240	516,524
Porto Alegre (RS)	1,409,351	1,492,530

	North	Northeast	Central-West	Southeast	South
N° cases (%)	502 (6.0%)	616 (8.1%)	1,349 (16.2%)	5,364 (64.4%)	490 (5.9%)
Included states	AM, PA	BA, PE, PB, RN	GO, MS	MG, RJ, SP	RS, SC
N° laboratories	2	4	2	6	2

Figure 1. Distribution of the 8,321 cases of lip, oral cavity, and oropharyngeal squamous cell carcinoma in the five Brazilian geographic regions (2010–2019).

and the gingiva/alveolar ridge (18%, 1,075/5,971 cases; Table 2). Based on the clinical aspect of the lesions (Figure 2B-D), most cases manifested as an ulcerated lesion (59.8%, 3,216/5,382 cases), with reddish coloration (50.6%, 2,305/4,555 cases), and hardened consistency (47.9%, 1,385/2,891 cases); most lesions measured less than or equal to 2 centimeters (40.7%, 1,514/3,722 cases), ranging from 0.2 to 24 centimeters at their maximum diameter (median: 3.0 centimeters). The majority of the individuals (74.2%, 3,238/4,361 cases) presented a symptomatic disease at diagnosis, with a median time of 3 months between perceiving signs and/or symptoms and being diagnosed (range: 0.1–360 months). Approximately 91% (4,982/5,475 cases) of the specimens consisted of incisional biopsies, and most of the clinical professionals had sent the obtained material for anatomopathological analysis

Table 1. Sociodemographic features of 8,321 patients with lip, oral cavity, or oropharyngeal squamous cell carcinoma diagnosed at sixteen public university oral pathology and maxillofacial laboratories (2010–2019).

Characteristics	Lips	Oral cavity	Oropharynx	All sites	p-value*
	N (%)	N (%)	N (%)	N (%)	
Total cases	951 (11.4)	5,971 (71.8)	1,399 (16.8)	8,321 (100.0)	
Brazilian region					
Southeast	699 (73.5)	4,026 (67.4)	639 (45.7)	5,364 (64,5)	
Central-West	78 (8.2)	696 (11.7)	575 (41.1)	1,349 (16.2)	
Northeast	72 (7.6)	505 (8.5)	39 (2.8)	616 (7.4)	< 0.0001
North	32 (3.4)	403 (6.7)	67 (4.8)	502 (6.0)	
South	70 (7.4)	341 (5.7)	79 (5.6)	490 (5.9)	
Period of diagnosis					
2010–2014	526 (55.3)	2,841 (47.6)	770 (55.0)	4,137 (49.7)	
2015–2019	425 (44.7)	3,130 (52.4)	629 (45.0)	4,184 (50.3)	
Gender					
Male	718 (75.5)	4,132 (69.3)	1,161 (83.0)	6,011 (72.3)	< 0.0001
Female	233 (24.5)	1,832 (30.7)	238 (17.0)	2,303 (27.7)	
Age at diagnosis (years)					
Mean ± SD	63.7 ± 13.7	61.9 ± 13.0	59.2 ± 10.8	61.7 ± 12.8	
≤ 30	15 (1.6)	52 (0.9)	4 (0.3)	71 (0.9)	
31 – 40	43 (4.6)	201 (3.5)	42 (3.0)	286 (3.5)	
41 – 50	94 (10.1)	809 (13.9)	244 (17.6)	1,147 (14.1)	< 0.0001
51 – 60	216 (23.2)	1,783 (30.6)	522 (37.6)	2,521 (31.0)	
61 – 70	278 (29.9)	1,563 (26.8)	390 (28.1)	2,231 (27.4)	
≥ 71	285 (30.6)	1,414 (24.3)	188 (13.5)	1,887 (23.2)	
Race/Ethnicity					
Caucasian	702 (85.3)	2,833 (58.2)	556 (45.8)	4,091 (59.3)	< 0.0001
Non-Caucasian**	121 (14.7)	2,034 (41.8)	658 (54.2)	2.813 (40.7)	
Schooling level					
Illiterate	55 (13.8)	227 (10.6)	81 (12.6)	363 (11.4)	
Elementary/Middle school	228 (57.3)	1,290 (60.0)	410 (63.7)	1,928 (60.4)	0.049
High school	77 (19.3)	431 (20.0)	110 (17.1)	618 (19.4)	
University	38 (9.5)	202 (9.4)	43 (6.7)	283 (8.9)	
Alcohol consumption					
Never	276 (58.6)	1,262 (35.0)	186 (18.1)	1,724 (33.7)	
Former	31 (6.6)	319 (8.8)	189 (18.4)	539 (10.5)	< 0.0001
Current	164 (34.8)	2,029 (56.2)	654 (63.6)	2,847 (55.7)	
Smoking status					
Never	204 (39.2)	859 (22.0)	79 (7.4)	1,142 (20.8)	
Former	51 (9.8)	347 (8.9)	95 (8.8)	493 (9.0)	< 0.0001
Current	265 (51.0)	2,699 (69.1)	900 (83.8)	3,864 (70.3)	

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Continuation					
Clinical appearance					
Ulceration	562 (64.3)	3,216 (59.8)	713 (61.5)	4,491 (60.6)	
Plaque	95 (10.9)	553 (10.3)	67 (5.8)	715 (9.6)	
Nodule	123 (14.1)	1,018 (18.9)	268 (23.1)	1,409 (19.0)	
Papule	4 (0.5)	18 (0.3)	0 (0.0)	22 (0.3)	
Macule	9 (1.0)	52 (1.0)	14 (1.2)	75 (1.0)	< 0.0001
Erosion	3 (0.3)	4 (0.4)	6 (0.5)	13 (0.2)	
Nodule and ulceration	55 (6.3)	381 (7.1)	79 (6.8)	515 (6.9)	
Plaque and ulceration	19 (2.2)	120 (2.2)	11 (0.9)	150 (2.0)	
Nodule and plaque	4 (0.5)	20 (0.4)	2 (0.2)	26 (0.4)	
Color					
White	126 (17.5)	605 (13.3)	67 (8.6)	798 (13.2)	
Red	338 (46.9)	2,305 (50.6)	474 (60.5)	3,117 (51.5)	
Yellow	44 (6.1)	122 (2.7)	15 (1.9)	181 (3.0)	
Purple	7 (1.0)	47 (1.0)	8 (1.0)	62 (1.0)	
Black	4 (0.6)	13 (0.3)	0 (0.0)	17 (0.3)	< 0.0001
Brown	17 (2.4)	15 (0.3)	9 (1.1)	41 (0.7)	
White/Red	114 (15.8)	1,087 (23.9)	144 (18.4)	1,345 (22.2)	
White/Yellow	4 (0.6)	7 (0.2)	1 (0.1)	12 (0.2)	
Red/Yellow	19 (2.6)	36 (0.8)	2 (0.3)	57 (0.9)	
Normal mucosa	47 (6.5)	318 (7.0)	63 (8.0)	428 (7.1)	
Consistency					
Fibrous	208 (40.4)	1,254 (43.4)	177 (37.8)	1,639 (42.3)	
Soft	17 (3.3)	200 (6.9)	36 (7.7)	253 (6.5)	0.005
Hard	280 (54.4)	1,385 (47.9)	244 (52.1)	1,909 (49.3)	
Similar to surrounding tissues	10 (1.9)	52 (1.8)	11 (2.4)	73 (1.9)	
Symptoms duration					
Median (range)	6 (0.2–360)	3 (0.1–360)	4 (0.25–120)	4 (0,1–360)	
Mean (months)	15.2	7	5.4	7.9	
≤ 4	256 (36.5)	2,594 (62.0)	581 (58.3)	3,431 (58.3)	< 0.0001
> 4	445 (63.5)	1,591 (38.0)	415 (41.7)	2,451 (41.7)	
Signs and symptoms					
Asymptomatic	377 (57.6)	1,123 (25.8)	222 (20.5)	1,722 (28.2)	< 0.0001
Symptomatic***	277 (42.4)	3,238 (74.2)	863 (79.5)	4,378 (71.8)	
Clinical lesion size****					
Median (range)	1.5 (0.2–15)	3 (0.1–24)	3 (0.2–15)	1.8 (0.1–24)	
Mean (centimeters)	1.9	3.2	3.2	2.9	
T1	527 (74.6)	1,514 (40.7)	247 (38.1)	2,288 (45.1)	
T2	125 (17.7)	1,389 (37.3)	246 (37.9)	1,760 (34.7)	< 0.0001
T3	47 (6.7)	804 (21.6)	121 (18.6)	972 (19.1)	
T4	7 (1.0)	15 (0.4)	35 (5.4)	57 (1.1)	

Continue

Continuation					
Biopsy type					
Incisional biopsy	729 (80.6)	4,982 (91.0)	1,210 (92.1)	6,921 (90.0)	< 0.001
Excisional biopsy	176 (19.4)	493 (9.0)	104 (7.9)	773 (10.0)	
Clinical hypothesis					
Reactive/inflammatory lesions	31 (3.4)	224 (4.2)	12 (1.1)	267 (3.7)	< 0.0001
Infectious lesions	26 (2.9)	129 (2.4)	18 (1.6)	173 (2.4)	
Cystic lesions	1 (0.1)	7 (0.1)	0 (0.0)	8 (0.1)	
Potentially malignant lesions	216 (23.9)	358 (6.8)	28 (2.6)	602 (8.3)	
Benign tumors	17 (1.9)	25 (0.5)	1 (0.1)	43 (0.6)	
Malignant tumors	607 (67.2)	4,502 (85.1)	1,028 (94.2)	6,137 (84.2)	
Immune mediated diseases or oral manifestations of systemic diseases	5 (0.6)	43 (1.6)	4 (0.4)	52 (0.8)	

SD: standard deviation. Missing data – Sex: 7 cases (0.1%); age at diagnosis: 178 cases (2.1%); race/ethnicity: 1,417 (17.0%); schooling level: 5,129 cases (61.6%); alcohol consumption: 3,211 cases (38.6%); smoking status: 2,822 cases (33.9%); signs and symptoms: 2,221 cases (26.7%); symptoms duration: 2,439 cases (29.3%); lesion size: 3,244 cases (39%); clinical appearance: 905 cases (10.9%); color: 2,263 cases (27.2%); consistency: 4,447 cases (53.4%); biopsy type: 627 cases (7.5%); clinical hypothesis: 1,039 cases (12.5%). *Comparison between the three topographies (lips, oral cavity, and oropharynx) and the sociodemographic variables. **Asian, black, brown, and indigenous; ***Pain, unhealed post-extraction, bleeding, paresthesia/hypoesthesia, discomfort, burning, dysphagia, and others; ****Based on the clinical staging of cancer (clinical TNM classification).

indicating a clinical hypothesis of malignant tumor (85.1%, 4,502/5,288 cases), with SCC being the most common hypothesis.

Oropharyngeal squamous cell carcinoma

Of the 8,321 patients, 1,399 (16.8%) were diagnosed with oropharyngeal SCC (OPSCC). Male and non-Caucasian patients comprised 83% (1,161/1,399 cases) and 54.2% (658/1,214 cases) of the sample analyzed, respectively, with a male-to-female ratio of 4.8:1. The patients' ages ranged from 30 to 94, with an average age of 59.2 ± 10.8 years. The most affected age group consisted of patients between 51 and 60 (37.6%, 522/1,390 cases). As to schooling level, the majority of patients (63.7%, 410/644 cases) had 1–8 years of formal education (Elementary/Middle school). Regarding lifestyle behavior, 63.6% (654/1,029 cases) and 83.8% (900/1,074 cases) of the individuals reported being current alcohol drinkers and tobacco smokers, respectively.

The soft palate accounted for 32.4% (453/1,399 cases) of the OPSCCs, followed by the base of tongue (28.9%, 405/1,399 cases), and the tonsils (20.5%, 287/1,399 cases; Table 02). As to the clinical aspect of the lesions (Figure 2E and 2F), most cases were characterized by an ulcerated lesion (61.5%, 713/5,382 cases), with reddish coloration (60.5%, 474/783 cases), and hard consistency (52.1%, 244/468 cases); most lesions measured less than or equal to 2 centimeters (38.1%, 247/649 cases), ranging from 0.2 to 15 centimeters at their maximum diameter (median: 3.0 centimeters). Most individuals (79.5%, 863/1,085 cases) presented a symptomatic disease at diagnosis, with a median time of 4 months between perceiving signs and/or symptoms and being diagnosed (range: 0.25–120 months). Approximately 92.1% (1,210/1,314 cases) of the specimens consisted of incisional biopsies. Most of the clinical professionals had sent the material for anatomopathological analysis indicating a clinical hypothesis of malignant tumor (94.2%, 1,028/1,091 cases), with SCC being the most common clinical diagnosis.

Discussion

Brazil is a country of continental dimensions, the most populous country in Latin America, and the seventh most populous country in the world. Additionally, Brazil has the highest incidence of LSCC, OSCC, and OPSCC in Latin America, up to three times higher than that of the other surrounding countries.[18,19] The INCA estimates that

Table 2. Distribution of the 8,321 cases of lip, oral cavity, and oropharyngeal squamous cell carcinoma according to tumor subsite (2010–2019).

Subsite	n (%)
Lips (n = 951)	
Upper lip	49 (5.1)
Lower lip	819 (86.1)
Commissure	34 (3.7)
Lip, NOS	49 (5.1)
Oral cavity (n = 5,971)	
Oral tongue	2,333 (39.0)
Floor of the mouth	1,297 (21.7)
Retromolar trigone	377 (6.3)
Hard palate	237 (3.9)
Palate, NOS	111 (1.9)
Gingiva/alveolar ridge	1,075 (18.0)
Buccal mucosa	373 (6.2)
Fornix region	61 (1.2)
Mouth, NOS	107 (1.8)
Oropharynx (n = 1,399)	
Base of tongue	405 (28.9)
Tonsil	287 (20.5)
Soft palate	453 (32.4)
Lateral wall	5 (0.6)
Vallecula	29 (2.0)
Uvula	18 (1.2)
Posterior wall	11 (0.9)
Anterior face of epiglottis	18 (1.2)

NOS: not otherwise specified.

approximately 83,751 cases of LSCC, OSCC, and OPSCC occurred between 2010 and 2019 in Brazil (available at: https://irhc.inca.gov.br/RHCNet/visualizaTabNetExterno.action, accessed 4 February 2023). Of these, 8,321 (9.9%) cases were diagnosed by the sixteen Brazilian public university OMPLs included in this study. It should be highlighted that the current study included 16 OMPLs from only 13 of the 27 Brazilian states; therefore, the percentage of cases diagnosed in these centers might be higher than that presented herein. To the best of our knowledge, there are 113 public universities throughout Brazil, most of which are concentrated in the Northeast and Southeast. Minas Gerais is the state with the greatest number of public universities. In addition, each state usually has more than one public university, and several other private ones; furthermore, most of these universities provide specialized services in diagnosing lesions affecting oral and maxillofacial tissues free of charge. However, the exact number of OMPLs in Brazilian public universities is unknown. Moreover, OMPLs not only contribute to the diagnosis of SCC but also to the training of new professionals to qualify them to work in regions that need oral pathologists (OPs). OMPLs in Brazil mostly belong to public and private universities.[6,9,11-13,20]

Corroborating our findings, nationwide data from the INCA (the main Brazilian database) show that the profile of Brazilian patients with LSCC and OSCC remains mostly Caucasian men with a mean age over 60. Conversely, most OPSCC patients are non-Caucasian males, with an average age of 58.7 years at the time of diagnosis.[14,21] Historically, LSCC, OSCC and OPSCC have been linked to socioeconomic status in low- and middle-income countries, with the highest prevalence rates occurring in the most disadvantaged population groups.[15,22–24] Accordingly, 71.8% of all patients in the current study had only up to 8 years of formal education, especially OPSCC individuals.

Notwithstanding the epidemiologic changes observed in the past decades, during which the incidence of HPV-related OPSCC has increased in several countries,[2] tobacco and alcohol consumption remain the most frequent risk factors in the development of OPSCC in the Brazilian population, corresponding to 83.8% and 63.3% of our sample, respectively. These results are compatible with data from the INCA database[21,22] and other low- and middle-income countries from Asia[25] and South America.[24] Therefore, the epidemiologic transition of oropharyngeal carcinogenesis may not have manifested itself among Brazilian patients.

After a diagnosis of OPSCC is made, the American Society of Clinical Oncology[4] recommends an investigation of HPV status of the tumor using surrogate marker p16 immunohistochemistry followed by a confirmatory HPV-specific test, such as in situ hybridization or polymerase chain reaction,

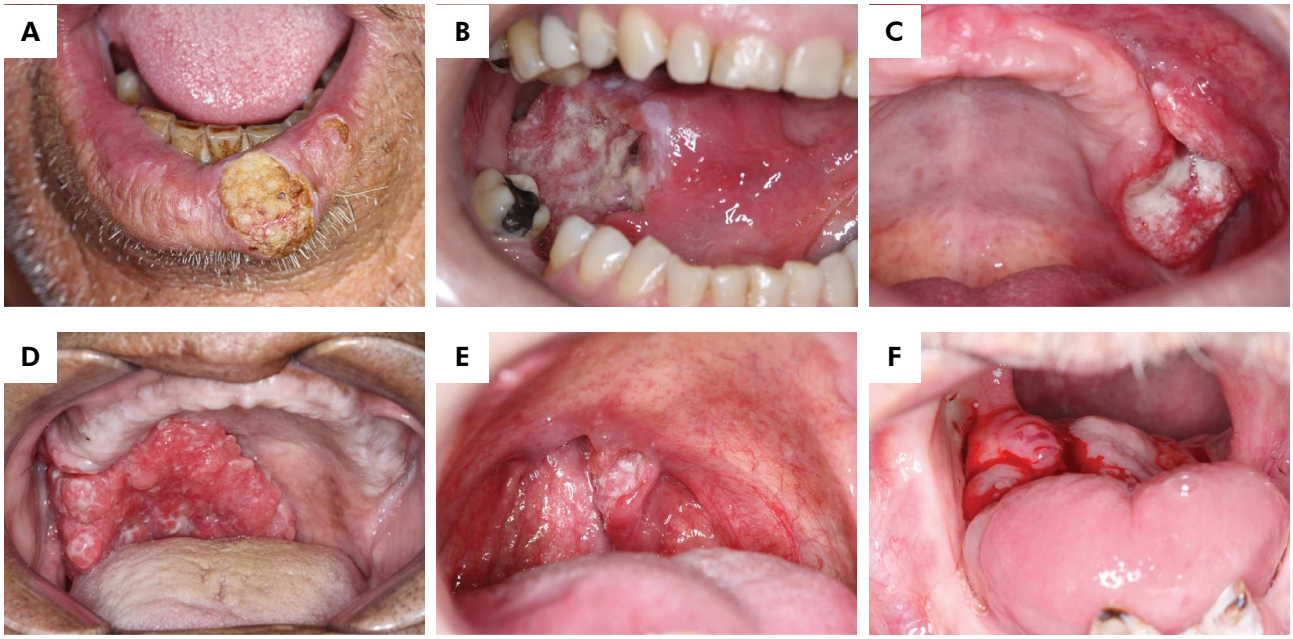

Figure 2. Clinical appearance of lip, oral cavity, and oropharyngeal squamous cell carcinomas. (A) Painless hard nodule with crusting and a yellowish surface, with a progression time of two months, located in the lower lip of a 59-year-old Brown man, who was a tobacco and alcohol user. (B) Painful ulceration with white areas and a progression time of four months in the lateral border of the tongue of a 58-year-old Caucasian woman, who was a nonsmoker and nondrinker. (C) Painful ulceration with white and red areas in the left alveolar ridge of a 78-year-old Caucasian man, who was a tobacco and alcohol user. (D) Large mass with superficial ulceration and bleeding, with a progression time of three months, encompassing the hard/soft palate and tonsillar pillar of a 67-year-old Brown man, who was a tobacco and alcohol user. (E) Ulceration with white areas and a progression time of 30 days in the tonsillar pillar of a 57-year-old Caucasian man, who was a tobacco and alcohol user. (F) Large painful swelling with a progression time of six months at the base of the tongue of a 76-year-old Caucasian man, who was a former smoker and alcohol user.

but these tests are not routinely applied in most Brazilian OMPLs due to their high cost.[9,20] Thus, it was not possible to establish the prevalence of HPV-related OPSCC in the current sample. In addition, the sociodemographic profile of patients with OPSCC in the present study was very similar to that observed in developing nations, with a reported low prevalence of HPV-related OPSCC, such as Thailand,[25] Sri Lanka,[26] and other South American countries.[24]

Brazilian public universities offer several services free of charge to local populations, including those of oral pathology laboratories. According to the last National census (available at: https://cidades.ibge.gov.br/brasil/panorama, accessed 4 February 2023), approximately 18% of the population (34,514,550 people) live in the 15 cities included in the present study (Figure 1). Therefore, the 16 OMPLs analyzed herein provide an important diagnostic service for a significant portion of the Brazilian population, more than 90% of which depend on the public healthcare system (SUS).[15]

Similarly to other countries such as the US,[7] Canada,[27] and Portugual,[5] most biopsy specimens are diagnosed as nonmalignant lesions in Brazilian public university OMPLs. Occasionally, biopsy specimens from oral lesions, including cancer cases, are sent to public or private general pathology services, but most of these services do not have OPs, generally considered the most appropriate professionals to diagnose these diseases.[28] Approximately 70% of the general pathologists belonging to these services had not referred or consulted an OP because they did not know one, or had difficulty communicating and sending the specimens to an OP.[29,30] In addition, general pathologists have trouble diagnosing odontogenic cysts and tumors, which despite being usually benign, may cause severe

morbidity.[28–30] Therefore, the current study aimed to highlight the importance of the oral pathologist among the dental, general pathology, and medical teams in Brazil.

In the current study, the lower lip, oral tongue, and soft palate were the subsites most commonly affected by LSCC, OSCC, and OPSCC, respectively. Contrasting with the results of our study, previous studies from Australia, New Zealand,[3] and the US[31] have reported that the most common subsite for OPSCC was the tonsils, whereas a study from Thailand has reported it to be the base of the tongue.[25] A number of factors may explain this finding. First, it may be associated with the high number of tobacco and alcohol users found in our sample, since, according to the most recent World Health Organization (WHO) classification, tobacco- and alcohol-attributed OPSCC more commonly involve the soft palate.[8,32] Second, most samples sent for biopsy come from dentists, and, since the soft palate is the most visible area, these samples tend to outnumber samples from other areas, such as the base of the tongue and tonsils, which are most commonly biopsied by otolaryngologists and sent to general pathology services.[9] A very robust hospital-based study previously conducted in Brazil found a higher prevalence of OPSCC at the base of the tongue and tonsils, which may confirm the latter hypothesis.[15]

Apart from LSCC, most cases of which involved an asymptomatic ulceration, more than half of the OSCC and OPSCC cases manifested as symptomatic indurated ulcerations. In addition, the mean duration of symptoms of OSCC and OPSCC was 7 and 5.4 months, respectively. Our findings are in line with those of other studies from Sri Lanka,[23] Uruguay,[33] and Brazil,[10] according to which most OSCC and OPSCC cases present with ulceration, but contrast with those of a Brazilian study by Pires et al.[10], which found a mean duration time of symptoms of 10 months. The presence of an ulceration with rolled margins and induration are the most significant features of malignancy.[34] In addition, discomfort, pain, reduced mobility of the tongue, and bleeding were the main complaints reported in the present study, especially in OSCC and OPSCC cases, and, according to the available literature, these signs are associated with an advanced stage of the disease.[8,34] Unfortunately, previous Brazilian studies have reported that most OSCC and OPSCC cases are diagnosed at an advanced stage.[15,32]

In the present study, most oral cavity and oropharyngeal lesions measured less than or equal to 4 centimeters in their greatest dimension, and were classified as T1 or T2. However, nationwide data show that most cases treated in tertiary care referral hospitals are classified as T3 or T4 (advanced tumor).[15,32,35] Some factors may explain this difference. First, the patient's clinical data are provided by the dentists who perform the biopsies and send the data to an OMPL. Therefore, this subjective information may not reflect the actual size of the clinical lesion. Second, most patients receive treatment 60 days or more after the initial diagnosis due to patient and healthcare factors.[15] Any delay in treatment can allow the disease to progress to more advanced stages.[24]

Although the university OMPLs provide an essential service to SUS, the Brazilian public databases do not keep records of the laboratories responsible for the diagnoses. For example, the Fundação Oncocentro de São Paulo (FOSP) collects data from all hospitals that perform cancer treatment in São Paulo State; however, its database only includes records concerning whether the patients arrived at the hospital with or without a previous diagnosis and concerning their origin (SUS, health insurance or private service).[15] Similarly, the INCA database collects cancer data from the population-based and hospital-based cancer registries of the five Brazilian geographic regions, but, just like the FOSP, only keeps records of whether the patient arrived at the hospital with or without a previous diagnosis.[21,22] Therefore, this lack of information on the laboratory responsible for the diagnosis means that the significant contribution made by public university OMPLs with respect to cancer diagnosis in the SUS remains unknown to society and the government.

Since its implementation in 2004, the Brazilian National Oral Health Policy (PNSB, its acronym in Portuguese) has provided increased access to oral health in primary care, in addition to implementing Dental Specialized Centers (CEOs, its acronym

in Portuguese) throughout the country. Between 2000 and 2013, coverage by oral health teams rose from 0% to approximately 40%, and the number of CEOs increased by 1,000%.[36] One of the priorities of the PNSB is the prevention and early diagnosis of LSCC, OSCC, and OPSCC. Biopsies of oral and maxillofacial lesions are one of the services offered by the CEOs, and the biopsed specimens are usually sent to a university OMPLs for anatomopathological analysis. Thus, public university OMPLs also provide crucial support to CEOs by diagnosing oral lesions, including cancer cases.[10,11] The available data indicates that the rate of advanced stage diagnoses and the risk of death due to oral cancer are higher in areas lacking CEOs and with poorer coverage with respect to oral health services.[36] These findings may also be linked to the lack of access to a university OMPL, since specialists need an anatomopathological report to be able to refer patients to a hospital for cancer treatment.

Interestingly, approximately 10% of the specimens sent for analysis consisted of excisional biopsies. Two factors may explain this finding: first, the small size of some lesions and their location, which may have led dentists to perform complete excision of the lesion, without a previous incisional biopsy, and, second, a significant number of cases with a clinical hypothesis of a benign lesion, such as a reactive or infectious lesion.

Despite the advances observed in the last decades, OSCC and OPSCC remain a major public health problem in Brazil, and one which may have been aggravated by the COVID-19 pandemic. Oral health procedures performed by the SUS decreased by 66% during the first half of 2020 compared to 2019.[37] Corroborating this data, a recent large multicenter study revealed a near 50% reduction in the number of oral cancer diagnoses by Brazilian university OMPLs during the first year of the COVID-19 pandemic.[12] Similarly, another study reported that the number of oral cancer diagnoses in a Brazilian reference center in oral pathology decreased by 32.2%, compared to the pre-pandemic period.[13] Worldwide, studies have revealed a notable decrease in cancer diagnosis when compared to the period before the COVID-19 pandemic.[38] However, the long-term damage caused by these delays, and the rate of undiagnosed cancer cases are yet unknown.

This study has some limitations. First, information regarding treatment, recurrence, and follow-up are scarce in OMPLs, since most services are not linked to oncology hospitals. Second, clinical and pathological staging is not included in the patients' histopathological records, since most specimens are referred by dentists who most often send in incisional biopsies. Third, most OMPLs in public universities do not have an immunohistochemistry service to assess the p16 status of OPSCCs. Because of these limitations, more complex populational statistical analyses were not performed.

Conclusion

In summary, this report highlights the fact that public university OMPLs provide essential diagnostic support for oral healthcare services in the SUS by diagnosing oral and maxillofacial lesions, including cancer cases. Sixteen public university OMPLs diagnosed 8,321 patients with LSCC, OSCC, and OPSCC, comprising approximately 9.9% of all the oral and oropharyngeal cancer cases diagnosed in Brazil between 2010 and 2019. Although a direct correlation cannot be made, the profile of patients being treated for oral SCCs in Brazilian hospitals is similar to that found in our study, highlighting the key role of public university OMPLs in the diagnosis of LSCC, OSCC, and OPSCC. Therefore, new public policies to encourage the work of oral pathologists in public university OMPLs can contribute to increasing the participation of these universities in the diagnosis of cancer cases in Brazil, especially in the current post-pandemic scenario where there is a large backlog of cases.

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