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Clinical and Epidemiological Aspects of Head and Neck Cancer Patients in a Brazilian North-Eastern Oncology Hospital: A Retrospective Study

Aspectos clínicos e epidemiológicos de pacientes com câncer de cabeça e pescoço em um hospital oncológico do Nordeste brasileiro: um estudo retrospectivo

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Carolina Raiane Leite Dourado Maranhão Diaz
ORCID: https://orcid.org/0000-0002-8308-8954
Universidade CEUMA, Brasil
E-mail: rai.011@hotmail.com
Camila Dayla Melo Oliveira
ORCID: https://orcid.org/0000-0001-5938-1766
Universidade CEUMA, Brasil
E-mail: camiladayla@yahoo.com.br
Laís Inês Silva Cardoso
ORCID: https://orcid.org/0000-0002-6478-5439
Universidade CEUMA, Brasil
E-mail: laisinescardoso@gmail.com
Thalisson Lima Silva
ORCID: https://orcid.org/0000-0001-8004-6313
Universidade CEUMA, Brasil
E-mail: thalissonlimasilva@hotmail.com
Antônio Victor Nascimento de Sousa
ORCID: https://orcid.org/0009-0002-1151-7120
Universidade CEUMA, Brasil
E-mail: vitorpqqq123@gmail.com
José Carlos Watanabe Neto
ORCID: https://orcid.org/0009-0000-9124-231X
Universidade CEUMA, Brasil
E-mail: watanabe.21neto@gmail.com
Ingrid Araújo Oliveira Consolaro
ORCID: https://orcid.org/0000-0002-4663-6405
Universidade de São Paulo, Brasil
E-mail: ingrid_ctbmf@yahoo.com.br
Erika Martins Pereira
ORCID: https://orcid.org/0000-0002-2247-0017
Universidade Federal do Maranhão, Brasil
E-mail: erika.mp@ufma.br
Cyrene Piazera Silva Costa
ORCID: https://orcid.org/0000-0002-9632-8304
Universidade CEUMA, Brasil
E-mail: cyrenepiazera@hotmail.com
Thalita Santana
ORCID: https://orcid.org/0000-0002-2172-9031
Universidade CEUMA, Brasil
E-mail: thalita005294@ceuma.com.br

ABSTRACT

The purpose of this study is to describe the head and neck cancer patients who are receiving treatment at an oncology facility in a state in northeastern Brazil. Fisher's Exact test was used to analyze the data, which were taken from medical records, tabulated, and statistically analyzed to see whether the factors and the disease result (death or remission) were related. $P < 0.05$ values were regarded as statistically significant. 74.4% of the 86 medical records that were examined were male, 89% of them were over 40, and 38.4% of them involved smoking. The tongue was the most common anatomical site of cancer (36%). Surgery was the most often used treatment approach (44.2%). A poorer prognosis was linked to the existence of distant metastases ($p = 0.041$). Compared to individuals with cancer in the oral cavity and maxillary sinus, those with cancer in the nasopharynx, larynx, and oropharynx had a better prognosis ($p=0.002$). Men of mixed ethnicity, over 40, and mostly with tongue lesions made up the patient profile. The majority of patients had advanced clinical stages at diagnosis, and 47.7% of the sample perished.

Keywords: Head and Neck Neoplasms; Mouth Neoplasms; Squamous Cell Carcinoma.

RESUMO

O objetivo deste estudo é descrever os pacientes com câncer de cabeça e pescoço em tratamento em um serviço oncológico de um estado do Nordeste do Brasil. Para análise dos dados foi utilizado o teste Exato de Fisher, que foram retirados dos prontuários, tabulados e analisados estatisticamente para verificar se os fatores e o resultado da doença (óbito ou remissão) estavam relacionados. Valores de $P < 0,05$ foram considerados estatisticamente significativos. Dos 86 prontuários examinados, 74,4% eram do sexo masculino, 89% deles tinham mais de 40 anos e 38,4% deles envolviam tabagismo. A língua foi o sítio anatômico mais comum de câncer (36%). A cirurgia foi a abordagem de tratamento mais utilizada (44,2%). Um pior prognóstico esteve associado à existência de metástases à distância ($p = 0,041$). Comparados aos indivíduos com câncer de cavidade oral e seio maxilar, aqueles com câncer de nasofaringe, laringe e orofaringe tiveram melhor prognóstico ($p=0,002$). Homens de etnia parda, acima de 40 anos e em sua maioria com lesões na língua compunham o perfil dos pacientes. A maioria dos pacientes apresentava estádio clínico avançado ao diagnóstico e 47,7% da amostra faleceu.

Palavras-chave: Câncer de Cabeça e Pescoço; Câncer de boca; Carcinoma de Células Escamosas.

INTRODUÇÃO

Cancer is an important public health problem worldwide, resulting in one of the main causes of death and, consequently, one of the main barriers to increasing life expectancy worldwide. One in five individuals will have cancer during their lifetime (SUNG *et al*, 2021; FERLAY *et al*, 2020). The third most common cancer in countries with low or medium Human Development Index (HDI) is head and neck[1]. The estimated number of new cases of cancer in the oral cavity in Brazil, for each year from 2023 to 2025, is 15,100 cases, 10,900 in men and 4,200 in women. Oral cavity cancer ranks eighth among the most common types of cancer in our country (MINISTÉRIO DA SAÚDE INSTITUTO NACIONAL DO CÂNCER, 2023).

Head and neck cancer is a collective term defined on the anatomical topographical basis, including malignant tumours of the upper digestive air tract, such as the oral cavity, pharynx, and larynx. It can originate anywhere in the upper airway, developing from the oral cavity (tongue, floor of the mouth, gums, oral mucosa, retromolar area and hard palate), oropharynx (tonsils, base of the tongue, soft palate, uvula), larynx, hypopharynx, up to the upper oesophagus (FERLAY *et al*, 2020; MINISTÉRIO DA SAÚDE INSTITUTO NACIONAL DO CÂNCER, 2023).

The main risk factors for head and neck cancer are smoking and excessive alcohol consumption, which increases in individuals who use tobacco and drink alcoholic beverages simultaneously due to the synergism between these substances (MINISTÉRIO DA SAÚDE INSTITUTO NACIONAL DO CÂNCER, 2023; CONWAY *et al*, 2018). Obesity and low consumption of fruits and vegetables are associated with an increased risk of mouth and pharyngeal cancer (CLINTON *et al*, 2020). Prolonged unprotected sun exposure is the risk factor for lip cancer (WORLD HEALTH ORGANIZATION: REGIONAL OFFICE FOR EUROPE, 2020). Human papillomavirus (HPV) infection is a recognized risk factor for the development of oropharyngeal cancer. Oropharyngeal cancer associated with HPV is often diagnosed in younger individuals, non-smokers, and non-alcohol users. Furthermore, studies have suggested that patients with HPV-related oropharyngeal cancer have a better prognosis compared to cases unrelated to the virus (MEHANNA *et al*, 2023).

About 90% of all head and neck cancers are squamous cell carcinomas. According to GLOBOCAN 2020, a global cancer estimates, around 830,000 new cases of head and neck squamous cell carcinoma were recorded worldwide in 2020. These numbers include

cancers from different locations, such as the oral cavity, oropharynx, larynx, and other regions of the head and neck (SUNG *et al*, 2021; MORAIS *et al*, 2017)

To aid the classification and clinical staging of cancer, the American Committee on Cancer developed the TNM staging system based on the size of the primary tumour (T), quantification of lymph node metastases according to size, number, and distribution (N), and the presence of distant metastases (M). The TNM system is a clinical tool that helps choose treatment and reliably predicts the patient's prognosis, however, it has the limitation of not providing biological information regarding malignant cellular components (O'SULLIVAN *et al*, 2017).

The prognosis of patients with head and neck cancer is significantly related to the presence of a metastatic cervical lymph node. The lymphatic condition seems to be a determinant criterion of the patient's clinical evolution (MORO *et al*, 2018). For Ahmed and collaborators in a 2019 study, when the tumour depth exceeds 5 mm there is an increase in metastasis (approximately 64.7%) when compared to a tumour depth of less than 5 mm (approximately 5.9%). The authors assume that this occurs because the deeper connective tissue, the existence of lymphatic vases opens the way for cervical metastases (AHMED *et al*, 2019).

The advanced stage of the tumour is the main factor that negatively impacts the prognosis of SCC, as it requires aggressive, mutilating treatments and is generally associated with cervical metastasis (ILHAN *et al*, 2021). Five-year survival rates for oral and oropharyngeal carcinomas are approximately 50%, and most of these patients survive a short time after diagnosis. Most tumours are diagnosed late, compromising treatment, prognosis, and patient survival (MARTINEZ *et al*, 2016).

Data on head and neck cancer are important for the public health network in Brazil. This information allows for monitoring the incidence, mortality, and trends of these types of cancer, helping to formulate policies for prevention, early detection, and appropriate treatment. Based on epidemiological data, it is possible to identify groups at higher risk, such as geographic regions with high incidence, vulnerable populations, and specific risk factors. This makes it possible to target health resources and strategies more efficiently, including awareness campaigns, screening programs, and improving diagnostic and treatment capacity in affected areas. Furthermore, data is also essential for evaluating the impact of implemented interventions and policies, as well as for guiding future research in the field of head and neck cancer (MAHL *et al*, 2022; SANTOS *et al*, 2022).

Therefore, the objective of this study was to characterize patients diagnosed with head and neck cancer treated at a reference hospital for oncology in the State of Maranhão and to evaluate the association between the variables analysed and the clinical outcome of the disease.

MATERIALS AND METHODS

Characterization of the study

A retrospective case-cohort of patients with head and neck cancer was used in this investigation. The study employed secondary data obtained from patients who had treatment at the Maranhão Tarquínio Lopes Filho Cancer Hospital from January 1, 2012, to December 31, 2018. For cohort studies, the STROBE checklist was adhered to. The STROBE checklist for cohort studies was strictly followed to.

Ethical considerations

This research was submitted for analysis by the Research Ethics Committee of the CEUMA University, having been approved according to opinion no. 4,840,006. The sample comprised all cases of mouth and head and neck cancer that met the inclusion and exclusion criteria and had medical records accessible for the study, totalling 86 medical records analysed.

Eligibility Criteria

Inclusion criteria

Cases with histopathological diagnosis of squamous cell carcinoma, and located in the oral cavity, maxillary sinus, pharynx, nasopharynx, and oropharynx.

Exclusion criteria

Cases that did not have information about the histopathological diagnosis. Head and neck tumours of other origins (e.g., salivary gland tumours, thyroid tumours, or soft tissue sarcomas), as they present different clinical behaviour.

Data

Data were obtained from records in the medical records filled out by Social Services, admission and medical and nursing team evolution forms, and death certificates.

From the patients' records, sociodemographic information was obtained, including sex, age, skin colour, education, marital status, and place of residence, as well as information on lifestyle habits related to smoking and alcohol consumption and clinical information: location of the injury, type of treatment received, clinical staging, presence of lymphatic metastasis, distant metastasis, recurrence, and clinical outcome.

The outcome was assessed using data reported as the patient's last visit to the hospital. Based on these data, the cases were classified as remission (the patient was free of disease, without recurrences or metastases), disease in progression (when the patient was still undergoing oncological treatment in the hospital at the time of the last analysis) and death from cancer. This information was unavailable in some medical records due to patients abandoning treatment or changing hospitals.

Statistical analysis

The data were tabulated and subjected to statistical analysis. After the descriptive analysis, Fisher's Exact test was used to evaluate the association between the analysed variables and the outcome (death or remission). For comparative purposes, the cases were grouped according to their location in the oral cavity and maxillary sinus and oropharynx, nasopharynx, and larynx. This grouping was due to the proximity of locations. Values of $p < 0.05$ were considered statistically significant.

RESULTS

The sample for this research consisted of 86 cases of head and neck squamous cell carcinoma. Data regarding patient characteristics are listed in Table 1, and data regarding tumour characteristics are in Table 2. The patients' ages ranged from 22 to 91 years, with a mean of 61.6 and a standard deviation of 14.5 years. 55.8% (n=48) of these patients were over 60 years old. Of the cases studied, 74.4% were male patients, and most of the patients had brown skin colour (54.7%). More than half (51.16%) of the patients studied came from the state’s capital, São Luís.

Fifty-four (62.8%) patients were smokers, 33 (38.4%) were alcoholics, and 41.86% of these patients were alcoholics and smokers at the same time. The tongue was the anatomical site most affected by head and neck cancer (36%), followed by the larynx (23.3%) and the oropharynx (17.4%). Considering the treatment of choice, 44.2% of patients underwent surgery alone. Regarding metastasis, 27.9% of the patients in the study

presented lymphatic metastasis, and 15.1% presented distant metastasis. Analysing the cases of squamous cell carcinoma in the study, 52.3% of patients remained alive during the study period. Information regarding TNM staging was absent in most medical records (Table 3). In those who had such information, we noted that most tumours were T4, N0 and Mx.

Table 1- Patient characteristics: sociodemographic, habits and comorbidities

Variables	**N (%)**
Gender	
Feminine	22(25.6)
Masculine	64(74.4)
Age	
<40 years	8(9.3)
41-59 years	28(32.6)
60-74 years	33(38.4)
> 75 years	16(18.6)
Not obtained	1 (1.2)
Marital status	
Married	35(40.7)
Stable union	5(5.8)
Widower/widow	12(14)
Divorced	1(1.2)
Single	26(30.2)
Not obtained	7(8.1)
Skin colour	
White	13(15.1)
Brown	47(54.7)
Black	6(7)
Indigenous	2(2.3)
Not obtained	18(20.9)
Education level	
Illiterate	18(20.9)
Elementary school incomplete	6(7)
Elementary school complete and High school incomplete	23(26.7)
High school complete or University Education incomplete	14(16.3)
University Education	3(3.5)
Not obtained	22(25.6)

Alcoholism	
Yes	33(38.4)
No	17(19.8)
Not obtained	36(41.9)
Smoking	
Yes	54(62.8)
No	12(14)
Not obtained	20(23.3)
Diabetes	
Yes	7(8.1)
No	57(66.3)
Not obtained	22(25.6)
Arterial hypertension	
Yes	26(30.2)
No	42(48.8)
Not obtained	18(20.9)

Table 2- Tumour characteristics

Variables	**N (%)**
Anatomical location	
Tongue	31(36)
Palate	5(5.8)
Oropharynx	15(17.4)
Larynx	20(23.3)
Mouth floor	8(9.3)
Maxillary sinus	1(1.2)
Retromolar triangle	2(2.3)
Maxila	1(1.2)
Nasopharynx	3(3.5)
Treatment	
Surgery	38(44.2)
Surgery + Radiotherapy + Chemotherapy	19(22.1)
Surgery + Radiotherapy	2(2.3)
Surgery + Chemotherapy	14(16.3)
Radiotherapy + Chemotherapy	6(7)
Paliative	1(1.2)
Not obtained	6(7.0)
Lymph node metastasis	

Yes	24(27.9)
No	24(27.9)
Not obtained	38(44.2)
Distant metastasis	
Yes	13(15.1)
No	29(33.7)
Not obtained	44(51.2)
Disease status at last visit	
Remission	15(17.4)
Progression (in treatment)	17(19.8)
Death from cancer	41(44.7)
Not obtainet	13(15.1)
Outcome	
Live	45(52.3)
Dead	41(47.7)

Table 3- TNM Staging

Variables	**N (%)**
T	
T1	2(2.3)
T2	4(4.7)
T3	8(9.3)
T4	10(11.6)
Not obtained	62(72.1)
N	
N0	22(25.6)
N1	13(15.1)
N2	6(7)
N3	3(3.5)
Nx	1(1.2)
Not obtained	41(47.7)
M	
M0	7(8.1)
M1	2(2.3)
Mx	10(11.6)
Not obtained	67(77.9)

We observed that patients who died had more distant metastases than patients who had disease remission, and this association was statistically significant (p=0.041).

Furthermore, patients who had cancer in the nasopharynx, larynx and oropharynx had a better outcome when compared to patients who had cancer in the oral cavity and maxillary sinus (p=0.002). (Table 4)

Table 4 – Analysis of the association of variables with the outcome

Variables	Death (N)	Alive (N)	Total (N)	Value of P*
Sociodemographic characteristics				
Gender				0.87
Female	7	6	13	
Male	34	9	43	
Age				>0.99
<60 years	17	6	23	
> 60 years	24	9	33	
Marital status				0.17
Married	16	6	22	
Stable union	4	0	4	
Widower/widow	5	4	9	
Divorced	0	1	1	
Single	12	4	16	
Skin colour				>0.99
White	7	3	10	
Non-white	28	11	39	
Education level				>0.99
Iliterate or < 8 years of education	11	4	15	
> 8 years of education	21	6	28	
Life style				
Alcoholism				0.96
Yes	18	4	22	
No	5	5	10	
Smoking				0.65
Yes	26	9	35	
No	4	2	6	
Comorbidities				
Diabetes				0.39
Yes	3	3	6	
No	24	11	25	

Arterial hypertension				0.74
Yes	11	6	17	
No	20	8	28	
Tumour characteristics				
Anatomical location				
Oral cavity and e Maxillary sinus	12	13	25	**0.002***
Oropharynx, Larynx, Nasopharynx	3	28	31	
Treatment				0.77
Surgery	17	8	25	
Surgery + Adjuvant therapies	17	6	23	
Lympho node metastasis				0.39
Yes	8	2	10	
No	9	7	16	
Distant metastasis				**0.041***
Yes	8	2	10	
No	5	10	15	
T				0.13
T1 and T2	0	2	2	
T3 and T4	6	2		
N				0.66
N0	9	4	13	
N1, N2 and N3	8	2	8	
M				
M0	3	1	4	>0.99
Mx	2	1	3	

* Fisher's exact test. Values in bold indicate statistical significance.

DISCUSSION

In our research, we evaluated 86 medical records of patients with head and neck squamous cell carcinoma from a reference hospital in the State of Maranhão. Most of the sample were male patients, over 40 years of age and smokers. Alcohol and tobacco are well-established risk factors associated with head and neck cancer. Silva and collaborators in a 2020 study (SILVA *et al*, 2020), which sought to correlate alcohol and tobacco with mouth cancer, found a significant correlation between alcohol use and tumour size and the presence of nodules, as well as between alcohol use and smoking with tumour size and the presence of nodules. In our sample, 62.8% were smokers and 38.4% were alcoholics, confirming the description of other authors who correlate these habits with mouth cancer.

There is a consensus that the incidence of head and neck cancer increases with age, being less common in individuals under 40 years of age. That happens because older individuals are exposed to risk factors such as alcohol consumption, smoking, sun exposure and nutritional deficiency for a longer period compared to younger individuals (KOUKA *et al*, 2023). Therefore, the sample of this study had most patients aged between 41 and 74 years, and we observed that patients under 60 years of age survived longer than patients over 60 years of age, but this association was not statistically significant, possibly because in our sample age distribution was heterogeneous. Abrahão and collaborators, in 2020 research on survival predictors in patients with head and neck cancer with univariate analyses showed that older age, male gender, lower education, advanced stage at diagnosis, smoking and alcohol consumption were associated with rates of higher mortality (ABRAHAO *et al*, 2020).

According to many studies, including ours, males are the most affected by head and neck cancer. Our sample found that 64.4% of patients diagnosed with this type of neoplasm were male, females represented 25.6% of the sample. The magnitude of the male gender in the samples can be justified by the greater number of alcohol and cigarette users among men, associated with consumption of greater quantities. Furthermore, the association of alcohol and tobacco can make men more vulnerable to another risk factor, which is HPV infection. Therefore, the association of three risk factors can increase the incidence of head and neck cancer in males (OSAZUWA-PETERS *et al*, 2015; KHODE *et al*, 2014).

However, it is important to highlight that there is a wave of change in the incidence profile of mouth cancer, with an increase in females, which is believed to reflect changes in smoking and alcohol consumption habits and may be directly associated with HPV (KHODE *et al*, 2014). It is also necessary to consider that some researchers report that estrogen deficiency caused by menopause or hysterectomy may also contribute to the high rates of oral cancer reported among women (ZHANG *et al*, 2018)

As for systemic comorbidities being a relevant factor from the point of view of the patient's prognosis, most patients in our study were not diabetic (66.3%), or hypertensive (48.8%), however, the association between these comorbidities and the outcome of death and non-death was not statistically significant. This fact contrasts with the study by Boakye et al. (2019) which states that the presence of comorbidities is a dependent prognostic factor, as they can interfere with the diagnosis, severity, treatment

modality and response to treatment (ADJEI BOAKYE *et al*, 2019; ADJEI BOAKYE *et al*, 2020).

Regarding the anatomical location of the tumour, there was no statistically significant association with the outcome. In this sample, the most prevalent anatomical location was the tongue, like what was observed in other studies. Even though, worldwide, there is a surprising increase in tongue cancer in younger women, with no history of tobacco or alcohol consumption. In the US population, the rate of new cases of tongue cancer was 3.6 per 100,000 men and women per year, with the base years 2017-2021. The death rate was 0.7 per 100,000 men and women per year, with base years 2018-2022. According to the authors, approximately 0.4 per cent of men and women in the United States will be diagnosed with tongue cancer at some point in their lives (TRAMBY *et al*, 2020; NCI, 2020).

Distant metastases presented a statistically significant association with the outcome in this sample (p= 0.04), and most of the patients in this group died. This fact may be related to the fact that during staging, most of the tumours were classified as T4, in an advanced stage, and consequently more prone to distant metastases and a worse prognosis. For Gormley and collaborators (GORMLEY *et al*, 2022), stage IV is the most common stage in the diagnosis of oral and oropharyngeal cancer, while stage I is the most common for laryngeal cancer.

FINAL CONSIDERATIONS

This research is relevant for better identifying the profile of patients, and its results can be used to support the implementation of public policy programs for screening and raising awareness among the population about the risk factors of head and neck cancer, in addition to informing the signs and symptoms of the disease, and the importance of early diagnosis.

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