ORAL AND OROPHARYNGEAL CANCER IN A VENEZUELAN POPULATION

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ABSTRACT

The aim of this work was to analyze diagnosed cases of Oral Cancer (OC) and Oropharyngeal Cancer (OPC) in a Venezuelan population.

We clinically evaluated 130 patients with OC and OPC and a histopathologic diagnosis of squamous cell carcinoma. The patients were analyzed according to gender, age, and use of alcohol and tobacco and the tumors were classified based on anatomic location, staging parameters, and degree of differentiation.

Ninety one patients (70%) were male and 39 (30%) were female. Patients' age ranged from 26 to 86 years old. Use of smoking tobacco, alcohol or both was reported by 84.3%, 49.1% and 45.4% of patients, respectively, and was more frequent in males. The most common oropharyngeal anatomic location was the base of the tongue (22.3%), followed by the tonsils (13.9%), while the most frequently affected oral location was the oral tongue (19.2%) followed by the gingiva and alveolar mucosa (10.8%), and the floor of mouth (7.7%). The majority of tumors (77.7%) were diagnosed at an advanced stage (Stage III or IV); metastasis to the regional lymph nodes occurred in 53.1% of cases. According to degree of differentiation, well, moderately and poorly differentiated tumors accounted for 45.4%, 46.1% and 8.5% of cases, respectively. Well differentiated tumors accounted for 56.7% of OC cases, while the majority of OPC cases were classified as moderately or poorly differentiated (72.3%) ($p \leq 0.002$). Also, non-metastatic cases (N0) showed a predominance of well-differentiated tumors (61.2%), while metastatic tumors (N+) were classified as moderately or poorly differentiated in 89.8% of cases ($p \leq 0.0001$).

Our study population was characterized by a predominance of smokers and/or drinkers and a predilection for male patients. Most tumors were diagnosed at an advanced stage with a high incidence of metastatic spread to the regional lymph nodes, indicating possible delays in diagnosis. Less differentiated tumors were more frequently encountered among OPC cases and accounted for the vast majority of metastatic cases, supporting the prognostic value of assessing the degree of differentiation.

Key words: oral cancer, oropharyngeal cancer, squamous cell carcinoma, Venezuela.

CÁNCER BUCAL Y OROFARÍNGEO EN UNA POBLACIÓN VENEZOLANA

RESUMEN

El propósito del presente trabajo fue analizar los casos diagnosticados como Cáncer Bucal y Orofaríngeo en una población venezolana.

Se evaluaron clínicamente 130 pacientes con Cáncer Bucal y Orofaríngeo con diagnóstico histopatológico de carcinoma de células escamosas. Los pacientes fueron analizados de acuerdo al género, edad, consumo de alcohol y tabaco.

Noventa y un pacientes (70%) correspondieron al género masculino y treinta y nueve (30%) al femenino. El rango de edad de los pacientes fue de 26-86 años. El consumo de tabaco, alcohol y de ambos fue de 84.3%, 49.1% y 45.4% respectivamente en los pacientes estudiados. La localización anatómica orofaríngea mas común fue la base de la lengua con un 22.3%, seguida de amígdalas 13.9%, mientras que la localización bucal mas frecuente fue lengua (19.2%), seguida por encía y mucosa del reborde alveolar (10.8%) y piso de boca (7.7%). La mayoría de los tumores (77.7%) fueron diagnosticados en un estadio avanzado (III o IV); la metástasis a ganglios linfáticos regionales se presentó en un 53.1% de los casos. De acuerdo al grado de diferenciación se observó que un 45.4% correspondieron a carcinoma de células escamosas bien diferenciado, un 46.1% a moderadamente diferenciado y un 8.5% a pobremente diferenciado. Los casos de cáncer bucal fueron en un 56.7% bien diferenciados , mientras que la mayoría de los casos orofaríngeos fueron clasificados como moderadamente o pobremente diferenciados (72.3%) $p< 0.002$. Adicionalmente, los casos no metastásicos (N0) mostraron un predominio de tumores bien diferenciados (61.2%) mientras que los metastásicos (N+) fueron clasificados como moderadamente o pobremente diferenciados en un 89.8% ($p< 0.001$).

La población estudiada se caracterizó por un predominio de pacientes con hábitos tabáquicos y alcohólicos en el género masculino. La mayoría de los tumores se diagnosticaron en etapas avanzadas y presentaron extensión a ganglios linfáticos regionales, indicando posiblemente un diagnóstico tardío en esos casos. Los tumores poco diferenciados fueron mas frecuentemente encontrados entre los casos orofaríngeos y representaron los tumores metastásicos, enfatizando la importancia del valor pronóstico del grado de diferenciación.

Palabras clave: cáncer bucal, cáncer orofaríngeo, carcinoma de células escamosas, Venezuela.

INTRODUCTION

Cancer of the oral cavity and oropharynx represents a significant health problem, accounting worldwide for approximately 220,000 new cases per year in men (5% of all cancers) and 90,000 in women (2% of all cancers)[1,2]. The incidence of oral cancer (OC) and oropharyngeal cancer (OPC) varies widely among different continents and countries[2]. In certain parts of Asia, for example India, cancers of the oral cavity and oropharynx, especially in men, represent one of the most common types of cancer. Nonetheless, comparing different continents, Asia shows the broadest range in incidence rates of OC and OPC in both genders. Most European countries and the USA show lower annual incidence rates. Nevertheless, great variation exists among the various European geographic regions, as well as among different races in the USA[1-3]. While northern European countries have a relatively low incidence of OC and OPC, certain central and eastern European regions show strikingly high rates: for example, the highest combined rate for OC and OPC recorded worldwide was found in northern France (49.4 per 100,000 men). Among Eastern European countries the highest combined rates in males were noted in Slovakia (19.7/100,000) and Slovenia (18.9/100,00).[3] In the USA, the overall annual incidence rate for oral cancer alone is 7.7 per 100,000, while the combined death toll of OC and OPC is significant, accounting for 9.000 deaths yearly. Interestingly, marked racial differences in the annual incidence of these cancers have been recorded in the USA: white males have a two-fold lower incidence of OC and OPC compared to black males. The latter group shows the highest incidence rate in the Americas followed by Brazil (Porto Alegre) and Puerto Rico.[1] In contrast, other American countries, e.g. Colombia and Costa Rica exhibits relatively low rates[2,3].

The epidemiology and etiology of SCC is complex. It has been clearly documented that tobacco and alcohol use are the most commonly implicated factors in the etiology of oral cancer. Other risk factors have been suspected, including poor dentition, oral hygiene, and diet. However, their relative contribution is considered lower compared to tobacco and alcohol consumption[4]. A viral etiology, especially HPV-related has been suggested but remains inconclusive[5,6]. Recently, a positive family history of head and neck cancer has been considered a risk factor in SCC**,** especially in the case of the upper aerodigestive tract and lung cancer[7].

After many years of decline, the incidence and mortality for cancers of the oral cavity and pharynx have been rising for the last two to three decades in many developed countries, particularly in Southern and Eastern Europe. Such increases are chiefly attributable to changes in the levels of tobacco and alcohol consumption. An influence of dietary factors and certain infectious agents (such as HPV) is also possible[1].

Although, the available epidemiologic data of OC and OPC in many developed countries are of reasonably high quality, similar data from most developing countries are lacking. Knowledge of the epidemiologic profile of OC and OPC in developing regions of the world will help determine the extent of the problem and guide health policy decisions. Moreover, it will allow comparative analysis of different populations, identifying discrepancies that may point to disparate etiologic and predisposing factors. In this regard, this study is the first to present a sizeable series of OC and OPC cases from a Venezuelan referral oncology hospital and to analyze them according to gender, age, alcohol and tobacco use, anatomic location, histological type, and degree of differentiation. This study constitutes baseline data on Oral Cancer in Venezuela and represents a contribution for Latin America.

MATERIAL AND METHODS

One hundred and thirty patients with OC and OPC from the metropolitan area of Caracas and four different Venezuelan states attended the referral oncology hospital "Padre Machado Hospital", during the period 1995-1999. These patients were assessed clinically and the diagnosis of SCC was confirmed histopathologically using the WHO histological criteria. Other forms of cancer such as malignant salivary gland tumors, malignant mesenchymal tumors, nasopharyngeal carcinoma and lymphoma were excluded. The age and gender of the patients and the anatomical location of the tumor were recorded. Data regarding the use of tobacco or alcohol, the stage of the tumor, and the degree of differentiation were also collected. A statistical comparison between groups of categorical variables was performed by means of Fisher's test and statistical significance was set at $p \leq 0.05$.

RESULTS

Out of a total of 130 patients with OC or OPC, 91 were male (70%) and 39 were female (30%). Patients' age

ranged from 26 to 86 years old and the median age was 63; most patients were in the 6th decade of life.

Of 108 patients with available information about OC/OPC-related habits, use of smoking tobacco and alcohol was reported by 91 (84.3%) and 53 patients (49.1%), respectively. Combined tobacco smoking and alcohol use was recorded in 45.4% (49/108) of cases (Table 1). Comparative values for male vs. female patients were recorded for use of smoking tobacco (89.5% vs. 68.9), use of alcohol (59.5% vs. 20.7%) or use of both tobacco and alcohol (55.7% vs. 17.2%) (Table 1).

Table 1: Association between Gender and Use of Tobacco, Alcohol, and Tobacco/Alcohol

	Tobacco use	Alcohol use	Combined tobacco and alcohol use
Male n=79	(89.9%) n=71	(59.5%) n=47	(55.7%) n=44
Female n=29	(68.9%) n=20	(20.7%) n=6	(17.2%) n=5
TOTAL n=108	(84.3%) n=91	(49.1%) n=53	(45.4%) n=49

OC represented 51.5% (67/130) of the total cases, OPC accounted for 36.2% (47/130), whereas the exact anatomic oral or oropharyngeal site was not specified in 16/130 (12.3%). The most common oropharyngeal anatomical location was the base of the tongue (29/130 cases, 22.3%), while the most frequently affected oral location was the oral tongue (25/130, 19.2%) (Table 2).

Table 2: Distribution of Oral Cancer (OC) and Oropharyngeal Cancer (OPC) by Anatomic Site

Anatomic Location	%
OC	*51.5 n=67*
Tongue	19.2 n=25
Gingiva and Alveolar Mucosa	10.8 n=14
Floor of Mouth	7.7 n=10
Hard Palate	6.9 n=9
Retromolar Pad	5.4 n=7
Soft Palate	1.5 n=2
OPC	*36.2 n=47*
Base of tongue	22.3 n=29
Tonsils	13.9 n=18
Unspecified	*12.3 n=16*
Total	*100% n=130*

The tumors were distributed based on stage information according to the TNM staging system[8] (Table 3). The majority of the tumors were classified as Stages III (30.8%) and IV (46.9%), while Stages I and II corresponded to 9.2% and 13.8% of cases, respectively. According to T stage (size of primary tumor), large tumors predominated, T3 and T4 tumors accounting together for 61.5% of the total. According to N stage, 53.1% of tumors showed evidence of lymph node metastasis (N+). No distant metastases were reported. All tumors were histopathologically diagnosed as squamous cell carcinoma (SCC). According to

Table 3: Distribution of Oral Cancer (OC) and Oropharyngeal Cancer (OPC) by Stage according to TNM System

Stage	Total #	Stage T					Stage N			
		T0	T1	T2	T3	T4	N0	N1	N2	N3
I	12/130 (9.2%)	1	11				12			
II	18/130 (13.8%)			18			18			
III	40/130 (30.8%)			10	29		17	23		
IV	61/130 (46.9%)			10	14	37	15	12	28	6
		1/130 (0.8%)	11/130 (8.5%)	38/130 (29.2%)	43/130 (33.1%)	37/130 (28.4%)	62/130 (47.6%)	35/130 (26.9%)	28/130 (21.6%)	6/130 (4.6%)

Table 4: Association between Tumor Anatomic Site and Degree of Differentiation

	Tongue Base n=29	Tonsils n=18	All OPC n=47	Tongue n=25	Ging/Alveo Mucosa n=14	All OC n=67	TOTAL n=130
WD	(37.9%) n=11	(11.1%) n=2	(27.7%) n=13	(64%) n=16	(64.3%) n=9	(56.7%) n=38	(45.4%) n=59
MD	(55.2%) n=16	(72.2%) n=13	(61.7%) n=29	(32%) n=8	(35.7%) n=5	(35.8%) n=24	(46.1%) n=60
PD	(6.9%) n=2	(16.7%) n=3	(10.6%) n=5	(4%) n=1	(0%) n=0	(7.5%) n=5	(8.5%) n=11

WD: well differentiated; MD: moderately differentiated; PD: poorly differentiated; Ging: gingival; Alveol: alveolar.

Table 5: Association between Degree of Differentiation, Tumor Size and Regional Metastasis to the Lymph Nodes

	Tumor Size		Lymph Node Metastasis	
	T1,2 n=49	T3,4 n=90	N0 n=62	N+ n=69
WD	(44.9%) n=22	(41.1%) n=37	(61.2%) n=38	(10.2%) n=7
MD	(46.9%) n=23	(51.1%) n=46	(32.8%) n=20	(57.9%) n=40
PD	(8.2%) n=4	(7.8%) n=7	(6.6%) n=4	(31.9%) n=22

degree of differentiation, well differentiated and moderately differentiated tumors accounted for 45.4% (59/130) and 46.1% (60/130) cases respectively, whereas the remaining 8.5% (11/130) were classified as poorly differentiated.

Regarding anatomic location, most cases of OPC were classified as moderately differentiated (29/47, 61.7%), while moderately and poorly differentiated tumors accounted together for 72.3% of cases. Similarly, moderately or poorly differentiated tumors accounted for the majority of cases located in the base of tongue or tonsils (18/29, 62.1% and 16/18, 88.9%, respectively) (Table 4). In contrast, among OC cases, well differentiated tumors predominated (38/67, 56.7%) with moderately and poorly differentiated tumors accounting for 43.3% (29/67) (Table 4). Comparing OC and OPC cases, well differentiated tumors were significantly more frequent in the former category ($p \leq 0.002$).

When correlating the degree of differentiation with the tumor size, small (T1,2) and big (T3,4) tumors showed a similar distribution of cases into well differentiated (44.9% vs. 41.1%), moderately differentiated (46.9% vs. 51.1%) and poorly differentiated tumors (8.2% vs. 7.8%) ($p>0.05$) (Table 5). In contrast, considering regional lymph node metastasis, non-metastatic cases (N0) showed a predominance of well-differentiated tumors (61.2%), as opposed to metastatic tumors (N+) that were classified as moderately or poorly differentiated in 89.8% of cases; this difference was statistically significant ($p \leq 0.0001$) (Table 5).

DISCUSSION

Our study was the first to present the epidemiological, clinical and histopathologic characteristics of a sizeable cohort of Venezuelan patients with cancer of the oral cavity and oropharynx, allowing comparisons with the published features of SCC patient populations from different ethnic backgrounds and geographic locations. In most published studies, the vast majority of OC and OPC cases occur in males, with a higher incidence in older individuals and an average age between the sixth and seventh decades of life. However, the second predominant group was that of 26 years of age. Interestingly, in this particular age group, 26-40 years, a total of 13/130 cases were found. This fact could be related to an early age of initiating the smoking and drinking consumption. Similarly, the present study confirmed a male predominance corresponding to a 7:3 male to female ratio. Patients in the sixth decade were more commonly affected in agreement with previous reports from the literature[9-12,13].

The etiological factors more commonly associated with OC and OPC include tobacco in all forms (smoked, placed or chewed) and alcohol[7,14-18]. Moreover, the combination of both tobacco and alcohol has a synergistic effect. Nutritional deficiencies, poor dentition, and viruses have also been implicated as potential etiologic factors. In our study population, 84.3% of patients reported tobacco use, mainly cigarette smoking, and 49.1% of the population were alcohol consumers. Interestingly, the combination of both alcohol and tobacco use, which has been positively correlated with an increased risk of

oral cancer, was noticed in 45.4% of the individuals. Smoking, drinking or the combination of both habits was significantly more frequent in male patients, possibly indicating a more significant etiologic role of these habits in cancer development in males. Recently, De Stefani et al.[19], in their study of 335 cases of OC and 441 cases of pharyngeal cancer in Uruguay, noticed that the latter was more frequently associated with smoking and drinking.

Oral Cancer (OC) includes malignant lesions of the mucosa of the alveolar ridge, gingiva, buccal and labial mucosa, floor of the mouth, hard and soft palate and oral tongue. Oropharyngeal cancer (OPC) encompasses malignant tumors of the base of tongue, tonsils and retromolar pad. In the present study of both OPC and OC, the latter predominated. The most common sites for OPC and OC were the base of the tongue and oral tongue, respectively. These results are in accordance with previous reports indicating that the lateral borders and base of the tongue along with the floor of the mouth, constitute areas more prone to develop cancer and represent the most common intraoral anatomical locations in the majority of the epidemiological studies[20]. Some investigations have proposed that the predilection for those sites is due to the pooling of carcinogens in the saliva and the food reservoir, creating risk zones; this theory is also referred to as Lederman's hypothesis[10,20,21,22].

Conventional prognostic factors in OC and OPC include staging parameters (clinical stage, tumor size, evidence of metastatic lymph nodes) and, to a lesser extent, histological grading. In recent years, molecular analysis and immunohistochemical tumor markers have also been studied as promising prognostic indicators.[21] In our study, advanced stages (III and IV), large tumors (T3 and T4), and regional metastasis (N+) were noticed in the majority of cases. This finding indicates that most patients were referred, and possibly diagnosed, at an advanced stage, when the possibility for curative treatment is severely compromised.

Regarding degree of differentiation, well and moderately differentiated SCC corresponded to the vast majority of cases, while poorly differentiated tumors were considerably less frequent. It has been suggested that OC in an anterior localization is generally better differentiated and less aggressive compared to those affecting the base of the tongue[23]. In the present investigation, correlation of the degree of differentiation and the anatomical site revealed a predominance of moderately/poorly differentiated cases for OPC, as opposed to the higher frequency of well differentiated cases in oral locations.

A significant finding of our study was the correlation between degree of differentiation and regional metastasis: the vast majority of metastatic tumors (N+) were classified as moderately or poorly differentiated. It is well established that spread to the regional lymph nodes correlates strongly with poor prognosis and a 50% decline in 5-year survival rate[24]. Therefore, our study supports that assessment of degree of differentiation may be useful for determining the metastatic potential and thus the prognosis of SCC, in agreement with previous investigations that found correlation between histopathological parameters of differentiation and the likelihood of lymph node metastasis[25,26].

There is little reliable population-based data on OC and OPC from developing countries. In addition, no longitudinal epidemiological studies have been conducted in a Venezuelan population. To our knowledge, the present study constitutes the first systematic collection of baseline epidemiological data on OC and OPC in one major Venezuelan oncologic referral hospital. The present findings set the stage for further investigations of OC and OPC in Venezuela in comparison with similar data from other developing and developed countries. Screening and development of clinical guidelines for early detection of OC and OPC are recommended as a strategic plan in our population.

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REFERENCES

1. Franceschi S, Bidoli E, Herrero R, Munoz N. Comparison of Cancers of the Oral Cavity and Pharynx worldwide: etiological clues. Oral Oncol 2000; 36:106-115.
2. Moore S, Johnson NW, Pierce A, Wilson D. The epidemiology of tongue cancer: a review of global incidence. Oral Dis 2000; 6:75-84.
3. La Vecchia C, Lucchini F, Negri E, Levy F. Trends in oral cancer mortality in Europe. Oral Oncol. 2004; 40:433-439.
4. Marshall JR, Graham S, Haughey BP, Shedd D, O´Shea R, Brasure J, Wilkinson GS, West D. Smoking, alcohol, dentition and diet in the epidemiology of oral cancer. Eur J Cancer B Oral Oncol 1992; 28B:9-15.
5. Correnti M, Rivera H, Cavazza M. Detection of human papillomaviruses of high oncogenic potential in oral squamous cell carcinoma in a Venezuelan population. Oral Dis 2004; 10:163-166.
6. Tachezy R, Klozar J, Salakova M, Smith E, Turek L, Betka J, Kodet R, Hamsikova E. HPV and other risk factors of oral cavity/oropharyngeal cancer in the Czech Republic. Oral Dis 2005; 11:181-185.
7. Jefferies S, Foulkes W. Genetic mechanisms in squamous cell carcinoma of the head and neck. Oral Oncol 2001; 37:115-126.
8. Howaldt HP, Kainz M , Euler B, Vorast H. Proposal for modification of the TNM staging classification for cancer of the oral cavity. DOSAK. J Craniomaxillofac Surg 1999; 27:275-288.
9. Krolls S, Hoffman S .Squamous cell carcinoma of the oral soft tissues: a statistical analysis of 14,253 cases by age, sex and race of patients. J Am Dent Assoc 1976; 2:571-574.
10. Chen JK, Katz RV, Krutchkof DJ. Intraoral squamous cell carcinoma: epidemiologic patterns in Connecticut from 1935 to 1985. Cancer 1990; 66:1288-1296.
11. Jensen OM, Estève J, Møller H, Renard H. Cancer in the European Community and its member states. Eur J Cancer 1990; 26:1167-1256.
12. Scully C, Newman L, Bagan JV. The role of the dental team in preventing and diagnosing cancer: 2. Oral cancer risk factors. Dent Update 2005; 32: 261-262, 264-266, 269-270.
13. Morelatto RA, López de Blanc SA. Oral cancer mortality in the province of Cordoba, Argentine Republic in the period 1975-2000. A comparative study with other populations. Med Oral Patol Oral Cir Bucal. 2006 1; 11:E230-235.
14. World Health Organization. Alcoholic Beverages. International Agency for Research and Cancer. Lyon. IARC Scientific Publication 44, 1988.
15. Franceschi S, Barra S, La Vecchia C, Bidoli E, Negri E, Talamini R.. Risk factors for cancer of the tongue and mouth. A case control study from Northern Italy. Cancer 1992; 70:2227-2233.
16. Hindle I, Downer MC, Speight PM. The epidemiology of oral cancer. Br J Oral Maxillofac Surg 1996; 34:471-476.
17. Cox B, Taylor K, Treasure E. Trends in oral cancer by subsite in New Zealand. Eur J. Cancer B Oral Oncol 1995; 31B:113-117.
18. Nemes J, Boda R, Redl P, Marton I. Oral squamous cell carcinoma in north-eastern Hungary. II. Etiological factors. Fogorv Sz 2006; 99:179-185.
19. De Stefani E, Boffetta P, Deneo-Pellegrini H, Ronco AL, Acosta G, Ferro G, Oreggia F, Leiva J. The effect of smoking and drinking in oral and pharyngeal cancer: A case control study in Uruguay. Cancer Lett 2007; 246:282-289.
20. Moore S, Johnson NW, Pierce A, Wilson D. The epidemiology of mouth cancer: a review of global incidence. Oral Dis 2000; 6:65-74.
21. Johnson NW, Warnakulasuriya S, Tavassoli M. Hereditary and environmental risk factors: clinical and laboratory risk markers for Head and Neck, especially oral cancer and precancer. Eur J Cancer Prev 1996; 5:5-17.
22. Brandizzi D, Chuchurru JA, Lanfranchi HE, Cabrini RL. Analysis of the epidemiological features of oral cancer in the city of Buenos Aires. Acta Odontol Latinoam. 2005; 18:31-5.
23. Muir C, Weiland L Upper aerodigestive tract cancer. Cancer 1995; 75:147-153.
24. Leemans CR, Tiwari R, Nauta JJ, van der Waal I, Snow GB. Regional lymph node involvement and its significance in the development of distant metastases in head and neck carcinoma. Cancer 1993; 71:452-456.
25. Warburton G, Nikitakis NG, Roberson P, Marinos NJ, Wu T, Sauk JJ Jr, Ord RA, Wahl SM. Histopathological and lymphangiogenic parameters in relation to lymph node metastasis in early stage oral squamous cell carcinoma. J Oral Maxillofac Surg 2007; 65:475-84.
26. Lopes MA, Nikitakis NG, Reynolds MA, Ord RA, Sauk J Jr. Biomarkers predictive of lymph node metastases in oral squamous cell carcinoma. J Oral Maxillofac Surg 2002; 60:142-147.