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Demographic and Clinical Profile of Oral Squamous Cell Carcinoma from a Service-Based Population

Alessandro Menna Alves[1,2,3], Marcos Britto Correa[1], Karine Duarte da Silva[1,2], Lenita Maria Aver de Araújo[2], Ana Carolina Uchoa Vasconcelos[1,2], Ana Paula Neutzling Gomes[1,2], Adriana Etges[1,2], Sandra Beatriz Chaves Tarquinio[1,2]

[1]Graduate Program in Dentistry, UFPel – Universidade Federal de Pelotas, Pelotas, RS, Brazil
[2]Center of Diagnosis of Oral Diseases, UFPel – Universidade Federal de Pelotas, Pelotas, RS, Brazil
[3]Dental School, UNIVATES - Unidade Integrada Vale do Taquari de Ensino Superior, Lajeado, RS, Brazil

Correspondence: Sandra Beatriz Chaves Tarquinio, Rua Gonçalves Chaves 457, s/607, 96015-560, Pelotas, RS, Brasil. Tel: +55-53-98111-2894. e-mail: sbtarquinio@gmail.com

The aim of this study was to evaluate the demographic and clinical profile of the oral squamous cells carcinoma (OSCC) cases registered in a center of oral diagnosis in southern Brazil. Eight hundred and six individuals with OSCC from 1959 to 2012 were included in this study. The variables recorded were: sex, age, occupation according to workplace, alcohol and tobacco consumption, skin color, tumor location, histological type, clinical appearance, size, evolution time, presence of pain and lymph node metastasis. Descriptive analysis was performed and the associations between variables were assessed using the chi-square and Fisher's exact test, with a confidence level of 5%. OSSC was more common in males (76.6%) aged between 51 to 70 years (53.9%). The most frequent sites were lower lip vermilion (23.3%), tongue (20.2%) and gingiva/alveolar ridge (18.1%). There was a strong association between outdoor occupation and white skin color with lip squamous cell carcinoma (LSCC). OSCC intraoral lesions were commonly more painful, larger than 2 cm and presented lymphatic metastasis. In conclusion, most of the results confirm the data from literature about sex, age, tumor location and occupation. Moreover, the positive correlations between LSCC and occupation, between LSCC and white skin color, and between bigger lesions and presence of pain/cervical metastasis also corroborate the literature data.

Key Words: mouth neoplasms, epidemiology, population groups, oral health.

Introduction

Generally, oral cancer represents around 5% of all human malignancies (1), as observed by the wide geographical variation in its incidence (2). In some parts of the globe it is the most frequent type of cancer, such as in south Asia, including India and some islands in Melanesia, mainly due to smoking and chewing tobacco habits (2,3). In other areas oral cancer shows great incidence, such as Sri Lanka, Pakistan and Taiwan; and also in some European countries, and in Latin American countries such as Brazil, Uruguay, Puerto Rico and Cuba (3). In Brazil, oral cancer represents the sixth neoplasm, since the OSCC is the most prevalent one (94% of all oral tumors), which occurs mainly in individuals over 45 years old. Although several studies about OSCC have been performed, more than 50% of the patients died within 5 years after the diagnosis. The prognosis for OSCC is variable due to the multiple variables implicated in its development, such as extension and location of the primary tumor, degree of invasion of neighboring structures, presence of regional and distant metastasis, histological types, the chosen therapy and the general health status of the patient (3).

The etiologic factors strongly associated with the development of OSCC are the consumption of tobacco and alcohol (3,4). However, in recent decades, there has been an increasing trend of OSCC development in females and young adults, for whom other etiological factors like genetic heritage, dietary habits and Human Papilomavirus (HPV) infection have been pointed out as causes (5-7). It has been observed that environmental and cultural differences may be closely related to the average occurrence of OSCC. Therefore, the knowledge of demographic and clinical profile of OSCC in different populations is important and relevant. In this way, many other studies have approached it, with emphasis on Brazilian surveys (8-10) and revealed status of important considerations about this disease in specific populations.

In southern Brazil, the Center of Diagnosis of Oral Diseases (CDOD) is considered a reference service for clinical and histopathological diagnosis of oral diseases. CDOD attended approximately 20,000 biopsy samples from 1959 to present, amounting to around 1.500 patients per year. In mind with the importance of the impact of oral cancer campaigns in the prevention and early diagnosis of this disease (11,12), this oral diagnosis service has promoted campaigns of prevention and detection of oral cancer in the last 15 years. Until the present moment, no other epidemiological study about OSCC was carried out at this center and knowing the demographic and clinical

profile of the patients attended in this service can help the establishment of strategies for prevention and early detection of OSCC.

The aim of this study was to evaluate the demographic and clinical profile of OSCC cases registered at a center of clinical and histopathological diagnosis, located in southern Brazil.

Material and Methods

All cases of OSCC were retrieved from the CDOD files of, the Dental School, Universidade of the Federal de Pelotas, RS, Brazil, from 1959 to 2012. They represent 806 individuals. This study was approved by the Ethics Committee, Universidade Federal de Pelotas (protocol number 058/2008).

Demographic Data

The data were categorized as followed: age of individual in decades (9); sex (male and female); skin color in white and non-white (referred by the professional) (10); the occupation according to the workplace, exposed or non-exposed to chronic solar radiation (10) (indoor or outdoor occupation).

Clinical and Histopathological Data

Initially, were collected data about when the histopathological diagnosis of OSCC was done. Then, the habits of tobacco and alcohol consumption were registered as dichotomous variables, based on present or past consume of any quantity and frequency (8). The following clinical parameters collected from the files of CDOD were: tumor location (vermilion of lower and upper lip, labial mucosa, lateral border/ventral surface of the tongue, dorsum of the tongue, floor of the mouth, gingiva/alveolar ridge, buccal mucosa, palate and tonsils); tumor size (categorized as up to 2 cm, 2.1–4 cm and over 4 cm) and the reported evolution time of the lesions (up to 6 months, 6.1–12 months and over 12 months). Additionally, were registered: pain (dichotomic variable), clinical appearance and lymph node involvement (dichotomic variable). All clinical variables were categorized similarly to Pires et al. (8) and Marocchio et al. (9).

The evaluated histopathological variants of OSCC were basaloid squamous carcinoma, verrucous carcinoma and spindle cell carcinoma.

Statistical Analysis

Data were double-typed using EPIDATA version 3.1 (EpiData Association, Odense, Denmark) and the consistency of information was subsequently verified. For data analysis, the software STATA version 11.0 (Stata Corporation, College Station, TX, USA) was used. Descriptive analyses were performed to describe and to calculate the frequency of interest variables of the study. The associations between variables were assessed using the chi-square and Fisher's tests, with a confidence level of $p<0.05$.

Results

From January 1959 to December 2012, a total of 20.206 samples were processed in CDOD, with 806 (3.9%) cases being diagnosed as oral squamous cell carcinoma or its histological variants, with a high frequency in males (76.6% [73.5; 79.4]) and white individuals (92.2% [90.0; 94.0]) (Table 1). From all the OSCC, 186 (23.1%) were diagnosed from 1959 to 1996 (total number of biopsies in the period=8148). The other 620 cases (76.9%) were diagnosed from 1996 to 2012 (total number of biopsies=12 058). The mean age was 57.7 years (19–90), with the majority of cases distributed between 51 and 70 years old (53.9%) (Fig. 1).

The most frequent sites were lower lip vermilion, followed by lateral border/ventral surface of the tongue, gingiva/alveolar ridge and floor of the mouth (Table 2). Ulcer was the most common clinical appearance (Table 2). The data about histological variants, reported evolution time, size of the lesions, pain, and lymph nodes are also indicated in Table 2.

There is a strong association between outdoor occupation, mainly farmers and LSCC ($p<0.001$). While workers with outdoor occupation showed a 47.4% (n=129) frequency of OSCC. Individuals who worked in indoor occupations or were retired presented frequencies of 22.5% (n=53) and 23.5% (n=58), respectively. Skin color was also associated with this site. Lower lip vermilion lesions were also more commonly found in white individuals, 34.2% (n=226), in comparison with non-white, 1.8% (n=1) ($p<0.001$).

The association between size and lesions characteristics, Lymph node involvement and associations, and pain and associations are presented in Tables, 3, 4 and 5, respectively. The OSCC lesions located on the tongue were commonly greater than 2 cm (Table 3) and frequently presented lymph node involvement (Table 5). Similar positive and statistically significant associations were observed also for gingiva/alveolar ridge and floor of the mouth (Tables 4 and 5). On the contrary, lesions located in the lower lip demonstrated the smallest size at the time of the diagnosis (Table 3) and rare lymph node involvement (Table 4).

The present study showed an association between pain and intraoral OSCC lesions, especially with those located in the most frequent sites as the tongue, floor of the mouth, and gingiva/alveolar ridge (Table 5) and between pain and the size of the lesions (Table 5). The greater the lesions, more painful they were (Table 5).

Discussion

The present study is a retrospective analysis of demographic and clinical profile of OSCC cases registered

in an oral diagnosis center located in southern Brazil. This disorder is the most frequent type of oral cancer (2), what justifies the importance of epidemiological studies in this field. Regarding the frequency between sexs, OSSC was more frequent in males (76.6%), corroborating the global literature for OSCC (3,16) that demonstrate a two-fold index of oral cancer among males compared to females (5,16). The greater male indulgence of the main risk factors of OSCC such as tobacco and alcohol consumption for intra-oral OSCC and sunlight exposure for LSCC could explain it (3). However, some studies have reported a decrease in the male-female ratio, attributing this change to different factors such as alteration of tobacco and alcohol habits, cultural and geographic peculiarities (17,18).

Most diagnosed patients in this study were between 51 and 70 years old (53.9%), which is in accordance with the literature (3,9,16,19) indicating that age is probably a risk

Table 1. Descriptive analysis of individual variables (demographic and behavioral). Pelotas, Brazil (N=806)

Variable	Absolute frequency (nº)	Relative frequency [% (95%CI)]
Sex		
Female	189	23.4 (20.6; 26.5)
Male	617	76.6 (73.5; 79.4)
Skin color[1]		
White	661	92.2 (90.0; 94.0)
Non-white	56	7.8 (6.0; 10.0)
Smoking[2]		
Yes	427	89.5 (86.4; 92.1)
No	50	10.5 (7.9; 13.6)
Alcoholism[3]		
Yes	211	84.4 (79.3; 88.7)
No	39	15.6 (11.3; 20.7)
Occupation[4]		
Indoor	272	40.6 (36.9; 44.4)
Outdoor	236	35.2 (31.6; 39.0)
Retired	162	24.2 (21.0; 27.6)

Data not informed: 89[1], 329[2], 556[3], 136[4].

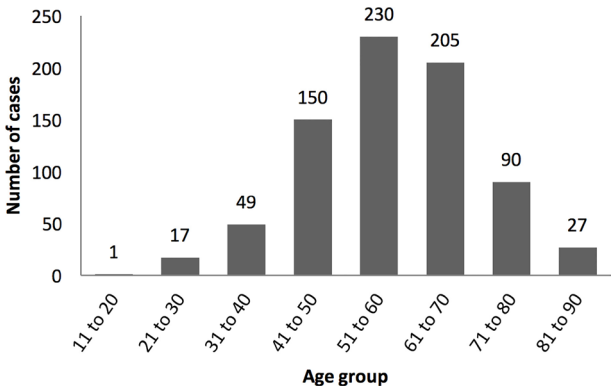

Figure 1. Distribution of cases according to age.

Table 2. Descriptive analysis of lesions characteristics (histological variant, referred time of evolution, clinical appearance, size, site, pain, and presence of lymph nodes). Pelotas, Brazil (N=806).

Variable	Absolute frequency (nº)	Relative frequency [% (95%CI)]
Histological variant		
Squamous cell carcinoma	780	96.8 (95.3; 97.9)
Verrucous carcinoma	24	3.0 (1.9; 4.4)
Basaloid squamous carcinoma	1	0.1 (0.0; 0.6)
Spindle cell carcinoma	1	0.1 (0.0; 0.6)
Referred evolution time[1]		
Up to 6 months	294	55.8 (52.3; 59.3)
6-12 months	114	21.6 (18.8; 24.6)
Over 12 months	119	22.6 (18.7; 25.6)
Clinical appearance[2]		
Ulcer	446	69.9 (66.6; 73.0)
Leukoplakia	81	12.7 (10.4; 15.1)
Erithroplakia	14	2.2 (1.3; 3.5)
Leukoerithroplakia	12	1.9 (1.0; 3.1)
Association	85	13.3 (11.0; 15.8)
Size[3]		
Up to 2 cm	272	50.4 (48.8; 55.9)
2.1-4 cm	180	33.3 (31.5; 38.1)
Over 4 cm	88	16.3 (14.5; 19.8)
Site		
Lower lip vermilion	241	23.3 (20.4; 26.4)
Upper lip vermilion	8	0.7 (0.2; 1.6)
Labial mucosa	18	1.7 (0.9; 2.9)
Lateral border/ventral surface of the tongue	209	20.2 (17.5; 23.2)
Dorsum of the tongue	9	0.9 (0.3; 1.8)
Buccal mucosa	62	6.0 (4.4; 7.8)
Floor of the mouth	154	14.9 (12.5; 17.5)
Gingiva/alveolar ridge	187	18.1 (15.5; 21.0)
Palate	66	6.4 (4.9; 8.4)
Tonsils	81	7.8 (6.0; 9.9)
Pain[4]		
Yes	285	66.1 (62.7; 69.4)
No	146	33.9 (30.6; 37.3)
Lymph node involvement[5]		
Yes	155	58.5 (55.1; 62.0)
No	110	41.5 (38.0; 44.9)

Data not informed: 279[1], 168[2], 286[3], 375[4], 541[5].

marker for OSCC (16). However, Patel et al. (6) showed an increased incidence among white female young individuals, aged 18 to 44 years, postulating that there may be a new and emerging head and neck cancer population.

Concerning all the anatomical oral sites, lower lip vermilion represented the most frequent location (23.3%), corroborating data from the literature (10,16). The major frequency of OSCC lesions in this site has great relevance when the studies are performed in tropical countries, in addition to the important influence by socio-demographic (like ethnic origin), main occupation and cultural aspects of the studied population (10,16,20).

It showed a strong association between outdoor occupation, mainly farmers and LSCC. Also between white skin color and this site, as previously demonstrated (10). Although the biopsy registers do not provide the occupation of the retired patients, it is possible that most of them live in rural areas, which would reinforce this correlation. Moreover, the lower lip is subjected to intense and chronic sun exposure and thus ultraviolet (UV) radiation, which may contribute to it being the most common site for OSCC in males and in populations of fair-skinned people (16,20,21). For women, the use of lipstick could be considered as a potential protective factor (17). In addition, factors like socio-demographic characteristics, lifestyle, immunosuppression and genetic susceptibility might produce a synergistic effect (10). Lower LSCC frequency was followed by lateral border/ventral surface of the tongue, gingiva/alveolar ridge and floor of the mouth. Considering the intraoral sites, the lateral border of the tongue has been pointed to as the most common OSCC site among European and United States populations (2,18). This study grouped lateral border and ventral surface of the tongue because many times both sites are concurrently affected. Mostly confirming the literature data, the tongue OSCCs in this study were more painful, frequently presenting lymph node involvement, and at least a T2 tumor or more (16,20). Similar positive and statistically significant associations were observed also for gingiva/alveolar ridge and floor of the mouth.

On the opposite, lesions located in lower lip demonstrated the smallest size at the time of the diagnosis, the least amount of pain and seldom lymph node involvement. One point that should be emphasized is that the lesions in the lip are promptly detected by self-examination compared with the intraoral lesions, which explains their minor size and by consequence have the lowest symptomatology and lowest incidence of cervical metastasis, which also allows for early diagnosis and better prognosis (9,10,16,18,20). The study results confirmed the reduced aggressiveness of LSCC, compared with intraoral cancer (20).

Cancer pain is also a public-health concern, as it creates a poor quality of life and limits normal function (22,23). The present study showed an association between pain and intraoral OSCC lesions and between pain and the size of the lesions. Ulcer was the most frequent OSSC clinical presentation. These findings agree with other authors (22-25) who demonstrated that pain in oral cancer may be associated with advanced, endophytic invasive tumors, delivering a poor prognosis for the patients. Although this symptom is very useful in evaluating cancer progression, it has some subjectivity in its evaluation.

The OSCC cases were distributed in two periods (1959–1996 and 1997–2012). The reason for categorizing the data into these periods of time was the beginning of oral cancer campaigns in November 1996. In the last two decades the CDOD has performed campaigns to raise awareness among citizens about the importance of oral self-examination and to promote the prevention and early detection of oral cancer. The majority of OSCC cases in this center were diagnosed after 1996 (76.9%), reflecting the impact of the campaigns. Nevertheless, the small number of samples in the first period of time limits the comparison between the two times. Moreover, the total number of

Table 3. Association between size and lesions characteristics

Variable/Category	Size, n (%)			
	<2 cm	2.1-4 cm	>4 cm	p value
Site				
Lower lip vermilion	140 (51.5)	27 (16.9)	5 (5.7)	<0.001
Upper lip vermilion	4 (1.5)	0 (0.0)	1 (1.1)	0.313
Labial mucosa	4 (1.5)	2 (1.3)	2 (2.3)	0.815
Lateral border/ventral surface of the tongue	51 (18.8)	54 (33.8)	28 (31.8)	0.001
Dorsum of the tongue	3 (1.1)	3 (1.9)	0 (0.0)	0.414
Buccal mucosa	10 (3.7)	13 (8.3)	12 (12.8)	0.008
Floor of the mouth	34 (12.5)	34 (21.3)	30 (34.1)	<0.001
Gingiva/alveolar ridge	22 (8.1)	42 (26.3)	37 (42.1)	<0.001
Palate	10 (3.68)	16 (10.0)	16 (18.1)	<0.001
Tonsils	11 (4.0)	17 (10.6)	13 (14.8)	0.002
Referred evolution time				0.214
Up to 6 months	102 (49.8)	72 (35.1)	31 (15.1)	
6–12 months	51 (64.6)	19 (24.1)	9 (11.4)	
Over 12 months	53 (59.6)	25 (28.1)	11 (12.4)	

biopsies after November 1996 was 12,058, with OSCC cases corresponding to 5.2%. This percentage is duplicated if compared with the same diagnosis done before November 1996 (2.3% from 8148).

Most of the epidemiological studies in oral cancer analyze hospital-based or oral-health-services-based cancer registries, which naturally gather biased information, since only part of the population has access to these centers, especially in developing countries (3). The present study has the same limitation, since it is a service-based study. However, it is important to highlight that the data show the OSCC frequency during the whole existence of the CDOD, which lasts more than 50 years. This study presents some other limitations such as lack of complete information on biopsy records. Missing data were not considered in the analysis of associations and could affect some of the findings. Lack of information in retrospective studies is common (8,9). Therefore, it is necessary to reinforce the importance of the correct filling by the surgeon of biopsy records sent with the specimens, avoiding the loss of data and minimizing this problem.

In conclusion, the study presents a demographic and clinical description of OSCC in a specific population in southern Brazil. Most of the results confirm the data from literature about sex, age, tumor location and occupation. Moreover, there was a significant correlation between LSCC and outdoor occupation and between LSCC and white skin color, highlighting the main socio-demographic and cultural characteristics of the studied population, who are mainly white, with European ascendency, and who work in agriculture. These lesions showed the smallest size, the lowest symptomatology, and the lowest incidence of cervical metastasis, because they are usually detected early. OSCC intraoral lesions were more common in sites such as tongue, gingiva/alveolar ridge and floor of the mouth, being more painful, frequently presenting lymph node involvement and at least a T2 size or more.

Table 4. Lymph node involvement and associations

Variable/Category	Yes, n (%)	No, n (%)	p value
Site			
Lower lip vermilion	16 (26.2)	45 (73.8)	< 0.001
Upper lip vermilion	2 (66.7)	1 (33.3)	0,773
Labial mucosa	1 (100.0)	0 (0.0)	0,399
Lateral border/ventral surface of the tongue	59 (71.9)	23 (28.1)	0,003
Dorsum of the tongue	3 (60.0)	2 (40.0)	0,945
Buccal mucosa	9 (52.9)	8 (47.1)	0,647
Floor of the mouth	46 (73.0)	17 (27.0)	0,007
Gingiva/alveolar ridge	45 (70.3)	19 (29.7)	0,028
Palate	16 (69.6)	7 (30.4)	0,259
Tonsils	28 (80.0)	7 (20.0)	0,006
Size			<0.001
Up to 2 cm	33 (38.4)	53 (61.6)	
From 2.1 to 4 cm	41 (63.1)	24 (36.9)	
Over 4 cm	37 (77.1)	11 (22.9)	
Referred evolution time			0.084
Up to 6 months	76 (65.5)	40 (34.5)	
From 6 to 12 months	22 (57.9)	16 (42.1)	
Over 12 months	14 (43.8)	18 (56.3)	
Number of sites			0,001
Single site	97 (51.9)	90 (48.1)	
Multiple sites	55 (75.3)	18 (24.7)	

Table 5. Pain and associations

Variable/category	Yes, n (%)	No, n (%)	p value
Site			
Lower lip vermilion	4 (34.4)	78 (65.6)	< 0.001
Upper lip vermilion	3 (75.0)	1 (25.0)	0,706
Labial mucosa	3 (37.5)	5 (62.5)	0,086
Lateral border/ventral surface of the tongue	103 (83.7)	20 (16.3)	<0.001
Dorsum of the tongue	4 (80.0)	1 (20.0)	0,51
Buccal mucosa	25 (71.4)	10 (28.6)	0,507
Floor of the mouth	70 (80.5)	17 (19.5)	0,002
Gingiva/alveolar ridge	79 (76.0)	25 (24.0)	0,015
Palate	31 (88.6)	4 (11.4)	0,003
Tonsils	34 (89.5)	4 (10.5)	0,001
Size			<0.001
Up to 2 cm	84 (53.5)	73 (46.5)	
2.1-4 cm	80 (76.2)	25 (23.8)	
Over 4 cm	37 (78.7)	10 (21.3)	
Referred evolution time			0,037
Up to 6 months	145 (71.1)	59 (28.9)	
From 6 to 12 months	40 (57.1)	30 (42.9)	
Over 12 months	47 (58.8)	33 (41.2)	
Number of sites			<0.001
Single site	197 (60.4)	129 (39.6)	
Multiple sites	83 (86.5)	13 (13.5)	

Resumo

O objetivo desse estudo foi avaliar o perfil clínico-demográfico dos casos de carcinoma de células escamosas oral (CCEO) oral registrados em um centro de diagnóstico bucal no Sul do Brasil. Oitocentos e seis indivíduos com CCEO de 1959 a 2012 foram incluídos no estudo. As variáveis coletadas foram: sexo, idade, ocupação de acordo com o ambiente de trabalho, consumo de álcool e tabaco, cor de pele, localização do tumor, tipo histológico, aparência clínica, tamanho, tempo de evolução, presença de dor e metástase linfonodal. Foi realizada análise descritiva e as associações entre as variáveis foram avaliadas usando qui-quadrado e teste exato de Fisher, com nível de confiança de 5%. CCE oral foi mais comum em homens (76,6%), entre 51 e 70 anos de idade (53,9%). Os sítios mais frequentes foram vermelhão de lábio inferior (23,3%), língua (20,2%) e gengiva/rebordo alveolar (18,1%). Houve uma forte associação entre ocupação em ambiente externo e cor de pele branca com CCEO em lábio. Lesões intraorais de CCEO foram comumente mais dolorosas, maiores que 2 cm e apresentaram metástase linfática. Em conclusão, a maioria dos resultados confirma os dados da literatura em relação a sexo, idade, localização do tumor e ocupação. Além disso, as correlações positivas entre CCE em lábio e ocupação, entre CCEO em lábio e cor de pele branca, e entre lesões maiores e presença de dor/metástase cervical também corroboram os dados da literatura.

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