UNIVERSIDADE ESTADUAL DE CAMPINAS
FACULDADE DE ODONTOLOGIA DE PIRACICABA

LIA MIZOBE ONO

ESTUDO EPIDEMIOLÓGICO RETROSPECTIVO DAS LESÕES BUCAIS DIAGNÓSTICADAS NA FUNDAÇÃO CENTRO DE CONTROLE DE ONCOLOGIA DO ESTADO DO AMAZONAS (FCECON) ENTRE OS ANOS DE 1998 A 2009

Tese de Doutorado apresentada à Faculdade de Odontologia de Piracicaba, da UNICAMP para obtenção do título de Doutor em Clinica Odontológica, na Área de Cirurgia e Traumatologia Buco-Maxilo-Faciais.

Orientador: Prof. Dr. Márcio de Moraes

Este exemplar corresponde à versão final da Tese defendida pela aluna, e orientada pelo Prof. Dr. Márcio de Moraes

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“Pensamos demasiadamente
Sentimos muito pouco
Necessitamos mais de humildade
Que de máquinas.
Mais de bondade e ternura
Que de inteligência.
Sem isso,
A vida se tornará violenta e
Tudo se perderá.”

Charles Chaplin

Resumo

A falta de estudos epidemiológicos a respeito de determinadas doenças, pode afetar o desenvolvimento de determinados programas de prevenção. Na região Norte do Brasil dados epidemiológicos sobre as lesões da cavidade bucal são escassos. Em muitos casos os tumores malignos são diagnosticados tardiamente em dois ou mais sítios de acometimento. Sendo assim, foi realizado um estudo retrospectivo dos prontuários dos pacientes atendidos pelos serviços de Cabeça e Pescoço e Odontologia da Fundação Centro e Controle de Oncologia do Estado do Amazonas (FCECON) no período de 1998 a 2009. No total foram selecionados 518 prontuários, seguindo os seguintes critérios de exclusão: ausência de dados e a impossibilidade de comprovar o laudo histopatológico das lesões. Dados a respeito do gênero, idade, raça, local de nascimento e residência, hábitos, sitio primário da lesão e o histológico da doença foram coletados. Todos os procedimentos estatísticos foram realizados no programa Statistica versão 5.1 (StatSoft Inc., Tulsa, USA). Foi observado que o gênero masculino (57,7%) foi predominante e que a média de idade dos pacientes foi de 47,8 anos (intervalo de 0 a 92 anos). As neoplasias malignas foram a maioria perfazendo 53,3% dos casos, seguidas pelas neoplasia benignas (18,0%) e patologias periodontais e gengivais (10,0%). A maioria dos casos dentro das neoplasias malignas foi do carcinoma de células escamosas (41,5%, n=215) e dentre as benignas foi o adenoma pleomórfico (9,5%, n=49). Uma ampla variedade de lesões foram encontradas e tabuladas para análise. A língua (17,8%) e a parótida (12,5%) foram as localidades mais acometidas pelas lesões. Essa distribuição varia nas diferentes regiões do Brasil e do mundo. Todos os dados analisados mostram que existe a necessidade de planejar novas estratégias para que os profissionais de saúde possam identificar precocemente as lesões que atingem o complexo maxilomandibular para minimizar possíveis sequelas que possam advir do tratamento e assim trabalhar por uma melhor qualidade de vida do paciente. Alem disso, a dificuldade de locomoção pelas barreiras geográficas, delimita a procura por atendimento por estes pacientes.

Palavras-chave: epidemiologia, saúde bucal, diagnóstico bucal, carcinoma de células escamosas, glândulas salivares.

Abstract

The lack of studies on the epidemiology of certain diseases may restrain the development of prevention and control programs. In the Northern region of Brazil, epidemiological data on oral lesions are rare and, in many cases, malignant tumors are frequently found in more than two sites. A retrospective study of patient medical records attended at the Department of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) from January 1998 to December 2009 was carried to better understand the oral and oropharynx lesions occurrence. The present study selected 518 medical records, using as exclusion criteria the lack of information and the impossibility to confirm its histopathology. Information concerning patient gender, age, race, birthplace, current residence, habits, primary lesion site and histological data of the disease were collected. All statistical analysis was done using the software Statistica 5.1 version (StatSoft Inc., Tulsa, USA). Male patients were more affected by lesions (57.7%) and mean age was 47.8 years (range of 0 to 92 years). Malignant neoplasias accounted for 53.3% of the cases, followed by benign neoplasia (18.0%) and periodontal and gingival pathologies (10.0%). Squamous cell carcinoma (41.5%, n=215) was the most common malignant neoplasia and the pleomorphic adenoma (9.5%, n=49) the most common among the benign ones. A wide variety of lesions was registered and tabulated for analysis. The tongue (17.8%) and the parotid (12.5%) were the primary sites affected by the lesions. The distribution of neoplasias varies according to the region in Brazil and worldwide. The present study highlights the need for better public health care plan strategies in order to promote the early diagnosis of lesions in the oral cavity and oropharynx to improve patient survival rates and quality of life, with the use of less radical and debilitating treatments. Besides, the geographical barriers and logistical difficulties restrain patient access to treatment.

Keywords: epidemiology, oral health, oral diagnosis, squamous cell carcinoma, salivary glands.

SUMÁRIO

INTRODUÇÃO

A epidemiologia define-se como estudo da distribuição e dos determinantes das doenças em populações humanas (Czeresnia & Ribeiro, 2000). Os estudos epidemiológicos mostram-se valiosos na reafirmação de tendências previamente estabelecidas e/ou na identificação de novos padrões de uma determinada doença (Gomes, 2004). A importância de estudos epidemiológicos é contemplada pela Lei dentro do Sistema Único de Saúde (Lei 8080, de 19 de Setembro de 1990), a fim de se planejar e executar programas de saúde para a população. Esses estudos devem ser desenvolvidos nas suas diversas regiões, já que as diferenças socioeconômicas, culturais e climáticas observadas apontam para uma possível distinção na prevalência dessas lesões (Volkweis et al., 2010).

As lesões na cavidade bucal são comumente encontradas na prática clínica. O seu diagnóstico e tratamento são partes integrantes do processo de recuperação da saúde bucal (Patel et al., 2011) e devem ser estudadas em todas as faixas etárias para uma melhor compreensão (Mandali et al., 2010; Shulman, 2005).

Estudos epidemiológicos são conduzidos para verificar a prevalência de determinadas alterações clínicas na mucosa bucal (Kniest et al., 2010; Shulman et al., 2004), onde encontramos trabalhos que tratam de lesões específicas ou de grupos fechados de estudo (Buchner et al., 2010; An et al., 2008; Santos, 2002) e outros que documentam a prevalência das lesões diagnosticadas histopatologicamente que afetam o complexo bucomaxilofacial (Kovac-Kavcic e Skaleric, 2000; Deboni et al., 2005). Contudo, condições específicas podem variar entre grupos selecionados dentro de uma população, resultante de fatores como a idade, gênero e etnia. Inferências gerais de estudos populacionais podem, muitas vezes, ser aplicadas a uma população geral (Jones e Franklin, 2006). A epidemiologia das lesões bucais na população adulta de países em desenvolvimento é praticamente desconhecida devido a ausência de grandes pesquisas de base populacional (Carrard et al., 2011). Na região Norte do Brasil as informações sobre a prevalência dessas lesões na população são escassas. Apenas um trabalho foi encontrado em pacientes com doenças sexualmente transmitidas (An et al., 2008).

Jones e Franklin (2006) realizaram um estudo de 30 anos na Inglaterra onde analisaram 44.000 lesões histologicamente diagnosticadas. Dessas lesões a maioria era benigna e 5.4% eram neoplasias malignas, estando de acordo com outros estudos (Carrard et al., 2011; Patel et al.,

2011). O Brasil tem a maior prevalência de câncer bucal na America Latina (Losi-Guembarovski et al., 2009). Quando estudamos a região de cabeça e pescoço, o carcinoma de células escamosas tem alta taxa de prevalência, sendo que na cavidade bucal é o mais prevalente (Scully e Bagan, 2009). Sendo assim o conhecimento do seu comportamento em determinada localização anatômica pode auxiliar no diagnóstico precoce e minimizar as possíveis sequelas.

Os tumores de glândulas salivares são incomuns e somam menos de 6% de todas as neoplasias na região de cabeça e pescoço. Por não serem comuns, sua epidemiologia não está adequadamente descrita (Pinkston e Cole, 1999; Zini et al., 2010) em algumas regiões do Brasil e, ainda, os estudos mostram que variações geográficas influenciam na prevalência dos tumores (Oliveira et al., 2009). Na região Norte não existem estudos nessa área.

O objetivo geral desse trabalho foi realizar um estudo retrospectivo através da revisão de prontuários dos pacientes atendidos no serviço de Cabeça e Pescoço e de Odontologia na Fundação Centro de Controle de Oncologia do Estado do Amazonas (FCECON) de 1998 a 2009 e analisar as características clínico-demográficas desses pacientes. Os objetivos específicos foram analisar as doenças malignas e benignas que acometem a cavidade bucal, dentre elas em destaque o carcinoma de células escamosas e os tumores de glândulas salivares.

CAPÍTULO 1

Oral lesions prevalence: A twelve-year (1998-2009) study performed at FCECON in Manaus - Amazonas

Objective: Characterize the patients attended at the Departments of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON).

Study design and setting: Five hundred and eighteen patient medical records were selected, using as the inclusion criterion the presence of oral lesions and the exclusion criteria was the lack of data in medical records and incapacity in confirming the histopathological diagnosis. Data regarding patient age, gender, race, diagnosis and tumor location were collected.

Results: The data revealed that the majority of patients were males from European-Amerindians descendents, at mean age of 47.8 years and the malignant tumors were more common than benign ones.

Conclusion: The large race variety of the Brazilian population make the analysis on a national level very difficult, but the data collected can contribute for the improvement of the health care planning in Northern Brazil.

Introduction

Diagnosis methods of oral lesions frequently include complementary exams such as the radiological, laboratorial and histological study. With reference to histological exams, biopsy consists in removing a fragment of a patient's tissue for macro and microscopical study, which combined to the clinical and radiographic signs, allow the dental surgeon to give a final diagnosis to the patient.

Although the biopsy is the most recommended procedure to provide diagnosis for the majority of the orofacial lesions, its use is relatively low[1]. In addition, only a few studies have documented the range of histologically diagnosed lesions that affect the maxillofacial complex. Most studies on the prevalence of disease are epidemiological in nature and so specific conditions may vary among selected groups. Data like age, gender, race and others can often be applied to the general population[2]. These data are important because they could help the professionals in the development of diagnostic hypotheses, providing them with data on the prevalence of disorders and diseases, making it possible to estimate its frequency in their clinical practice[3].

Oral health is an important part of the quality of life and oral lesions can cause discomfort or pain interfering with mastication, swallowing and speech. These factors can interfere with daily social activities[4]. Stomatology is an important field in health caring because the oral cavity is the site where malignant or benign neoplastic conditions may occur[5]. Oral cancer is considered a public health issue, because its worldwide incidence continues to increase[6] and also because of its high incidence and mortality rates. Some regions in Asia and on Indian subcontinent, oral cancer remains one the most common form of cancer[7]. In Brazil, among men, oral cancer is the 5th and in females the 7th most common site for cancer occurrence (National Cancer Institute – INCA)[8]. In the oral cavity and pharynx cancer can be located on the lip, tongue, gingival (gums), floor of the mouth, soft and hard palate, tonsils, salivary glands, oropharinx, among other less frequent sites[9].

Epidemiology of oral lesions has been described worldwide[2] and in some regions of Brazil[3], but in the Northern region these information are scarce. According to the 2010 data of IBGE[10] (Brazilian Institute of Geography and Statistics), the urban population in Northern Brazil is represented by 23.6% white, 4.7% African descendent, 71.2% mixed race called "pardo" and 0.4% Amerindians. In the State of Amazonas the "pardo" people are the most numerous, representing 70% of the population. Among the "pardo" people, the most common are the "caboclo", who were originated from the miscigenation between Ameridians and Europeans since the 19th century.

The geographical barriers and logistical difficulties in the Amazonas restrain patient access to treatment which, in many cases, means that they have to travel by boat for many days to reach treatment centers. Thus, in cases where accessibility to treatment centers is difficult, efficient oral cancer prevention programs are the only alternative to alleviate patient suffering and to reduce morbidity and mortality rates[11].

The present study is a retrospective study of oral lesions diagnosed from the Departments of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) located in Manaus, Amazonas, Northern Brazil. The survey included patient records from January 1998 to December 2009 and aimed to characterize the biopsied patients from this region of Brazil.

Material and Methods

This retrospective study was approved by the Research Ethics Committee of Amazonas State University (protocol number 143/09). The medical records of patients treated at the Departments of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) located in Manaus, State of Amazonas, from January 1998 to December 2009 were retrieved. FCECON is the only public hospital for cancer treatment in the State of Amazonas, where the population is over three million people and is also the referral hospital for cancer treatment in the Northern region of Brazil.

Information concerning age at diagnosis, gender, race, histopathological exam, as well as, tumor location were obtained from the patient records. All cases of oral and pharyngeal cancer treated at FCECON were evaluated and the data tabulated and analyzed. The inclusion criterion was the presence of oral and pharyngeal lesions. The exclusion criteria were the lack of data in medical records and incapacity in confirming the histopathological diagnosis. Five hundred eighteen medical records were selected and the data were organized in subcategories as presented in the results.

The data were analyzed by using Microsoft Office Excel (Microsoft Excel for Windows, release 11.0, 2003, Microsoft Corporation, Redmond, WA, USA) and all statistical analysis was done using the software Statistica 5.1 version (StatSoft Inc., Tulsa, USA) applied Fisher's exact test or the chi-square test, p value 0.05.

Results

During the 12-year period, 518 (9.9%) medical records were retrieved for analysis, where 57.7% were males and 42.3% were females (M:F = 1.4:1). The mean age at presentation were 49.3 and 45.8 years for males and females, respectively, within a general age range of 0 to 92 years. Thirty-nine patients (7.5%) were children between the age 0 and 16 years. The race distribution was 82.2% European-Amerindians descents, 14.9% white, 2.5% Afro-Brazilian and 0.4% Amerindians.

A total of 73 different diagnosis were analyzed, where 276 (53.3%) were malignant, 93 (18.0%) were benign tumors, followed by 52 (10.0%) cases of non-neoplastic proliferative lesions and gingival pathology (Table 1). Malignant tumors were more common among males (70.3%) while benign tumors in females were more common (57.0%).

Lesions were found on all parts of the oral region, but the tongue and parotid were the most commonly affected. In the case of malignant tumors, a higher percentage of two or more site tumors were observed (12.0%) (Table 2).

Squamous cell carcinoma was the most frequent malignant tumor (77.9%), followed by gland salivary tumors, the adenoid cystic carcinoma (5.4%) and mucoepidermoid carcinoma (4.0%). Squamous cell carcinoma was more prevalent in males while pleomorphic adenoma and adenocarcinoma were more common in females. Only a case of carcinoma *in situ* was found in this study and 4 (1.4%) cases of a rare oral melanoma were found (Table 3). Mean age of patients with malignant tumors was 50.7 years.

Amongst benign tumors, pleomorfic adenoma (52.7%) and focal fibrous hyperplasia (16.1%) were more common, some uncommon tumors like haemangiopericytoma (1.1%) and meningioma (1.1%) were also found (Table 4). The mean of age of these patients was 36.4 years.

Non-neoplastic proliferative lesions and gingival pathology showed female:male ratio 3:1 and pyogenic granuloma (48.1%) and fibrous epulis (46.2%) were the most frequent (Table 5 in Appendix 2). In the case of salivary gland pathologies (excluding neoplasia), sialadenitis was the most frequent (29.6%) followed by ranula (18.5%) and mucocele (14.8%). If the ranula and mucocele are considered a unique entity they become the most frequent. (Table 6 in Appendix 3).

In this study, ossifying fibroma (41.2%) and capillary haemangioma (55.6%) affected more bone and connective tissues, respectively (Table 7 in Appendix 4). The odontogenic tumors, ameloblastoma (43.8%) and keratocystic odontogenic tumor (25.0%) were the most common, as well as dentigerous cyst (71.4%) that was the most common amongst odontogenic cysts (Table 8 in Appendix 5). Patients with odontogenic tumors and odontogenic cysts presented same mean age (33.1 years old).

Leucoplakia (29.4%) and epithelial hyperplasia (23.5%) were the most frequent pathology observed in the mucosa (Table 9 in Appendix 6). Others pathologies less common are presented in Table 10 (Appendix 7).

Discussion

Worldwide published information on the prevalence of maxillofacial pathologies is scarce[2,4,5] and a similar situation is found in Brazil. These studies are important for monitoring the disease incidence within a population and for future planning and implementing preventive and therapeutic health care services[12].

Many patient medical records were disconsidered in the present study because of the occurrence of some pathology exclusively at the neck and also because many medical records were incomplete.

Recent studies have revealed that benign tumors and lesions were prevalent when compared to malignant tumors[2,12,13,14]. In this study malignant tumors were more frequent than benign ones[5]. The opposite pattern found in the present study is probably associated to the fact that the FCECON is the referral hospital for cancer treatment in Northern Brazil and many patients are screened in other medical facilities beforehand and mainly the patients with malignant tumors are forwarded to be treated at that hospital. On the other hand, most of the studies are normally performed in oral pathology centers that attend patients in general, without prior triage. In our sampling females account for 56.9% of all benign tumors and the mean-age of the patients was lower than for the group with malignant tumors (36.4 vs. 50.7 years) and these data were in accordance to the other studies[2].

The State of Amazonas presented, in 2010, a population of 3,480,397, distributed in 1,751,328 males and 1,729,609 females (IBGE, 2011)[15]. The male/female ratio in this study was 1.4:1. This observation was in contrast to the data reported by Jones and Franklin (2006)[2] and Patel et al (2011)[12]. They related male/female ratio 0.9:1 and 0.74:1, respectively, according to a study performed with individuals aged 60 years or above[16]. In some studies tumors are mainly found in the age group of 50 to 59 years[12]. These data are not in accordance to those of the present study in which lesions were found in patients of a mean of age 47.8 years. In a study carried out in the United States, 9.7% of 10,030 patients between 2 and 17 years of age presented oral lesions[17], while in other study with patients from 0 to 16 years, 8.2% presented oral lesions[18], which were slightly higher than of the present study (7.5%). Although the prevalence of oral mucosal disease has been found to be higher in older subjects, age is not considered to be the only factor correlated with oral mucosal disorders[19]. This race distribution is in accordance to the data presented by IBGE (2010)[10].

Tongue followed by parotid was the site most commonly affected by lesions, corresponding together for 30.3% of the cases. Shulman et al (2004)[20] after examined 17,235 adults, found that most of the lesions were in the hard palate, but other research referred that tongue is the most common site for intraoral cancer[21] among European and US populations[7,22]. Jones et al (2006)[2] discussed that their study was limited to patients who were 17 years and over; therefore, direct comparisons with previous reports are difficult. Most studies are rather limited to specific population groups.

Carcinomas represent 98.1% of oral and head and neck cancers, with nearly 87% specifically diagnosed as squamous cell carcinoma[6]. This was also the most frequent histological type of malignant diseases in the present study, representing 77.9% of the malignant cases and this finding is in accordance to other studies[2,23,24]. In the majority of the published information, as well as the results observed in this study, carcinoma has been diagnosed in patients older than 50 years old[25,26,27,28] . Patient mean age diagnosed with squamous cell carcinoma in this study was 63.7 years.

Although a high percentage of oral cancer was observed in this study, apparently they had a weak relationship with leukoplakia[29] because of its low occurrence, considering that only five patients (n= 518, 0.96%) presented leucoplakia. According to Zhang et al. (2010)[30] the incidence of leukoplakia was 9.18% in a study carried out in China, but other surveys showed a frequency of 1.46% to 15.56%.

The second most frequent type of malignant diseases was the adenoid cystic carcinoma, a salivary gland tumor that accounted for 5.4% of our cases. The predominance of adenoid cystic carcinoma observered in the patients of the present study has also been reported[31,32,33,34], but many studies also reported mucoepidermoid carcinoma as being the most common type of malignant salivary gland tumor[35,36,37] . Jones & Franklin (2006a)[1] found similar values to mucoepidermoid (10.4%) and to adenoid cystic carcinoma (9.9%) and Ajavi et al (2007)[24], in a study performed in Nigeria, found the adenocarcinoma as the second most common pathology of malignant diseases.

While some studies pointed females as the most affected gender[33,38], in our study the adenoid cystic carcinoma was more frequent in males[23] and the mean age of 50.7 years was compatible with the findings of Vargas et al (2002)[38] but a slightly high when compared with the data from Eveson and Cawson (1985)[33].

Head and neck sarcomas are very infrequent and generally account for 5 to 15% of all adult sarcoma cases[39]. In a study carried out in China, its frequency was 8.77%[40] while in another study done in Nigeria, the occurrence rate was 18%[24]. In the present survey, this type of cancer accounted for only 2.8% of all malignant neoplasm found (one case), a much lower rate than those found in other studies. A different aspect observed in the present study was that the patient was a 13-year old female, while analyzing a 10-year period of head and neck sarcoma occurrence, Mücke et al (2010)[41] found that males were more affected and mean age was 49.4 years for males and 46.4 years for females.

Han et al (2010)[40] found 5.92% of lymphomas, a high percentage compared to 2.1% in the present study. All cases of this study were only non-Hodgkin lymphomas, in agreement with other studies in which this type of lesion was the most common lymphoma[2,23,24].

Malignant melanoma is rare in the oral cavity and accounted for only 0.2 to 8% of all melanomas[42]. In our study there were four cases of this pathology, accounting for 1.4% of all malignant diseases. This value is consistent with the date from other studies[23,24], but ethinicity is indicated to influence its prevalence[43]. According to Mendenhall et al (2005)[44], the mean age of patients was 60 years with a male preponderance, which was confirmed by our findings.

In general, malignancies affected more male patients (70.2%) older than 50 years of age. This date is in agreement with those of Chidzonga (2006)[23], Jones & Franklin (2006)[2] and Ajayi et al. (2007)[24]. Benign to malignant tumor ratio in our study was almost 1:3, a much larger prevalence of malignancies than found in literature, as Jones and Franklin (2006)[2] found a 1:1 ratio.

In case of benign tumors, pleomorfic adenoma was the most common benign neoplasm (52.7%), followed by focal fibrous hyperplasia (16.1%) and squamous papilloma (6.5%). The present study showed differences when compared to Jones and Franklin (2006)[2] findings, in which papilloma was the most frequently, followed by pleomorfic adenoma and focal fibrous hyperplasia.

Most common periodontal and gingival pathologies were pyogenic granuloma (48.1%) and fibrous epulis (46.2%) as shown in other studies and females were more affected in all studies[2,16,44,45]. The higher incidence of fibrous epulis in females is probably due to their more frequent and longer use of complete dentures compared to men[44]. The prevalent age distribution for both type of lesions was 34 to 44 years in the present study. Buchner et al (2010)[45] found the

highest occurrence of pyogenic granuloma in the same age range, while other studies showed the greatest incidence of fibrous epulis in patients older than 60 years[16].

The analysis of salivary gland pathologies in this study, excluding neoplasias, indicates a major incidence of sialodenitis (29.6%) followed by ranula (18.5%) and mucocele (14.8%), which was in accordance with the results of Jones et al (2006)[2]. In the present study, mean age of patients with sialodenite was 37.1 years, while Jones et al. (2006)[2] found 49.7 years during a study carried out in England. In relation to mucocele, many studies indicated its predilection to children and young adults[46], which was confirmed by our findings (mean age of 15.5 years), but Kovac-Kavcic and Skaleric (2000)[13] found a major incidence in patients of 65 to 75 years of age in a study performed in Slovenia.

Ossifying fibroma (41.2%) was the most prevalent in this study while in other study its prevalence was 2.9%[2]. According to Ribeiro et al. (2010)[47], this type of lesion is mainly diagnosed in patients between the second and fourth decade of life, which is in accordance to our findings, in which patients mean age was 26.0 years. Oral vascular lesions are uncommon on the oral mucosa and the jaws[48], but the haemangiomas were the most frequently found in this study, in accordance with previous study carried out in United Kingdom[2].

In this study odontogenic tumors and cysts presented equal male to female ratio. Odontogenic tumors in females are more common in the second and third decade of life[49,50], but our findings differed on gender. Reports on the incidence of odontogenic tumors are not frequent[49]. The ameloblastoma was also the most frequent in this study[2,50] but Santos et al (2001)[49] found odontoma as the most common. Our findings showed that dentigerous cyst accounted for 71.4% and patient mean age was 25.2 years. These data are in accordance with another odontogenic cysts study performed in Brazil, being only the male:female (1.7:1) ratio different[51]. The low occurrence of cists and odontogenic tumors in this survey may be biased because FCECON is a referral hospital for the treatment of malignant neoplasias.

Conclusion

The results of the present study provide information on the prevalence of oral lesions in Manaus – Amazonas population and it should be of interest to health care professionals. These results do not represent the actual prevalence within the national general population, and is restricted to the incidence in the Northern region of Brazil. The wide racial variance within Brazil

and even within the Northern region makes the interpretation of the results difficult since some of the lesions are directly related to the ethnical characteristic of the population. Studies that evaluate the prevalence of diseases are much important for health care planning in order to set prevention programs, early diagnosis and treatment for the improvement of health conditions of the population.

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Table 1 – Distribution of patients treated at FCECON by diagnostic category and gender (1998-2009 period).

Diagnostic category	M		F		p	M+F	
	n	%	n	%		n	%
Malignant disease	194	65.3	82	37.1	<0.001*	276	53.3
Benign tumors	40	13.5	53	24.0	0.002 *	93	18.0
Non-neoplastic proliferative lesions and gingival pathology	13	4.4	39	17.6	<0.001 *	52	10.0
Salivary Gland pathology excluding neoplasia	15	5.1	12	5.4	0.847 ns	27	5.2
Mucosal and skin pathology	8	2.7	9	4.1	0.384 ns	17	3.3
Bone pathology	10	3.4	7	3.2	0.900 ns	17	3.3
Odontogenic tumours	8	2.7	8	3.6	0.547 ns	16	3.1
Connective tissue pathology	2	0.7	7	3.2	0.032 *	9	1.7
Odontogenic cysts	4	1.3	3	1.4	0.992 ns	7	1.4
Miscellaneous pathology	3	1.0	0	0.0	0.134 ns	3	0.6
Non-odontogenic cyst	0	0.0	1	0.5	0.246 ns	1	0.2
TOTAL	297	100.0	221	100.0		518	100.0

* – statistically significant difference between the gender ($p<0.05$)
ns – no statistically significant difference between the gender

Table 2 – Distribution of patients treated at FCECON by lesion site (1998-2009 period).

Site	n	%
Tongue	92	17.8
Parotid	65	12.5
Two or more sites	62	12.0
Gingiva	57	11.0
Hard or soft palate	51	9.8
Floor of the mouth	45	8.7
Buccal mucosa	32	6.2
Mandible	26	5.0
Submandibular gland	24	4.6
Lip	22	4.2
Maxila	17	3.3
Oropharinx or tonsils	8	1.5
Submental or submandibular	8	1.5
Vestibular fornix	5	1.1
Retromolar área	4	0.8
TOTAL	518	100.0

Table 3 – Distribution of patients treated at FCECON by malignant disease and gender (1998-2009 period).

Diagnostic category	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Squamous cell carcinoma	162	83.5	53	64.6	<0.001 *	215	77.9	60.6
Adenoid cystic carcinoma	10	5.2	5	6.1	0.752 ns	15	5.4	50.7
Mucoepidermoid carcinoma	7	3.6	4	4.9	0.622 ns	11	4.0	42.7
Non-Hodgkin's lymphoma	4	2.1	2	2.4	0.844 ns	6	2.2	46.7
Melanoma	3	1.5	1	1.2	0.836 ns	4	1.4	53.5
Carcinoma ex-pleomorphic adenoma	0	0.0	4	4.9	0.002 *	4	1.4	54.0
Metastatic carcinoma	0	0.0	3	3.7	0.007 *	3	1.1	48.3
Carcinoma - Undifferentiated	3	1.5	0	0.0	0.258 ns	3	1.1	49.3
Plasmocytoma	0	0.0	2	2.4	0.029	2	0.7	68.5
Acinic cell carcinoma	2	1.0	0	0.0	0.356 ns	2	0.7	66.0
Adenocarcinoma	0	0.0	2	2.4	0.029 *	2	0.7	56.0
Rhabdomyosarcoma	1	0.5	1	1.2	0.529 ns	2	0.7	24.5
Angiosarcoma	1	0.5	0	0.0	0.515 ns	1	0.4	64.0
Malignant Langerhans cell histiocytosis	0	0.0	1	1.2	0.123 ns	1	0.4	45.0
Malignant disease - undifferentiated	0	0.0	1	1.2	0.123 ns	1	0.4	69.0
Osteosarcoma	1	0.5	0	0.0	0.515 ns	1	0.4	31.0
Sarcoma	0	0.0	1	1.2	0.123 ns	1	0.4	13.0
Carcinoma *in situ*	0	0.0	1	1.2	0.123 ns	1	0.4	52.0
Myoepithelial carcinoma	0	0.0	1	1.2	0.123 ns	1	0.4	65.0
TOTAL	194	100.0	82	100.0		276	100.0	50.7

* – statistically significant difference between the gender ($p<0.05$)
ns – no statistically significant difference between the gender

Table - 4 Distribution of patients treated at FCECON by benign tumor and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Pleomorphic adenoma	19	47.5	30	56.6	0.409 ns	49	52.7	36.8
Focal fibrous hyperplasia	7	17.5	8	15.1	0.755 ns	15	16.1	43.1
Squamous papillomas	2	5.0	4	7.5	0.621 ns	6	6.5	37.0
Lymphangioma	3	7.5	1	1.9	0.187 ns	4	4.3	17.0
Warthin tumor (adenolymphoma)	4	10.0	0	0.0	0.031 *	4	4.3	53.8
Fibrous histiocytoma	1	2.5	2	3.8	1.000 ns	3	3.2	47.0
Lipoma	1	2.5	2	3.8	1.000 ns	3	3.2	56.3
Fibrolipoma	1	2.5	1	1.9	1.000 ns	2	2.2	37.0
Basal cell adenoma	1	2.5	1	1.9	1.000 ns	2	2.2	56.0
Haemangiopericytoma	0	0.0	1	1.9	1.000 ns	1	1.1	20.0
Meningioma	1	2.5	0	0.0	1.000 ns	1	1.1	20.0
Neurofibroma	0	0.0	1	1.9	1.000 ns	1	1.1	46.0
Melanotic neuroectodermal tumor of infancy	0	0.0	1	1.9	1.000 ns	1	1.1	0.0
Myoepithelioma (myoepitelial adenoma)	0	0.0	1	1.9	1.000 ns	1	1.1	40.0
TOTAL	40	100.0	53	100.0		93	100.0	36.4

* – statistically significant difference between the gender ($p<0.05$)
ns – no statistically significant difference between the gender

CAPÍTULO 2

Oral Squamous cell carcinoma: the patient's profile in Manaus - Amazonas, Brazil

Abstract

The incidence of oral squamous cell carcinoma in Northern Brazil still remains scarce, mainly in Manaus – Amazonas where oral cancer is the fifth most common site among men and the seventh most common among women. The medical records of patients treated at the Departments of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) from January 1998 to December 2009 were retrieved and analyzed. Patient information such as age, gender, race, birthplace, city of residence, habits, the tumor location and treatment were obtained. Males were more affected than females (3.1:1). The mean age of the patients diagnosed was 60.6 years and tongue was the most affected site. The majority of patients did not consume tobacco or alcohol and received radiotherapy, radiotherapy associate with chemotherapy or surgery during treatment. Twenty per cent of the patients had two or more sites on their initial diagnosis. This may indicate the deficiency of the health caring professionals in the Amazonas in early diagnosing the disease, which reinforce the need to improve public health planning in order to improve patient survival rates and quality of life, with the use of less radical and debilitating treatments.

Introduction

The first written medical documents with reference to cancer are the Edwin Smith Papyrus (1600 B.C.) and the Ebers Papyrus (1550 B.C.). In 460 B.C., Hippocrates was the first to use the term carcinoma[1]. Nowadays cancer is one of the most common causes of morbidity and mortality, with more than 10 million new cases and more than 6 million deaths worldwide every year [2]. More than 20 million people around the world live with a diagnosis of cancer and more than a half all cancer cases occur in the developing countries. Cancer is responsible for about 20% of all deaths in high income countries and 10% in low income countries. It is projected that by 2020 there will be every year 15 million new cases of cancer and 10 million deaths caused by this disease[3].

The majority of cancer in the head and neck is the squamous cell carcinoma and the oral squamous cell carcinoma is the most common among them[4,5,6]. Oral cancer is a serious and

growing problem in many parts of the globe. Oral and pharyngeal cancer, as a group, is the sixth most common type of cancer in the world[7] and the oral cancer is a malignant tumor that occurs in different locations in the oral cavity[8].

Oral lesions can cause discomfort or pain interfering with mastication, swallowing and speech, while symptoms such as halitosis, xerostomia or oral dysaesthesia can interfere with daily social activities diminishing patient's quality of life[9]. The etiology of oral cancer is multifactorial and factors such as the use of tobacco and excess consumption of alcohol act separately or synergistically[7].

The etiology of malignancies in general is considered to be multifactorial[10]. Uses of tobacco and alcohol consumption[6] are among the various risk factors for oral squamous cell carcinoma occurrence. Hashibe et al (2007)[11] confirmed previous findings that cigarette smoking is a strong risk factor for head and neck cancer.

According to the 2010 data of IBGE[12] (Brazilian Institute of Geography and Statistics), the urban population in Northern Brazil is represented by 23.6% white, 4.7% African descendent, 71.2% mixed race called "pardo" and 0.4% Amerindians. In the State of Amazonas the "pardo" people are the most numerous, representing 70% of the population. Among the "pardo" people, the most common is the "caboclo", who were originated from the miscigenation between Amerindians and Europeans since the 19th century. Brazil presents the highest incidence of oral cancer in Latin America[13]. According to the National Cancer Institute – INCA[14] (2008), oral cancer is the fifth most common among men and the seventh most common among women in the Amazonas State and also in Brazil.

Moore et al (2000)[15] reported that Brazil had the highest rate of mouth cancer in the world. There are innumerous epidemiologic studies on oral cancer throughout the world, even in Brazil, but in Northern Brazil these data are scarce[16], mainly in the Amazonas State. The present study is a retrospective study of oral squamous cell carcinoma cases from FCECON located in Manaus, Amazonas, and aimed to build the profile of oral squamous cell carcinoma patients.

Material and Methods

The medical records of all patients treated at the Department of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) from January 1998 to December 2009 were retrieved and 215 cases of oral squamous cell carcinoma

were analyzed. Basic patient information such as age, gender, race, birthplace, city of residence, habits, the tumor location, as well as, treatment were obtained. The exclusion criteria were lack of data in medical records and impossibility to verify the histopathology exam of the patients. The race distribution of the present study was done according to the IBGE[12] as white, African descendents, Amerindians and European-Amerindian descendents.

Oral cavity sites were defined as oral mucosa (C00.3,4/C06.0-C06.2)[16], gingiva or alveolar ridge (C03.0-C03.1)[16], hard palate (C05.0)[16], tongue (C02.0,1-C02.2)[16] and floor of the mouth (C04)[16], but in this study we divided in: tongue, gingiva or alveolar ridge, floor of the mouth, palate, buccal mucosa, retromolar area, lip and other sites. The term "lip" was used when referring to lesions of the upper and lower lip and lesions affecting the vermilion border, and the term "tongue" was used to indicate lesions located in all regions of the tongue. The term "two or more sites" was used for lesions that involved multiple anatomical sites in the oral cavity. The term "other sites" was applied for the other regions of the oral cavity and oropharynx.

The treatments applied were surgery, radiotherapy, chemotherapy, surgery and adjuvant radiotherapy, radiotherapy and chemotherapy, surgery plus adjuvant chemotherapy, surgery plus adjuvant radio and chemotherapy. When patients were not able to undergo one of the treatments presented above, "no treatment" was noted.

The data were analyzed by using Microsoft Office Excel (Microsoft Excel for Windows, release 11.0, 2003, Microsoft Corporation, Redmond, WA, USA) and all statistical analysis was done using the software Statistica 5.1 version (StatSoft Inc., Tulsa, USA) applied Fisher's exact test or the qui-square test, p value 5%.

The present study was performed in accordance to the Research Ethics Committee – Amazon State University, process number 143/09.

Results

Out of a total of 215 patient records, 162 were male (75.3%) with mean age of 57.4 years, 53 were female (24.7%) with mean age of 60.6 years. The highest of occurrence for male of oral squamous cell carcinoma was at 41-70 years, whilst the occurrence for females were most frequent at 51-70 years and at 81-90 years of age (Table 1).

The majority of the patients were European-Amerindian descendents (80%), some were white (16.7%) and 3.3% were African descendents. Eighty-one patients had been living in

Manaus, sixty were from the country side of Amazonas and seventy-four came from other States. Among these last, third-three patients were living in Manaus and forty-one were coming to Manaus only for treatment. European-Amerindian descendents accounted for 172 and were the most affected (80%) followed by the white 36 (16.74%) and only 7 (3.26%) were African descendents.

The most frequent site of the tumor was the tongue (31.6%), followed by two or more sites (20.9%) and the floor of the mouth (13.5%) (Table 2). Among the patients that presented two or more anatomical sites at the diagnosis, 33.3% were from Manaus, 31.1% from the country side of the State of Amazonas and 35.6% originated from other States. These patients were primarily treated with radiotherapy and radiotherapy associated with chemotherapy and presented mean age of 59.3 years and were prevalently males.

The majority of the patients (59.1%) did not report any habits (alcohol or tobacco consumption). The association of these two habits was present in 20.5% of the patients, followed by tobacco consumption (19.1%). Only 1.9% of the patients did not report alcohol consumption (Table 3).

Analyzing all cases combined, radiotherapy represented the most frequent treatment used (29.3%), followed by surgery (24.2%) and radiotherapy associated with chemotherapy (23.7%) (Table 5). However, when the data was analyzed in two different periods, radiotherapy associated with chemotherapy was the most common treatment, followed by surgery (Table 6).

Discussion

Many patient medical records were disconsidered in the present study because of the occurrence of some pathology exclusively at the neck and also because many medical records were incomplete.

In this study, oral squamous cell carcinomas occurred more frequently among males than females. In countries considerer of high-risk, such as, Sri Lanka, India, Pakistan and Bangladesh, oral cancer is the most common cancer in men[7]. This greater ratio of males in the occurrence of oral squamous cell carcinoma was seen in innumerous studies[18,19,20,21,22,23,24,25]. However, Llewellyn et al (2003)[26] observed higher oral cancer occurrence in young women than in young men, but in older patients (mean 58.6 years) they observed even a ratio of 6.6:1.0 male to female[13].

In the present study, mean age of women diagnosed with oral squamous cell carcinoma was 60.6 years and similar values were observed in other studies[4,27]. Kruse et al (2010)[28] reported male:female ratio of 46:53 to mean age of 79 years old. In this study, it was also observed an increase in the incidence of oral squamous cell carcinoma in women of 81 to 90 years of age. The frequency of oral cancer in young people is extremely low[10].

Some studies performed in Southern Brazil showed that white patients were the most affected[22,29,30,31], but Gervásio et al (2001)[18] showed that white patients were the least affected. These data can be compared with those of the Northern region of Brazil, where European-Amerindian descendents were the most affected, as well as the Northeastern region where non-white were the most affected[25]. Comparing the incidence of oral squamous cell carcinoma among races in Brazil is rather difficult due to the large miscegenation in the Brazilian population[31].

Marocchio et al (2003)[31] observed that dentists are much aware of their role as health care professionals and they can detect oral cancer early. However, this was not the case in the present study, since 20% of the patients were diagnosed with cancer in two or more anatomical sites. This may indicate the deficiency of these professionals in the Amazonas in early diagnosing the disease. It is also important to consider that in the present study, several patients came from the country side of the Amazonas State which, in many cases, means that they had to travel by boat for many days to seek treatment.

No site within the oral cavity is immune to the squamous cell carcinoma. However, certain sites are well recognized as locations where cancer occur more frequently[4]. Tongue is the most common site for intraoral cancer[17] among European and US populations[15, 32] and buccal cancer is more common among Asian populations[7]. Studies carried out in California among a diverse of racial and ethnical populations, tongue was the most common subsite for oral squamous cell carcinoma[8,33]. Llewlyn & Mitchell (1994)[34] found the highest incidence in the floor of the mouth and tongue. The tongue was the most affected site (53%) followed by the buccal mucosa (9.5%) and maxillary gingiva (9%). However, on a study performed in Iran, the floor of the mouth was the least involved[23] and in two other studies carried out in Southern Brazil a greater number of cases were found occurring in the gingiva[29,31].

Women are more likely to develop carcinoma of the gingiva (rigde included), whereas men have more propensity to develop cancer in the floor of the mouth[32]. Oral squamous cell carcinoma in floor of the mouth in this study was prevalent in males but in the gingiva gender

ratio was 1:1. The retromolar trigone is a relatively uncommon site for oral squamous cell carcinoma[35] as observed in the present study. Epidemiological studies have shown that the sites of occurrence of oral cancer differ widely[18].

The lower lip vermilion is by far the most common site of oral cancer[18] because this anatomical site usually receives a higher exposure of solar radiation[36]. Lip cancer is particularly a problem of older people and is a disease that affects especially males, being a common lesion of the lower lip in Caucasians living in hot climates[6]. In Tropical cities high incidences of lip squamous cell carcinoma is expected, although in this study only 6.0% was observed. The high miscegenation in the Amazon may have been beneficial to its population considering that Bertotto et al (2003)[37] found no occurrence of lip cancer among Indians despite their constant exposure to the sun.

Since 1965, the relation between alcohol and tobacco use and cancer of the mouth has been studied[38]. Nowadays, it is well known that smoking is a strong risk factor for head and neck cancer independently of alcohol consumption[11]. In some cases, alcohol consumption is the major risk factor to cancer[15]. Within the Europe countries, the highest incidence rates occur in males from France and Hungary where alcohol consumption is high, while the lowest rates are found in Greece and Cyprus[7].

According to the 2008 National Home Sample Survey (PNAD)[39] carried out by the Brazilian Institute of Geography and Statistics (IBGE), the State of Amazonas presents one of the lowest rates of smokers in Brazil. These data are in accordance to those of the present study where the majority of the patients (59.1%) did not report alcohol and tobacco consumption. However, some individuals who had minimal levels of tobacco or alcohol use might have been included in the "never used tobacco" and "never drink"[11].

Kruse et al (2010)[28] discussed the tongue and floor of mouth sensitivity to the carcinogenic effects of tobacco or alcohol. In this study, no correlation was found between the anatomical sites and the patient habits to consume alcohol or tobacco.

Despite the low rate of tobacco users in this study, the incidence of oral cancer was similar to those of other States in Brazil[14]. In a study carried out in the United States, a significant portion of the patients with oral cancer reported no history of smoking[40], thus the etiology of oral squamous cell carcinoma on those who never smoked is still unclear[28]. Llewellyn et al (2003)[26] reported in their study that one quarter of all cases had no major risk factors associated, such as,

the exposure to tobacco or excessive levels of alcohol, and 6% of these had never smoked or drunk alcohol regularity. The incidence of cancer of the head and neck varies throughout the world and the etiology has been described to local carcinogenesis that produces this variation[34].

Surgery remains the most well established definitive treatment at first for the majority of patients with oral squamous cell carcinoma[41]. Radiotherapy can be used on early-stages and locally in advanced disease, alone or combined with surgery and/or chemotherapy[42]. Also, chemotherapy has been used for local treatment or as a palliative therapy[43]. In the present study, the most common treatment used was the radiotherapy in the period from 1998 to 2009. However, when analyzing the period from 2004 to 2009, the radiotherapy associated with chemotherapy was the most common treatment applied. The major advance in the concomitant treatment chemotherapy-radiotherapy has been improving the treatment in locally advanced cases[42,43].

Our results were similar to those of patients in Northeastern of Brazil, except for the fact that in the present study the patients had the lowest rate of lip cancer and the consumption of tobacco and alcohol were lower than in other regions.

Cancer registries are part of a surveillance system. Efforts to prevent and control cancer are hampered by the low priority frequently given by governments. The excessive expenditure on treatments and the considerable unbalance between resources allocated to basic cancer research and those directed to its prevention and control also contribute to the expansion of the disease.

It is important to consider that in the present study, 81 patients had been living in Manaus, another 74 patients came from other States and 60 came from the countryside of the Amazonas State which, in many cases, meant that they traveled many days to be treated. Therefore, many patients looked for treatment only when the disease caused too much pain or disability to eat, which can also explain why some tumors had two or more sites. The Oncology Center Control Foundation of the Amazonas (FCECON) is a referral center in the oncology treatment in Northern Brazil, therefore many patients come from other States seeking for treatment. As a result, the follow up of the disease and results of the treatments is difficult for those patients from the country side and for those coming from other States.

Conclusion

Based on data from a 12-year period from the only Amazonas State Public Oncology Center, patient with oral squamous cell carcinoma in this region were most commonly man

(75,3%); European-Amerindian descendent (80%); with mean-age of 57.4 years; no consumer of alcohol or tobacco (59.1%). These characteristics were similar to those of patients in Northeastern Brazil, except for the fact that in the present study the patients had the lowest rate of lip cancer and the consumption of tobacco and alcohol were lower than in other regions.

The Amazon region presents geographical barriers and logistical difficulties, aggravated by poor and expensive transport infrastructure which restrain patient access to treatment. As a result, the diagnosis of pathologies may be delayed considering the lack of health care professionals in the countryside of the Amazonas State, indicated by 20.9% of patients that presented two or more sites affected by the disease. Thus, a more comprehensive health care planning is required compared to other regions of Brazil, where road transport is available.

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Table 1 – Age and gender distribution of patients with squamous cell carcinoma.

Age (year)	F		M		F+M	
	n	%	n	%	n	%
21-30	1	1.9	2	1.2	3	1.4
31-40	3	5.7	9	5.6	12	5.6
41-50	7	13.2	35	21.6	42	19.5
51-60	12	22.6	58	35.8	70	32.6
61-70	12	22.6	36	22.2	48	22.3
71-80	7	13.2	16	9.9	23	10.7
81-90	11	20.8	6	3.7	17	7.9
Total	53	100.0	162	100.0	215	100.0

Table 2 – Frequency of cancer site distribution according to gender.

Site	Gender						
	M		F		p	M+F	
	n	%	n	%		n	%
Tongue	54	33.3	14	26.4	0.347 ns	68	31.6
Two or more sites	33	20.4	12	22.6	0.724 ns	45	20.9
Palate	21	13.0	9	17.0	0.464 ns	30	14.0
Floor of the mouth	23	14.2	6	11.3	0.594 ns	29	13.5
Lips	8	4.9	5	9.4	0.233 ns	13	6.0
Gingiva	5	3.1	5	9.4	0.057 ns	10	4.7
Other anatomical location	10	6.2	0	0.0	0.064 ns	10	4.7
Buccal mucosa	7	4.3	2	3.8	0.863 ns	9	4.2
Retromolar trigone area	1	0.6	0	0.0	0.566 ns	1	0.5
TOTAL	162	100.0	53	100.0		215	100.0

ns – no statistically significant difference between the gender

Table 3 – Frequency of patient's habits according to gender.

Site	Gender		
	M	F	M+F
	n(%)	n(%)	n(%)
Tobacco	30(18.5)	11(20.7)	41(19.1)
Alcohol	0(0.0)	3(5.7)	3 (4.1)
Both[a]	36(22.2)	8(15.1)	44(20.5)
No habits[b]	96 (59.3)	31(58.5)	127(59.1)
Total	162(100.0)	53(100.0)	215(100.0)

Tobacco and Alcohol consumption[a] / No tobacco or alcohol consumption[b]

Table 4 – Distribution of cancer site of patients by habits.

Site	Tobacco	Alcohol	Both	Anyone
Tongue	12	2	14	40
Floor of the mouth	5	1	10	13
Palate	3	0	6	21
Gingiva	3	0	2	5
Buccal mucosa	3	0	1	5
Lip	4	0	1	8
Two or more sites	9	0	8	28
Retromolar trigone area	0	0	0	1
Other mouth	2	0	5	3
Total	41	3	47	124

P value = 0.59977 – Fisher's exact test

Table 5 – Distribution of treatment by gender in a 12-year period.

Treatment	M		F		p	M+F	
	n	%	n	%		n	%
Surgery	36	22.2	16	30.2	0.240 ns	52	24.2
Radiotherapy	45	27.8	18	34.0	0.391 ns	63	29.3
Chemotherapy	5	3.1	1	1.9	0.645 ns	6	2.8
Surgery + adjuvant radiotherapy	12	7.4	5	9.4	0.635 ns	17	7.9
Radiotherapy + chemotherapy	44	27.2	7	13.2	0.038 *	51	23.7
Surgery + adjuvant chemotherapy	2	1.2	1	1.9	0.725 ns	3	1.4
Surgery + adjuvant radio and chemotherapy	10	6.2	1	1.9	0.219 ns	11	5.1
No treatment	8	4.9	4	7.5	0.473 ns	12	5.6
TOTAL	162	100.0	53	100.0		215	100.0

* – statistically significant difference between the gender ($p<0.05$)
ns – no statistically significant difference between the gender

Table 6 – Frequency of treatments according to gender in two periods.

Treatment	1998 – 2003				2004 - 2009				p
	F	M	M+F	%	F	M	M+F	%	
Surgery	5	16	21	21.2	11	20	31	26.7	0.347 ns
Radiotherapy	8	30	38	38.4	10	15	25	21.6	0.007 *
Chemotherapy	-	2	2	2.0	1	3	4	3.4	0.526 ns
Surgery + adjuvante radiotherapy	3	7	10	10.1	2	5	7	6.0	0.271 ns
Radiotherapy + chemotherapy	2	16	18	18.2	5	28	33	28.4	0.078 ns
Surgery + adjuvante chemotherapy	-	2	2	2.0	1	-	1	0.9	0.471 ns
Surgery + adjuvante radio and chemotherapy	-	2	2	2.0	1	8	9	7.8	0.057 ns
No treatment	2	4	6	6.1	2	4	6	5.2	0.777 ns
TOTAL	20	79	99	100.0	33	83	116	100.0	

* – statistically significant difference between period ($p<0.05$)
ns – no statistically significant difference between period

CAPÍTULO 3

Salivary Gland Tumors: A Retrospective study in Northern Brazil.

BACKGROUND: The aim of this study is to present a retrospective study of salivary gland tumors cases in Manaus – Amazonas (Northern Brazil), over a 10-year period (1998-2009).

METHODS: The medical records of all patients treated at the Department of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) were retrieved and data on the patient with salivary gland tumors with epithelial or mesenchymal origin were analyzed.

RESULTS: Salivary gland tumors were 58.3% benign and 41.7% were malignant. For benign tumor, females were more affected than males, but for malignant tumors the occurrence was almost two times higher for males. The average age of patients with benign tumors was 48.0 years for males and 45.0 years for females, while for malignant tumors the average age was 54.5 years for males and 48.6 years for females. In the group of benign tumors, the predominant type was pleomorphic adenoma, whilst amongst the malignancies, the adenoid cystic carcinoma was the most frequent.

CONCLUSIONS: The present study showed that many clinical characteristics of salivary gland tumors are similar to those found elsewhere in the world and in other regions in Brazil, contributing for better understanding and treating the disease.

Keywords: intra-oral neoplasm, salivary gland tumors

INTRODUCTION

Salivary tumors are uncommon and comprise less than 6% of all neoplasms of the head and neck region[1,2,3], but generate considerable interest because of their variation in histological and clinical presentation[4]. Salivary gland tumors present a yearly incidence of about 1.0 to 6.5 per 100,000 worldwide and about 2.5 to 3.0 per 100,000 in the Western world. Since 1991, the World Health Organization (WHO) named almost 43 epithelial tumors in salivary glands[2,5].

Salivary glands are anatomical and functional adnexae of the oral cavity. Therapy of tumors of these glands involves various specialists but the disease is mainly treated by maxillofacial surgeons[6]. The knowledge on the most current diseases is important to the

epidemiologists, to public health policy and to the health professionals, allowing the planning of specific therapeutical approaches for each disease[7].

According to the 2010 data of the Brazilian Institute of Geography and Statistics (IBGE)[8], the urban population in Northern Brazil is represented by 23.6% white, 4.7% African descendents, 71.2% mixed race called "pardo" and 0.4% Amerindians. In the State of Amazonas "pardo" people are the most numerous, representing 70% of the population. Within those, the most common is the "caboclo", who were originated from the miscegenation of Amerindians and Europeans since the 19th century.

The epidemiology of salivary gland tumors has been described in some regions of Brazil[9] but in the Northern region these information are scarce. The present study is a retrospective study of salivary gland tumor cases from a single institution located in the State of Amazonas, Northern Brazil.

MATERIAL AND METHODS

This retrospective study was approved by the Research Ethics Committee of Amazonas State University (protocol number 143/09). The medical records of all patients treated at the Department of Head and Neck and Odontology of the Oncology Center Control Foundation of the Amazonas (FCECON) from January 1998 to December 2009 were retrieved. FCECON is the only public hospital for cancer treatment in the state of Amazonas, which has a population of over three million inhabitants, and is also the referral hospital in the entire Northern region. Ninety-six cases of salivary gland tumors with epithelial or mesenchymal origin were analyzed. Information concerning age at diagnosis, gender, race, birthplace, as well as, the tumor location, were obtained from the patient records. Rare cases of salivary gland neoplasms were also analyzed.

The criterion for inclusion in the study was the histological diagnosis of salivary gland tumor based on the second edition of the WHO's Histological Classification of Salivary Gland Tumors[10] and the exclusion criterion was the lack of adequate information.

The data were analyzed by using Microsoft Office Excel (Microsoft Excel for Windows, release 11.0, 2003, Microsoft Corporation, Redmond, WA, USA) and all statistical analysis was done using the software Statistica 5.1 version (StatSoft Inc., Tulsa, USA) applied Fisher's exact test or the qui-square test, p value 5%.

RESULTS

The total number of salivary gland diseases was 127. Salivary tumors accounted for 75.6% (96) of all salivary gland diseases and for 1.83% of all neoplasm treated in this hospital. In this study 58.3% (56) of salivary gland tumors were benign and 41.7% (40) were malignant. The male:female ratio was 1:1.3 for benign tumor while for malignant tumors the ratio was almost two times higher for males (table1).

The average age at diagnosis of benign tumors was 40.6 years for males and 38.2 years for females and for malignant tumors average age was 53.0 years for males and 45.2 years for females (table 2). The high incidence for patients with benign tumors was in the second and third decades. However, for the patients with malignant tumors the majority of incidence was in the fifth and sixth decade.

Children/adolescents were the minority (7.2%) and the average age was 18.1 years, the youngest was 15 years old. Most of the tumors were pleomorphic adenoma (71.4%), another 28.6% were adenoid cystic carcinoma and mucoepidermoid carcinoma both on a same proportion.

In the group of benign tumors, the predominant type was pleomorphic adenoma, while amongst the malignancies, the adenoid cystic carcinoma (15.6%) was most frequent (table 3) and mucoepidermoid carcinoma was the second (11.5%). Although uncommon, one case of myoepithelial carcinoma was found.

Two cases of acinic cell carcinoma were diagnosed in two 66 years old male patients, one located in the parotid gland and another in the floor of the mouth. Basal cell adenoma was detected in two patients, one of each gender; both arisen in the parotid gland. Male patient was 55.0 years old and female was 57.0. Non Hodgkin's lymphoma was detected in the parotid gland in four patients, who were all males with mean age of 43.5 years old. A case of myoepithelial carcinoma was diagnosed in a 65.0 years-old woman, located in the parotid gland and other 40.0 years-old woman presented a myoepithelioma in the parotid gland.

The parotid gland was the most common site of salivary tumors (56%), followed by the submandibular gland (13%) and the minor salivary gland in the palate (10%). Five patients had malignant tumor in two or more sites and due to their large extension, the primary sites were not determined. Two patients had tumor on the tongue, a pleomorphic adenoma and an adenoid cystic carcinoma and one patient had a mucoepidermoid carcinoma in retromolar trigone area.

Statistical analysis showed that pleomorphic adenoma occurred more in females than males, p = 0.007 (table 3).

The majority of the patients were European-Amerindian descendents, some were white and only one was African descendent. Thirty five patients had been living in Manaus, 31 were from the country side of Amazonas and 31 came from other States.

The benign salivary gland tumors are the most common in different regions where pleomorphic adenoma was the most frequent for all regions in Brazil. Among the malignant tumors, adenoid cystic carcinoma was the most frequent in Northern and Northeast regions. In the Southern and Southeast regions of Brazil, mucoepidermoid carcinoma was the most frequent (table 4).

DISCUSSION

Ninety six cases of salivary gland tumors were found, accounting for 1.84% of all neoplasms treated in this hospital. This number is consistent with the frequency often found in the literature[1,2,3]. There was a predominance of benign salivary gland tumors (57.1%) over malignant tumors. This predominance of benign tumors had been seen in other studies [1,9,11,12,13,14], but a study carried out in Thailand found 52.7% of malignant tumors while benign accounted 47.3%[15]. It was justified by having the dental school occasionally receiving referred cases of malignant tumors. It was also discussed if it reflected the true incidence in their geographic region and their racial population or not.

In the present study, benign tumors were more prevalent in females and patients with malignant tumors commonly were older and males. Greater ratio of females in the occurrence of benign tumors was seen in innumerous studies[1,9,11,12,15], but Tian et al (2010)[16] showed a slight propensity toward males. Other studies showed no gender predominance for both benign and malignant tumors[6,17,18,19]. Sun et al (1999)[20] described that salivary gland cancer was slightly higher among females than males until the age range of 40-44 years, after which males were at a higher risk. Some differences can be attributed to race and geographical location[21].

In this study, the highest of incidence of benign salivary tumors was found in the second and third decades, the same values seen in a Chinese study[12]. However, Eveson & Cawson (1985)[22] found benign salivary tumors most frequently in the sixth decade. Ito et al (2005)[9] found the most frequent occurrence in patients at the fifth decade and Subhashraj (2008)[18] found at the

fifth and the sixth decade of life. In the case of malignant salivary gland tumors, this study found the prevalent incidence in the seventh decade[9,22], but Subhashraj (2008)[18] and Moreira et al (2009)[11] found in the sixth decade the highest incidence of malignant tumors. Epithelial malignances of the salivary glands are not limited to a certain age. They can occur in children as well as in adults[19].

Patients with a benign tumor which occurs at a young age have higher risk of developing a malignant parotid carcinoma[23]. Sun et al (1999)[20] found that the incidence of salivary gland cancer increased markedly with aging. They described that females until the age range of 40-44 had a slightly higher incidence than males but after that, males were at a higher risk. In children/adolescents, the occurrence of salivary gland tumors is rare[24].

The most common site for the occurrence of tumor in this study was the parotid gland (n= 54), followed by the minor salivary gland (n= 17) and submandibular gland (n= 13)[4,9,12,13,17,18,22]. Others studies showed that the majority of salivary gland tumors was the parotid gland, followed by submandibular gland and minor salivary gland[11,14]. Tilakaratne et al (2009)[25] found the majority of the tumors occurrence in the minor salivary gland followed by parotid gland. The data from the statistical analysis indicated that the histological type of tumor depends on its location, which can explain the difference in the incidence between benign and malignant of certain neoplasia. When malignancies were analyzed, the most common site was the minor salivary glands[11,16] and Speight & Barrett (2002)[2] related that the majority of tumors arising from the minor salivary glands and sublingual gland are malignant.

The predominant type of benign tumors in our study was pleomorphic adenoma, which is also listed universally as the most common tumor in other studies [2,6,9,10,11,13,15,26,27]. The predominance of adenoid cystic carcinoma in the patients of the present study had been related [6,11,22,26], but many studies reported mucoepidermoid carcinoma as being the most common type of malignant tumor [2,9,13,25,28,29]. Jones & Franklin (2006)[27] found similar values to mucoepidermoid (10.4%) and to adenoid cystic carcinoma (9.9%).

Dhanuthai et al (2009)[15] referring to studies from USA, Brazil, Venezuela, Australia, Libya and China revealed that mucoepidermoid carcinoma was the most common malignant salivary gland tumor. However, studies from UK, the Netherlands, Japan, China and South Africa found the adenoid cystic carcinoma the most common. In Brazil, when analyzing malignant tumors, it was found a predominance of adenoid cystic carcinoma in the Northern and

Northeastern regions. In the Southern and Southeastern Brazil, mucoepidermoid carcinoma was the most common (Table III). Perhaps, this variability observed in these studies performed in Brazil can be explained for its differences in the racial distribution. For example, in the Northern and Northeastern regions the predominance race is European-Amerindian and European-African descendents while in Southern and Southeastern white is the predominant (IBGE, 2010)[8].

The results of our survey with 96 patients showed the distribution of 87.5% European-Amerindian descendents, 12.5% white and 1.0% African descendent and were, in accordance to the race distribution published by IBGE (2010). Pinkston & Cole (1999)[1] showed that incidence rates varied considerably by race. In opposition, the present study indicated no significant difference in the incidence rate by race. Other studies carried out in Brazil by Ito et al (2005)[9] and Vargas et al (2005)[13] in Southeastern and Southern Brazil, respectively, reported different incidence of salivary gland tumors[30] compared to the present study.

Some rare cases were diagnosed in this study, acinic cell carcinoma is one and two cases were diagnosed in two male patients. Omlie & Koutlas (2010)[31] found that males were more affected than female, but other studies showed males were the least affected[32,33]. Age range in the studies was 48-70 years old. This neoplasm comprises approximately 7% to 15% of all malignant tumors arising in salivary glands, with majority affecting the parotid gland, which was the location of one of the lesions. The other lesion was detected in the floor of the mouth, a rare location for this kind of tumor[32].

The real frequency of intraoral myoepithelial carcinoma remains unknown[34]. This type of neoplasm represents only about 0.4 to 0.6% of all salivary gland tumors, but in a Chinese study it represented 3%[16]. The incidence ratio of male:female was approximately equal. The majority of myoepithelial carcinoma affects the major salivary gland[34], as diagnosed in one female patient in our records, who presented the parotid gland affected.

Malignant lymphomas of the oral region are rare and account for approximately 3.5% of all oral malignancies[35]. This incidence was confirmed in a Chinese study with 6,982 patients where no case of oral malignant lymphoma was found[16]. In this study, two cases were found in males and were located in the parotid. It represented 2.16% in our oral malignancies study.

Basal cell adenoma accounts for 1-3% of all salivary gland tumors[36], and in this study two male patients were diagnosed with this type of tumor, differently from other studies in which females were the most affected[37]. The basal cell adenoma is a benign neoplasm that typically

affects major salivary glands, in which 75% of the cases occur in the parotid gland[35], the same location seen in the patients of this study.

A case of myoepithelioma was diagnosed in the parotid gland of a female patient of the present study. This benign tumor is rare, accounting for less than 1% of all salivary gland tumors in some studies[38] while others have shown an occurrence of 3%[11]. In most cases, this type of tumor affects the parotid gland, as seen in the patient in our records. Also, there is no apparent predilection for any gender[11].

It is important to consider that in the present study, 35 patients had been living in Manaus and 31 came from the country side of the Amazonas State which, in many cases, means that they had to travel by boat for many days to seek treatment. Therefore, many patients living in the country side look for treatment only when the disease causes too much pain or disability to eat, what can also explain why some tumors had two or more sites. Another 31 patients came from other States to be treated at the Oncology Center Control Foundation of the Amazonas (FCECON), which is a referral center in the oncology treatment in Northern Brazil. As a result, the follow up of the disease of these patients was also very difficult.

CONCLUSION

This group of patients do not represent the whole country of Brazil, but in summary, the majority of the tumors were benign, found in the parotid gland and in females. Pleomorphic adenoma was the most frequent histological type, followed by the adenoid cystic carcinoma, Warthin's tumor and mucoepidermoid carcinoma. These results showed that many clinical characteristics of disease are similar to those found elsewhere in the world and in other regions of Brazil. Salivary gland tumor distribution is indicated to be related to race and the group of patients on this study may represent the occurrence in Northern and Northeastern Brazil. Many clinical characteristics of disease found in this study are similar to those found elsewhere in the world and in other region of Brazil, contributing for better understanding and treating salivary gland tumors.

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Table 1 - Frequency of benign and malignant tumors according to gender.

Gender	Benign		Malignant		Total
	n	%	n	%	
Male	24	45.3	29	54.7	53
Female	31	72.1	12	27.9	43
Total	55	57.3	41	42.7	96

P = 0.008* (statistically significant difference between the gender (p<0.05))

Table 2 - Frequency of salivary tumors according to gender and age.

Tumor	Gender							Mean age (years)		
	M		F		P	M+F				
	n	%	n	%		n	%	M	F	M+F
Benign (n = 56)										
Pleomorphic adenoma	19	38.0	30	65.2	0.007*	49	51.0	37.1	36.7	36.8
Warthin tumor (adenolymphoma)	4	8.0	0	0.0	0.118 ns	4	4.2	53.8	-	53.8
Basal cell adenoma	1	2.0	1	2.2	1.000 ns	2	2.1	55.0	57.0	56.0
Myoepithelioma (myoepitelial adenoma)	0	0.0	1	2.2	0.479 ns	1	1.0	-	40.0	40.0
Malignant (n = 40)										
Adenoid cystic carcinoma	10	20.0	5	10.9	0.218 ns	15	15.6	56.3	45.0	52.5
Mucoepidermoid carcinoma	7	14.0	4	8.7	0.664 ns	11	11.5	49.6	35.8	44.5
Malignant lymphomas	4	8.0	0	0.0	0.118 ns	4	4.2	43.5	0.0	43.5
Carcinoma ex-pleomorphic adenoma	3	6.0	1	2.2	0.618 ns	4	4.2	46.7	64.0	51.0
Acinic cell carcinoma	2	4.0	0	0.0	0.496 ns	2	2.1	66.0	-	66.0
Adenocarcinoma	2	4.0	0	0.0	0.496 ns	2	2.1	56.0	-	56.0
Squamous cell carcinoma	1	2.0	0	0.0	1.000 ns	1	1.0	69.0	-	69.0
Mioepithelial carcinoma	0	0.0	1	2.2	0.479 ns	1	1.0	-	65.0	65.0
TOTAL	50	100.0	46	100.0		96	100.0			

* – statistically significant difference between the gender (p<0.05)
ns – no statistically significant difference between the gender

Table 3 - Histological classification and site of salivary gland tumors.

Tumor	Parotid	Submandibular	Palate	Buccal	Floor of the mouth	Lip	Retro-molar trigone area	Tongue	Two or more sites	Total	(%)
Benign											
Pleomorphic adenoma	36 (73%)	9 (18%)	2 (4%)			1 (2%)		1 (2%)		49	51.0%
Myoepithelioma (myoepitelial adenoma)	1 (100%)									1	1.0%
Basal cell adenoma	2 (100%)									2	2.1%
Warthin tumor (adenolymphoma)	3 (75%)	1 (25%)								4	4.2%
Malignant											
Acinic cell carcinoma	1 (50%)				1 (50%)					2	2.1%
Mucoepidermoid carcinoma	4 (36%)		3 (27%)		1 (9%)		1 (9%)		2 (18%)	11	11.5%
Adenoid cystic carcinoma	2 (13%)	2 (13%)	3 (20%)	2 (13%)	4 (27%)			2 (13%)		15	15.6%
Adenocarcinoma									2 (100%)	2	2.1%
Carcinoma in pleomorphic adenoma	2 (50%)		2 (50%)							4	4.2%
Squamous cell carcinoma		1 (100%)								1	1.0%
Malignant lymphomas	2 (50%)							1 (25%)	1 (25%)	4	4.2%
Myoepithelial carcinoma	1 (100%)									1	1.0%
TOTAL	54 (56%)	13 (14%)	10 (10%)	2 (2%)	6 (6%)	1 (1%)	1 (1%)	4 (4%)	5 (5%)	96	100.0

Table 4 – Comparison of reported distribution of salivary gland tumors in different regions in Brazil

Brazil Region	Total (n)	Years Covered	Benign	Malignant	Salivary glands Major	Salivary glands Minor	Pleomorphic adenoma	Adenoid cystic carcinoma	Mucoepidermoid carcinoma
Southern[1]	496	1972-2001	335 (67.5%)	161 (32.5%)	383 (77.2%)	113 (22.8%)	269 (54.2%)	39 (7.9%)	67 (13.5%)
Southeastern[2]	124	1993-1999	99 (79.8%)	25 (20.2%)	118 (95.2%)	6 (4.8%)	84 (67.7%)	5 (4.0%)	13 (10.5%)
Northern[3]	97	1998-2009	57 (58.8%)	40 (41.2%)	68 (70.1%)	23 (23.7%)	49 (50.5%)	15 (15.5%)	11 (11.3%)
Northeastern[4]	484	1985-2005	259 (53.5%)	225 (46.5%)	302 (62.4%)	109 (22.5%)	205 (42.3%)	108 (22.3%)	22 (4.5%)
Northeastern[5]	245	1980-1999	187(76.3%)	58 (23.7%)	199 (81.2%)	46 (18.8%)	168 (68.6%)	13 (5.3%)	11 (4.5%)

Ito et al (2005)[1], Vargas et al (2002)[2], present study[3], Moreira et al (2009)[4], Lima et al (2005)[5].

DISCUSSÃO GERAL

A Fundação Centro de Controle de Oncologia (FCECON) realiza o atendimento dos pacientes com neoplasias malignas e, em muitos casos, de neoplasias benignas. Localizada na cidade de Manaus, é o único hospital dedicado ao tratamento de pacientes com câncer no Estado do Amazonas, tornando-se uma referência na região Norte. Outro hospital que realiza atendimento aos pacientes oncológicos é o Hospital Ophyr Loyola em Belém – PA e o Hospital Regional de Santarém que desde 2008 vem realizando tratamento quimio e radioterápico.

Similar a este estudo, Parkins et al. (2008) achou um maior número de neoplasias malignas quando comparado as neoplasias benignas. Os autores relataram que as neoplasias benignas eram mais comuns aos pacientes mais jovens e as neoplasias malignas aos pacientes mais velhos. Quando avaliamos a media de idade deste estudo para neoplasias malignas (52,6 anos de idade) e para as neoplasias benignas (36,5 anos de idade) deste estudo, constatamos a mesma distribuição.

As barreiras geográficas da maioria das cidades do interior do Amazonas fazem com que o acesso a determinadas cidades sejam apenas por via fluvial. Esse fato resulta em um difícil acesso a algumas cidades cuja viagem pode demorar mais de 15 dias. Outro agravante encontrado é que na época da vazante muitas cidades ficam isoladas, sem meio de transporte e consequentemente sem possibilidade de locomoção a outras cidades. Muitas comunidades e cidades menores dependem das cidades maiores para o primeiro atendimento na área de saúde, onde existe a carência de profissionais da área da saúde.

O Amazonas é conhecido ainda, por ter na sua população algumas etnias indígenas, esses também são atendidos no FCECON, no entanto dependendo da etnia, muitos se recusam ao tratamento, pois quando o mesmo causa mutilação, os mesmos não são aceitos de volta na sua aldeia. Os índios que não podem colaborar com a aldeia são abandonados por ela.

A prevenção através do exame da cavidade bucal é tradicionalmente preferido no diagnóstico de lesões por não ser uma técnica invasiva e ser de fácil execução. Segundo Steele e Meyers (2011), o uso do exame bucal como programa de detecção de lesões em estágio precoce é controverso, pois os mesmos afirmam que há evidências insuficientes que suportem ou refutem, como mostra o estudo de Sankaranarayanan et al. (2005). No entanto, esse mesmo estudo mostrou uma melhora na sobrevida dos pacientes diagnosticados com câncer bucal.

CONCLUSÕES

As adversidades encontradas no Estado do Amazonas levam ao atraso do diagnóstico de muitas doenças e lesões, fazendo com que haja o diagnóstico tardio. Além disso, o acompanhamento desses pacientes após a alta hospitalar é sempre prejudicada pela distância, pois muitos não retornam. As lesões malignas foram mais incidentes nesse estudo e dentre elas o carcinoma de células escamosas, onde muitos pacientes já tinham dois ou mais sítios anatômicos envolvidos e a maioria desses pacientes eram do interior do Amazonas ou de outros Estados, isso nos leva a acreditar que houve o atraso no diagnóstico da lesão, por carência de profissionais ou pela dificuldade de diagnóstico devido as barreiras geográficas.

A alta prevalência encontrada de câncer bucal, a despeito dos baixos índices de tabagismo e etilismo, mostra que é necessário que as autoridades competentes iniciem campanhas de prevenção para a população em geral e viabilize o atendimento de saúde nas áreas menos favorecidas do Estado.

Quando os tumores de glândula salivares foram analisados, o adenoma pleomórfico apresentou maior preval ência. Existem na literatura relatos do seu potencial de transformação maligna. Sendo assim, se faz necessário uma conscientização dos profissionais da área de saúde do Estado do Amazonas para que possa ser diagnosticado e tratado precocemente.

Alguns prontuários não traziam o laudo histopatológico, apenas a anotação do profissional da área de saúde. Por serem realizados em outra instituição, não puderam ser confirmados. A falta de dados em muitos prontuários pesquisados reflete a falta de conhecimento da importância desse por parte dos profissionais da área de saúde no Amazonas, isso levou a exclusão de muitos prontuários, que poderiam ter contribuído com esse estudo. Como melhoria reuniões frequentes com orientações e a melhoria da ficha de anamnese do prontuário deveria ser estudada.

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Anexo 1

METODOLOGIA GERAL

Foi realizado um estudo retrospectivo com prontuários dos pacientes atendidos nos serviços de Cabeça e Pescoço e de Odontologia da Fundação Centro de Controle de Oncologia do Estado do Amazonas (FCECON) de janeiro de 1998 a dezembro de 2009.

Para determinar o objeto do estudo, foram estabelecidos os seguintes critérios: de inclusão deveria haver a presença de lesão bucal; e o de exclusão foram o preenchimento incorreto do prontuário e/ou a incapacidade de verificar o diagnóstico do exame histopatológico.

O projeto inicial foi aprovado pelo Comitê de Ética e Pesquisa (CEP) da Universidade do Estado do Amazonas (UEA) sob o protocolo de número 143/09 (Anexo 2). Os dados foram coletados num formulário (Anexo 3) previamente estabelecido visando gênero, idade, local de nascimento, município de residência, raça, hábitos, localização da lesão, diagnóstico histopatológico e tratamento.

Todos os procedimentos estatísticos foram realizados no programa Statistica versão 5.1 (StatSoft Inc., Tulsa, USA). Os dados qualitativos foram descritos por meio de frequência absoluta (n) e relativa (%). A variável idade foi descrita pela média.

Para comparação entre os grupos, quando o "n" era menor que 20, ou quando o valor ficava entre 20 e 40 e a casela com a menor freqüência esperada tinha valor menor ou igual a 5, utilizou-se o Teste Exato de Fisher. Nas outras situações utilizou-se o teste do qui-quadrado. Em todos os testes adotou-se nível de significância de 5% ($p<0,05$).

Anexo 2

UEA
UNIVERSIDADE
DO ESTADO DO
AMAZONAS

GOVERNO DO ESTADO DO
AMAZONAS

UNIVERSIDADE DO ESTADO DO AMAZONAS
ESCOLA SUPERIOR DE CIÊNCIAS DA SAÚDE
COMITÊ DE ÉTICA EM PESQUISA

IDENTIFICAÇÃO
Proc. Nº. 143/09-CEP/UEA – Projeto de Pesquisa **"Estudo Epidemiológico das lesões bucais diagnosticadas na Fundação Centro e Controle de Oncologia do estado do Amazonas (FCECON)".**
Interessado (a): – MSc. Lia Mizobe Ono.
Data de apreciação – 25/09/2009.

D E C I S Ã O

Nesta data, o Comitê de Ética em Pesquisa (CEP) da Escola Superior de Ciências da Saúde da Universidade do Estado do Amazonas, acatando voto do(a) eminente relator(a), **APROVOU** o processo supra identificado, com base no caput do item VII, na alínea a do sub-ítem VII.13 e na alínea a do sub-ítem IX.2 da Resolução CNS 196/96, ficando, portanto, autorizado o início da pesquisa proposta.

Plenário do Comitê de Ética em Pesquisa da Escola Superior de Ciências da Saúde da Universidade do Estado do Amazonas, em Manaus, 25 de setembro de 2009.

Profª. Drª. Ivete de Araújo Roland
Coordenadora

Anexo 3

FICHA DE COLETA DA DADOS

NOME:			
DATA DO 1o ATENDIMENTO:____/____/_____ RH:			
IDENTIFICAÇÃO:			
Endereço			
Bairro:	CEP:	Cidade:	UF:
Tel:	Rec:	Naturalidade(cidade):	
Data de nascimento: ____/____/_____		Profissão:	
Cor: Branca Negra Indígena	Gênero: ( )M ( )F		
HISTÓRIA MÉDICA:			
Vícios: Fumo Ácool Droga NãoEV Droga EV			
Frequência:			
EXAME FÍSICO INTRABUCAL:			
Localização da lesão:			
DIAGNÓSTICO HISTOPATOLÓGICO:			
TRATAMENTO:			

Anexo 4
(Appendix 1)

Table 5 - Distribution of patients treated at FCECON by non-neoplastic proliferative lesions and gingival pathology and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Pyogenic granuloma	7	53.8	18	46.2	0.752 ns	25	48.1	34.2
Focal fibrous hyperplasia	6	46.2	18	46.2	1.000 ns	24	46.2	44.4
Peripheral ossifying fibroma	0	0.0	2	5.1	1.000 ns	2	3.8	60.0
Gingival hyperplasia	0	0.0	1	2.6	1.000 ns	1	1.9	28.0
TOTAL	13	100.0	39	100.0		52	100.0	41.6

ns – no statistically significant difference between the gender

Anexo 5
(Appendix 2)

Table 6 - Distribution of patients treated at FCECON by salivary gland pathology excluding neoplasia and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Sialadenitis	5	33.3	3	25.0	0.696 ns	8	29.6	37.1
Ranula	3	20.0	2	16.7	1.000 ns	5	18.5	17.8
Mucocele	2	13.3	2	16.7	1.000 ns	4	14.8	15.5
Sialolithiasis	3	20.0	0	0.0	0.230 ns	3	11.1	51.3
Epidermal cyst	0	0.0	2	16.7	0.188 ns	2	7.4	30.0
Benign lymphoepithelial lesion	1	6.7	1	8.3	1.000 ns	2	7.4	43.5
Sjögren's syndrome	0	0.0	2	16.7	0.188 ns	2	7.4	47.5
Sialosis	1	6.7	0	0.0	1.000 ns	1	3.7	63.0
TOTAL	15	100.0	12	100.0		27	100.0	38.2

ns – no statistically significant difference between the gender

Anexo 6
(Appendix 3)

Table 7 - Distribution of patients treated at FCECON Bone and connective tissue pathology and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Bone pathology								
Fibrous dysplasia	2	20.0	2	28.6	1.000 ns	4	23.5	23.5
Ossifying fibroma	4	40.0	3	42.9	1.000 ns	7	41.2	41.2
Osteomielytis	2	20.0	0	0.0	0.485 ns	2	11.8	11.8
Central giant cell granuloma	2	20.0	2	28.6	1.000 ns	4	23.5	23.5
Sub-total	10	100.0	7	100.0		17	100.0	100.0
Connective tissue pathology								
Haemangioma – capillary	1	50.0	4	57.1	1.000 ns	5	55.6	55.6
Haemangioma – cavernous	1	50.0	2	28.6	1.000 ns	3	33.3	33.3
Normal tissue	0	0.0	1	14.3	1.000 ns	1	11.1	11.1
Sub-total	2	100.0	7	100.0		9	100.0	100.0
TOTAL	12		14			26		

ns – no statistically significant difference between the gender

Anexo 7
(Appendix 4)

Table 8 - Distribution of patients treated at FCECON by odontogenic tumors and cysts and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Odontogenic tumor								
Ameloblastoma	3	37.5	4	50.0	1.000 ns	7	43.8	31.9
keratocistic odontogenic tumour	3	37.5	1	12.5	0.569 ns	4	25.0	38.8
Odontogenic myxoma	0	0.0	2	25.0	0.467 ns	2	12.5	62.0
Calcifying epithelial odontogenic tumour	1	12.5	0	0.0	1.000 ns	1	6.3	12.0
Adenomatoid odontogenic tumour	1	12.5	0	0.0	1.000 ns	1	6.3	35.0
Odontogenic fibroma	0	0.0	1	12.5	1.000 ns	1	6.3	19.0
Sub-total	8	100.0	8	100.0		16	100.0	33.1
Odontogenic cysts								
Dentigerous cyst	3	75.0	2	66.7	1.000 ns	5	71.4	25.2
Calcifying odontogenic cyst	0	0.0	1	33.3	0.428 ns	1	14.3	32.0
Odontogenic cyst – unclassified	1	25.0	0	0.0	1.000 ns	1	14.3	42.0
Sub-total	4	100.0	3	100.0		7	100.0	33.1
TOTAL	12		11			23		

ns – no statistically significant difference between the gender

Anexo 8
(Appendix 5)

Table 9 - Distribution of patients treated at FCECON by mucosal and skin pathology and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Leucoplakia	3	37.5	2	22.2	0.620 ns	5	29.4	59.6
Epithelial hyperplasia	1	12.5	3	33.3	0.576 ns	4	23.5	47.8
Melanocytic nevus	1	12.5	1	11.1	1.000 ns	2	11.8	28.0
Paracoccidiodomycosis	1	12.5	1	11.1	1.000 ns	2	11.8	50.0
Ectodermal dysplasia	0	0.0	1	11.1	1.000 ns	1	5.9	13.0
Epidermolysis bullosa	1	12.5	0	0.0	0.471 ns	1	5.9	6.0
Papillary hyperplasia	0	0.0	1	11.1	1.000 ns	1	5.9	71.0
Lichen planus	1	12.5	0	0.0	0.471 ns	1	5.9	64.0
TOTAL	8	100.0	9	100.0		17	100.0	42.4

ns – no statistically significant difference between the gender

Anexo 9
(Appendix 6)

Table 10 - Distribution of patients treated at FCECON for other diagnosed diseases by type and gender (1998-2009 period).

Diagnosis	M		F		p	M+F		
	n	%	n	%		n	%	mean age
Miscellaneous pathology								
Ectopic thyroid	1	33.3	0	0.0	-	1	33.3	8.0
Leishmaniasis	1	33.3	0	0.0	-	1	33.3	45.0
Chronic lymphadenitis	1	33.3	0	0.0	-	1	33.3	19.0
Sub-total	3	100.0	0	0.0		3	100.0	
Non-odontogenic cyst								
Lymphoepithelial cyst	0	0.0	1	100.0	-	1	100.0	34.0
TOTAL	3		1			4		

ns – no statistically significant difference between the gender

Anexo 10

Table 11 - Histological classification and site of pathologies.

PATHOLOGY	Tongue	Parotid	Floor of the mouth	Sub-mandibular	Palate	Buccal mucosa	Lips	Gengiva	Retromolar trigone area	Vestibule	Two or more sites	Other mouth	Mandible	Maxilla	TOTAL
Squamous cell carcinoma	68		29	1	30	9	13	10	1		45	10			216
Acinic cell carcinoma		1	1												2
Mucoepidermoid carcinoma		4	1		3				1		2				11
Adenoid cystic carcinoma	2	2	4	2	3	2									15
Adenocarcinoma											2				2
Carcinoma in pleomorphic adenoma		2			2										4
Malignant lymphomas	1	2									1				3
Myoepithelial carcinoma		1													1
Non-Hodgkin's lymphoma				1							1				2
Melanoma					2	1					1				4
Metastatic carcinoma									1						1
Carcinoma - Undifferentiated		2		1											3
Plasmocytoma													2		2
Rhabdomyosarcoma											2				2
Angiosarcoma		1													1
Langerhans cell histiocytosis											2				2
Malignant disease - undifferentiated													1		1
Osteosarcoma														1	1
Sarcoma											1				1
Carcinoma in situ			1												1
Myoepithelial carcinoma		1													1
Pleomorfic adenoma	1	36		9	2		1								49
Myoepithelioma		2													2
Basal cell adenoma		2													2
Warthin tumor		3		1											4
Focal fibrous hyperplasia	2					7	5	1							15
Squamous papillomas	3				1			7							11
Lymphangioma	1		1	1							1				4
Fibrous histiocytoma		1					1								2

PATHOLOGY	Tongue	Parotid	Floor of the mouth	Sub-mandibular	Palate	Buccal mucosa	Lips	Gengiva	Retromolar trigone area	Vestibule	Two or more sites	Other mouth	Mandible	Maxilla	TOTAL
Haemangiopericytoma											1				1
Meningioma														1	1
Neurofibroma			1												1
Melanotic neuroectodermal tumor of infancy											1				1
Pyogenic granuloma	5				2	3	2	7	1						20
Fibrous epulis	1		1		3	1	1	15		3					25
Peripheral ossifying fibroma													1		1
Gingival hyperplasia								1							1
Sialadenitis		1		6											7
Mucocele and ranula			5		1		3								9
Sialolithiasis			1												1
Epidermal cyst		1													1
Benign lymphoepitelial lesion		1		2											3
Sjögren syndrome				2											2
Sialosis				1									3		4
Fibrous displasia													1	3	4
Ossifying fibroma													4	3	7
Osteomielytis													2		2
Central giant cell granuloma													3	1	4
Haemangioma - capillary	2						2	1							5
Haemangioma - cavernous	3														3
Normal tissue												1			1
Ameloblastoma													6	1	7
Keratocistic odontogenic tumour													3	1	4
Odontogenic myxoma													1	1	2
Calcifying epithelial odontogenic tumour														1	1
Adenomatoid odontogenic tumour														1	1

PATHOLOGY	Tongue	Parotid	Floor of the mouth	Sub-mandibular	Palate	Buccal mucosa	Lips	Gengiva	Retromolar trigone area	Vestibule	Two or more sites	Other mouth	Mandible	Maxilla	TOTAL
Calcifying odontogenic cyst													4	1	5
Dentigerous cyst													1		1
Odontogenic cyst - unclassified														1	1
Ectodermal dysplasia												1			1
Epidermolysis bullosa							1								1
Leucoplakia						2	1	2							5
Melanocytic nevus					1			1							2
Paracoccidiodomycosis				1			1								2
Epithelial hyperplasia						1	1	2							4
Papillary hyperplasia	1														1
Lichen planus						1									1
Ectopic thyroid	1														1
Leishmaniasis														1	1
Chroinic lymphadenitis				1											1
Lymphoepithelial cyst		1													1
TOTAL	91	65	46	30	50	27	32	48	4	3	61	12	32	18	518