Characteristics and in-hospital morbidity trends associated with oral cavity cancer in Brazil

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Abstract

Objectives: To analyze epidemiological aspects, including temporal trends, of in-hospital morbidity from oral cavity cancer in Brazil.

Methods: Observational study based on information from the entire Brazilian territory, where data on hospital admissions for oral cancer were analyzed, obtained from the Information System of the Brazilian Cancer Registry. For the temporal series analysis, generalized linear regression model was used with the Prais-Winsten method.

Results: Of the 121,971 patients hospitalized with oral cavity cancer, 76.40% were male and 23.60% were female, resulting in a M:F ratio of 3.24:1. Regarding the anatomical region of involvement among hospitalized patients with oral cavity neoplastic lesions, there was a predominance in non-specific places in the mouth, such as the floor of the mouth, soft and hard palate, among others (32.68%), followed by lesions in the region of tongue (28.89%). In this population, the predominant age group was between the fifth (31.09%) and sixth decades of life (24.99%); men had oral cavity neoplastic lesions at an earlier age than women. In all regions of the country, the staging of cases diagnosed in the tertiary health network accredited to the José Alencar Gomes da Silva National Cancer Institute (INCA) was late, with an increased tendency for metastasis. The temporal trend of the adjusted in-hospital morbidity rates showed to be increasing in the Northeast, South and Midwest regions for the male gender. For females, they were increasing in the Northeast and South regions.

Conclusions: It is concluded that the distribution of in-hospital morbidity rates for oral cavity cancer in the country is irregular, with a predominance of male patients and higher in the Southeast and South regions, and there is a trend for this rate to increase in both genders.

Introduction

Neoplastic lesions primarily located in the lips, oral cavity, salivary glands and oropharynx are classified as oral cavity cancer, according to the José de Alencar National Cancer Institute (INCA, Instituto Nacional do Câncer)\(^1,\)\(^2\).

In Brazil, 11,180 new cases of oral cavity cancer in men and 4,100 in women are estimated for each year of the 2020-2022 triennium, being, respectively, the 5th and 13th most frequent cancer among all neoplasms\(^1\). Also, a notable increase in the incidence of this disease has been verified among younger people and women\(^3\).

Some risk factors are common for oral cavity cancer, such as the habits of smoking/chewing tobacco and drinking alcohol above the recommended levels, especially when they are associated\(^4,\)\(^5\). Other risk factors, such as the presence of human papillomavirus (HPV) infection and excessive exposure to the sun, are determinant for cancers of the oropharynx and mouth, respectively\(^6\).
In turn, an early diagnosis favors the implementation of usually less invasive and more effective treatments\textsuperscript{5}. Behaviors associated to primary prevention, early detection and adequate and timely treatment are associated, among other factors, to the organization and quality of the provided health services\textsuperscript{7,8}. In fact, the incorporation of the monitoring of morbidity and mortality from cancer in the health management routine is of utmost importance to implement actions aimed at preventing and controlling cancer and its risk factors\textsuperscript{9,10}.

Hence, Brazil has experienced an expansion of the population's access to oral health policies after the creation of the Unified Health System (SUS, Sistema Único de Saúde), with the consolidation of Primary Health Care (PHC) and the incorporation of dental care at the three levels of care through the National Oral Health Policy (PNSB, Política Nacional de Saúde Bucal) created in 2004\textsuperscript{10–12}.

The National Cancer Prevention and Control Policy establishes that cancer treatment in Brazil is carried out in qualified health establishments, which generate data from hospital cancer records in Brazil, called the Integrating Module of Hospital Cancer Records (RHC Integrator)\textsuperscript{13}.

Considering the scarcity of information, it was decided to study temporal series of in-hospital morbidity from oral cavity cancer, aiming at characterizing disease burden variations by Brazilian macroregion. The trend analysis for this indicator, during the assessed period, is unprecedented in Brazil. Therefore, the aim of this study was to analyze epidemiological aspects, including the temporal trend, of in-hospital morbidity from oral cavity cancer in Brazil, considering hospitalizations in an INCA-accredited health network.

**Method**

**Ethical aspects**

This study was exempted from the analysis by the Ethics Committee because it used data obtained from public and unrestricted access databases. This study is reported in accordance with the STROBE (Strengthening the reporting of observational studies in epidemiology) guidelines\textsuperscript{14}.

**Study design and context**

This is an observational study of temporal series, in which data on hospital admissions due to oral cavity cancer were analyzed, obtained from the Information System of the Cancer Hospital Registry (SisRHC, Sistema de Informação do Registro Hospitalar do Câncer) in Brazil\textsuperscript{13}.

The study covers data from the entire national territory, between the years 2000 and 2015. The database acquisition took place through the IRHC/INCA website (download of databases containing occurrences in all states, per year, from 2000 to 2015) and this was organized and tabulated using the MS Excel software.

All reported cases of hospitalization and classified during the first hospital visit as malignant neoplasms with primary location in the lips, oral cavity, salivary glands and oropharynx (ICD-10 codes C00-C10),
according to the INCA\textsuperscript{1} classification, were included in the study. Therefore, no sample calculation was performed.

**Analyzed variables**

Table 1 shows the variables analyzed in this study, their descriptions and the statistical treatment applied to each one.
Table 1
Variables, descriptions and statistical treatments shown in the database of the Information System of the Cancer Hospital Registry. Brazil, 2000-2015.

| Variables                        | Description and statistical treatment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| In-hospital morbidity rate       | Related to the number of hospital admissions for cancer of the oral cavity per 100,000 inhabitants in the studied period, per macroregion of Brazil. The data related to the Brazilian population necessary for the calculation were obtained from the SUS IT Department (DATASUS), which aggregates information from the Demographic Censuses, Intercess Projections and IBGE Population Estimates. The coefficients were later standardized by gender and age group (0 to 4; 5 to 9; 10 to 14; 15 to 19; 20 to 29; 30 to 39; 40 to 49; 50 to 59; 60 to 69; 70 to 79 years and 80 years and over), by the direct method, using as a standard the distribution of the world's population created by the World Health Organization for this purpose. The standardization aims to consider and remove the effect of factors related to the population distribution that interfere with the risk of developing the disease, allowing comparisons to be made. |
| Anatomical site                   | The codes were grouped by anatomical region for better data presentation. Thus, for this study, the lesions were presented as: “lip” – originally classified at the IRH/INCA as C00 (lip); “tongue” – originally C01 (base of the tongue) and C02 (other parts and unspecified parts of the tongue); “other parts of the mouth” – originally C03 (gingiva), C04 (floor of the mouth), C05 (palate) and C06 (other unspecified parts of the mouth: mucosa, vestibules, retromolar area); “salivary glands” – originally C07 (parotid gland) and C08 (other major salivary glands and unspecified major salivary glands); and “oropharynx” - originally C09 (palatine tonsil) and C10 (oropharynx) |
| Macropopulation                   | Variable organized according to the distribution of the Brazilian Institute of Geography and Statistics (IBGE, Instituto Brasileiro de Geografia e Estatística) as North, Northeast, Southeast, South and Midwest regions. This variable was identified based on the hospitalized patient's place of residence, as described in the notification form.                                                                                                                                                                                                                               |
| Gender                           | Variable categorized into female, male and no information.                                                                                                                                                                                                                                                                                                                                                                                                          |
| Ethnicity                         | Variable categorized as white, black, yellow, brown, indigenous or without information, according to the classification of the Brazilian Institute of Geography and Statistics (IBGE).                                                                                                                                                                                                                                                                                     |
| Level of schooling                | Variable categorized according to the presentation in the original database as none, incomplete elementary level, complete elementary level, high school level, higher education level or no information.                                                                                                                                                                                                                                                                               |
| Age range                         | Variable categorized as 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 years old, 80 years old and over and "no information", considering the sum of these age groups as the total number of cases. This classification was chosen for age group presentation, as the assessed pathology shows a relevant incidence from adulthood onwards. There was a disproportionate frequency of cases classified as 0 years old, which were considered "no information", indicating problems with registration in the database. |
### Variables and Statistical Treatment

| Variables                  | Description and statistical treatment                                                                 |
|----------------------------|--------------------------------------------------------------------------------------------------------|
| Alcohol consumption        | Variable categorized into: never consumed, ex-consumer, consumer and not evaluated.                     |
| Smoking status             | Variable recategorized according to the original database into: never smoked, ex-smoker, smoker and not evaluated (the latter also included - not applicable and no information). |

### Statistical Analysis

With the exception of the in-hospital morbidity rates, data were presented as relative frequency (percentage of cases). To analyze the trend of the in-hospital morbidity rates, generalized linear regression was used with the Prais-Winsten method, which allows first-order autocorrelation correction to be carried out in the analysis of series of values organized in time. This procedure allowed classifying the rates as increasing (p<0.05 and positive regression coefficient), decreasing (p<0.05 and negative regression coefficient) or stationary (p>0.05) and enabled the quantification of annual averages of increase or decrease of the coefficients (annual percent change - APC) and its 95% confidence interval (95% CI).\(^\text{18}\)

This technique was applied on the logarithm of rates. In the analysis of trend and annual variation, the coefficients were unstable in the first and last two years of the “2000 to 2015” series. Thus, it was decided to conduct the temporal trend analysis, excluding the years 2000, 2001, 2014 and 2015. Statistical analyzes were performed using the Stata\(^\text{®}\) software, version 14.0, and the graphs were prepared using the R\(^\text{®}\) software, version 3.5.0.

### Results

There were 121,971 hospitalizations for oral cavity cancer from 2000 to 2015 in Brazil. Of these cases, 76.40% were male, 31.09% were aged between 50 and 59 years, 32.23% were White and 36.58% had incomplete elementary education. Moreover, the neoplasms classified as occurring in other parts of the mouth at the time of the first consultation were the most frequent cause of hospitalization (32.68%) and tumors already diagnosed with metastasis were more frequent (13.61%) than tumors with less severe staging (0.52%).

Table 2 shows the distribution of hospital admissions by case (C00 to C10) according to the macroregion of the notifying city and by gender, anatomical site, ethnicity/skin color, level of schooling, age group, alcohol and tobacco consumption.
Table 2
Distribution of hospital admissions due to oral cavity cancer; percentage by anatomical site, gender, ethnicity/skin color, level of schooling, age group, alcohol and tobacco consumption, by macroregion. Brazil, 2000-2015.

| Variables                      | Macroregion (%) | Total Brazil |
|--------------------------------|-----------------|--------------|
|                                | North | Northeast | Southeast | South | Midwest | n   | %     |
| Anatomical site                |       |           |           |       |         |     |       |
| Lip                            | 3.83  | 6.29      | 6.81      | 8.32  | 3.95    | 8,315| 6.82  |
| Tongue                         | 27.04 | 28.49     | 29.44     | 27.73 | 31.24   | 35,240| 28.89 |
| Other parts of mouth           | 38.14 | 35.89     | 31.75     | 30.49 | 33.87   | 39,855| 32.68 |
| Oropharynx                     | 20.39 | 20.40     | 25.30     | 24.97 | 22.32   | 29,196| 23.94 |
| Gender                         |       |           |           |       |         |     |       |
| Male                           | 67.33 | 68.65     | 78.69     | 80.30 | 77.61   | 93,184| 76.40 |
| Female                         | 32.67 | 31.34     | 21.30     | 19.69 | 22.39   | 28,780| 23.60 |
| No information                 | 0.00  | 0.01      | 0.00      | 0.01  | 0.00    | 7    | 0.01  |
| Ethnicity/skin color           |       |           |           |       |         |     |       |
| White                          | 21.81 | 17.34     | 21.44     | 83.56 | 36.41   | 39,313| 32.23 |
| Black                          | 4.97  | 4.75      | 5.21      | 3.62  | 6.05    | 5,894 | 4.83  |
| Yellow                         | 0.70  | 1.09      | 0.23      | 0.40  | 0.91    | 590  | 0.48  |
| Brown                          | 55.21 | 67.54     | 16.82     | 4.65  | 41.74   | 33,677| 27.61 |
| Indigenous                     | 0.29  | 0.17      | 0.05      | 0.03  | 0.17    | 99   | 0.08  |
| No information                 | 17.02 | 9.10      | 56.24     | 7.74  | 14.72   | 42,393| 34.76 |
| Level of schooling             |       |           |           |       |         |     |       |
| None                           | 18.93 | 23.49     | 23.49     | 5.90  | 12.19   | 14,705| 12.06 |
| Incomplete Elementary          | 40.05 | 30.90     | 30.90     | 36.36 | 25.46   | 44,622| 36.58 |
| Complete Elementary            | 11.03 | 9.00      | 9.00      | 17.47 | 13.20   | 17,006| 13.94 |
| High School                    | 9.46  | 6.76      | 6.76      | 9.26  | 6.21    | 10,435| 8.56  |
| Higher Education               | 2.46  | 1.70      | 1.70      | 2.74  | 1.82    | 3,436 | 2.82  |
| No information                 | 18.03 | 28.12     | 28.12     | 28.26 | 41.10   | 31,767| 26.04 |
The highest mean in-hospital morbidity rate for men was identified in the Southeast region (9.36/100,000 inhab.), whereas, for women, it was identified in the Northeast region (2.29/100,000 inhab.). The trend of in-hospital morbidity rates was increasing in Brazil, for the entire population and by gender, as well as in the Northeast, South and Midwest regions.

Table 3 shows the standardized in-hospital morbidity rates due to oral cancer created to show an equitable distribution of hospital admissions for cases notified to INCA between the regions, considering the differences in population distribution.

**Table 3.** Adjusted in-hospital morbidity rates due to oral cavity cancer per 100,000 inhabitants, by macroregion, by gender. Brazil, 2000-2015.
Table 4 shows the trend of in-hospital morbidity rates for oral cancer, between 2002 and 2013, by macroregion and the total of Brazil, by gender and by overall distribution. The temporal trend of the adjusted in-hospital morbidity rates was increasing in the Northeast, South and Midwest regions for males, whereas, for females, it was increasing in the Northeast and South regions.
Table 4
Trend and annual variation (APC – annual percent change) of the adjusted in-hospital morbidity rates due to cancer of the oral cavity, by macroregion, gender and by overall distribution. Brazil, 2002-2013*.

| Variables       | APC (%) | CI (95%) | P-value | Trend  |
|-----------------|---------|----------|---------|--------|
|                 | Lower   | Upper    |         |        |
| Both genders    |         |          |         |        |
| North           | -0.18   | -1.42    | 1.07    | 0.75   | Stable |
| Northeast       | 5.67    | 3.90     | 7.47    | <0.001 | Increasing |
| Southeast       | 0.38    | -0.64    | 1.41    | 0.43   | Stable |
| South           | 6.97    | 1.83     | 12.37   | 0.01   | Increasing |
| Midwest         | 5.97    | 0.40     | 11.86   | 0.04   | Increasing |
| Total Brazil    | 2.62    | 1.20     | 4.06    | 0.00   | Increasing |
| Male gender     |         |          |         |        |
| North           | -0.08   | -1.38    | 1.23    | 0.89   | Stable |
| Northeast       | 6.22    | 4.36     | 8.12    | <0.001 | Increasing |
| Southeast       | 0.26    | -0.74    | 1.27    | 0.57   | Stable |
| South           | 7.03    | 1.50     | 12.86   | 0.02   | Increasing |
| Midwest         | 6.70    | 0.73     | 13.03   | 0.03   | Increasing |
| Total Brazil    | 2.60    | 1.14     | 4.07    | 0.00   | Increasing |
| Female gender   |         |          |         |        |
| North           | -0.30   | -2.55    | 2.00    | 0.77   | Stable |
| Northeast       | 4.34    | 2.74     | 5.96    | <0.001 | Increasing |
| Southeast       | 0.81    | -0.44    | 2.07    | 0.18   | Stable |
| South           | 7.26    | 3.90     | 10.74   | 0.00   | Increasing |
| Midwest         | 3.85    | -0.59    | 8.48    | 0.08   | Stable |
| Total Brazil    | 2.68    | 1.26     | 4.11    | 0.00   | Increasing |

* Note: As the rates were unstable in the first and last years of the “2000 to 2015” series, it was decided to carry out the trend analysis without the years 2000, 2001, 2014 and 201518.

Figure 1 depicts the 2002-2013 temporal series, showing the trend of the adjusted in-hospital morbidity rates from oral cancer in Brazil (total), by gender.
Discussion

This study identified that cases of hospital admissions due to oral and oropharyngeal cancer in Brazil, from 2000 to 2015, comprised mostly men, with a predominance of individuals aged 50-59 years, with low level of schooling, white and brown ethnicity, and with more advanced stage tumors, with metastasis already identified. In addition, the temporal trend of the in-hospital morbidity rates for oral cavity cancer in the period 2002-2013 showed to be increasing, both for males and females. The analysis of this information is unprecedented, considering the in-hospital morbidity of this disease in Brazil.

In all regions, the smoking and alcohol consumption factors were relevant to the development of the disease among hospitalized patients, as the consumption or ex-consumption of alcohol and tobacco was shown to be at higher amounts than those who declared they had never drunk alcoholic beverages or used tobacco products. Moreover, the observed increase in the consumption of alcohol-tobacco has been associated with the increase in the disease prevalence, especially in female patients.

In all regions, the cases diagnosed at advanced staging (with metastasis) at the time of the first hospital admission showed higher percentages than cases classified as initial staging/with localized involvement. Data from the INCA Hospital Cancer Records warn that, as most patients arrive at hospitals at an advanced stage of the disease, the treatment is no longer curative, being in most cases mutilating.

It was found that, for the entire Brazilian territory, the trend of in-hospital morbidity rates for oral cancer, between the years 2002 and 2013, was increasing, both for males and females. An increasing trend was also observed when analyzing both genders together. According to this finding, a study analyzing the granting of social security benefits in Brazil for cancer of the oral cavity (2006-2013) showed this trend was increasing. Social security benefits related to cancer involvement in other parts of the mouth, nasopharynx, oropharynx, floor of the mouth and palate showed the same increasing trend.

The growing trend in the evidenced overall picture of hospitalizations may be linked to the initial hypothesis of better case registration after the consolidation of the nationwide hospital integrated information system. As the analysis of these data is unprecedented in the literature, it was not possible to compare them with other studies on hospitalization trends due to oral cavity cancer. However, considering the results of studies that indicate a stability or decrease in mortality rates related to neoplastic conditions of the oral cavity in contrast to the growing trend of hospitalization observed in the present study, this investigation suggests better access to health services throughout the historical series.

Users of the public health system who previously did not have access to treatment may be able to have access to the hospital network and attempt to be cured. This reasoning would also be compatible with the results indicated with advanced staging, since, as this is a chronic disease, people would come to the health service network with a previously established case severity.

It is worth mentioning that the inclusion and expansion of the family health network close to Brazilian communities experienced during the analyzed historical period has shown the potential to reach the
population at risk for the development of oral cavity cancer\textsuperscript{26,27}. In this sense, a recent study shows that the inclusion of oral health teams is associated with early and timely detection of these diseases\textsuperscript{8}. Which, associated with the possibility of access to treatments in the hospital network, would result in lower mortality rates, while in-hospital morbidity is increasing\textsuperscript{28}. A recent study indicated the association between the number of oral health teams and the timely diagnosis of oral cavity cancer\textsuperscript{8}.

Therefore, it is reiterated that studies of epidemiological surveys for oral cancer diagnosis and surveillance are of utmost importance, allowing better management of public policies in the health area and data that support planning by health professionals, so that users have greater chances of treatment and cure\textsuperscript{29,30}.

As Brazil is a country with a large territorial extension and has many regional variations, both geographical and populational, the importance of developing research by state to assess the specific characteristics of its population is highlighted. Thus, this study met its purpose of identifying trends and characterizing epidemiological aspects related to morbidity from oral and oropharyngeal cancer in Brazil, showing data that had not been published before in the literature.

We point out some limitations of the present study, since by using public information systems, it was observed that some data were under-recorded (classified as not applicable or missing), which seems to correspond to the failure to complete the medical records at the time of hospitalization and also the migration of some databases from regional platforms to a national platform, particularly in the state of São Paulo, which has a single state database\textsuperscript{15}.

Nevertheless, it is considered that the data shown here constitute the best and most comprehensive information on oral cancer morbidity available in the Brazilian territory. In addition, these data are already consolidated and have a policy of information monitoring and checking at state and national levels to avoid duplication of information\textsuperscript{13}, giving them reliability and robustness.

Our results demonstrate that greater attention should be paid to the early detection and treatment of oral cancer, reinforcing that dedicated professional action is still required in the fight against the disease and educating the population about risk factors and signs and symptoms of oral cavity cancer. Also, it is necessary to expand cancer care, by involving the Primary Health Care level and high complexity centers.

We conclude that the distribution of in-hospital morbidity rates for oral cavity cancer in the country is irregular, with a predominance of the male gender and in the Southeast and South regions, and that there is a trend for this rate to increase in both genders.

**Declarations**

**Ethics approval and consent to participate**

All information is of public domain, with no identification of patients and for that reason, there was no need for project approval by the Ethics Committee for Research with human beings. The exemption was taken by the Ethics Committee in Human Beings of the Federal University of Mato Grosso do Sul
Consent for publication

Not applicable

Availability of data and materials

The datasets generated and analyzed during the current study are available in the Hospital Cancer Registry of the National Cancer Institute of Brazil (RHC-INCA, in Portuguese abbreviation) repository, available in https://irhc.inca.gov.br/RHCNet/visualizaTabNetExterno.action.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors have approved the final version of the manuscript. DGMV and ADDC conceived and designed the study. DGMV collected data wrote the manuscript. ARC performed the data analysis and assisted in the writing of the article. ADDC, LFP, EJZ, PZP and EPST interpreted the analysis, and revised the manuscript for important intellectual content.

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**Figures**
Figure 1

Trend of adjusted in-hospital morbidity rates from oral cancer, per 100,000 inhabitants, by gender. Brazil, 2002-2013*.

*Note: As the coefficients were unstable in the first and last years of the “2000 to 2015” series, it was decided to carry out the trend analysis without the years 2000, 2001, 2014 and 2015.