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ORIGINAL ARTICLE

Impact of the COVID-19 Pandemic on Delay in Treatment Initiation for Oral Cavity and Oropharyngeal Cancer in Brazil

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ABSTRACT

Objective: To analyze the impact of the COVID-19 pandemic on the interval between diagnosis and initiation of treatment for oral cavity and oropharyngeal cancer in Brazil. **Material and Methods:** A time series study was conducted using secondary data extracted from the DATASUS system. The three-year period from 2019 to 2021 was selected to represent the baseline, onset, and peak of reported COVID-19 cases. The dependent variable of the study was the delay in starting anticancer treatment (>60 days after histopathologic diagnosis). Time series were analyzed using joint-point regression and monthly percentage changes (MPC) were estimated. **Results:** For oral cavity cancer, there were two periods of decrease in the delay in treatment initiation, from January 2019 to June 2020 (MPC= -0.75, 95% CI = -0.3 to -3.2, p=0.004) and from November 2020 to December 2021 (MPC= -1.41, 95% CI = -2.2 to -0.6, p=0.001). For oropharyngeal cancer, there was an increase in the percentage of delays in treatment initiation from January 2019 to February 2020 (MPC= 0.86, 95% CI = 0.2 to 1.5, p=0.014) and from May 2020 to December 2020 (MPC= 3.66, 95% CI = 1.2 to 6.2, p=0.005), with a decrease from December 2020 to December 2021 (MPC= -1.40, 95% CI = -2.3 to -0.5, p=0.003). **Conclusion:** The COVID-19 pandemic in Brazil had a greater impact on treatment initiation delay for oropharyngeal cancer than for oral cavity cancer. However, the percentage of delay in treatment initiation for oropharyngeal cancer showed fluctuation, with an increase in the pre-pandemic period and a decrease after December 2020.

Keywords: Mouth Neoplasms; Oropharyngeal Neoplasms; COVID-19; Time-to-Treatment.

Introduction

Cancer is a major cause of death worldwide and a significant public health concern. Brazil has one of the highest incidence rates of oral and oropharyngeal cancer globally. According to estimates, there will be approximately 15,100 new cases of oral cavity and oropharyngeal cancer in Brazil each year from 2023 to 2025, which corresponds to around 6.99 new cases per 100,000 inhabitants. Of these cases, 10,900 will be in men and 4,200 in women [1].

Brazilian law mandates that cancer treatment must begin within 60 days of a confirmed malignant neoplasm [2]. However, compliance with this law has not yet been fully established in the country. According to the Oncology Panel data, in 2020, 50% of oral cavity and oropharynx cancer cases diagnosed in Brazil were treated after 60 days, with the South Region having the lowest percentage at 37% and the North Region having the highest at 55% [3]. Therefore, Brazil's public health system, at the municipal, state, and federal levels, must reorganize the care network to reduce this delay in starting treatment, increasing the patient's chance of cure and survival [4].

On January 30, 2020, the World Health Organization (WHO) declared a Public Health Emergency of International Concern due to the rapid spread of the new coronavirus (SARS-CoV-2), which is responsible for the COVID-19 pandemic [5]. The first confirmed case in Brazil was reported in February 2020. In the same month, Law no. 13,979/2020 was enacted [6], which provides measures to combat COVID-19 and underwent subsequent changes in March of the same year. Brazilian states and municipalities have implemented several measures to control the spread of the virus [7].

The adaptations required by the COVID-19 pandemic in terms of environmental biosafety and social distancing had a negative impact on the provision and organization of the health care network, including the availability of beds and health professionals for cancer diagnosis and treatment services [8-10]. Thus, the objective of this study was to analyze the impact of COVID-19 pandemic on treatment initiation delay for oral cavity and oropharyngeal cancers in Brazil, defined as a delay of more than 60 days after diagnosis. The time series covers the period from January 2019 to December 2021. This time frame allows an assessment of the situation before, at the beginning, and at the peak of confirmed COVID-19 cases in Brazil. This analysis included the year before the start of the COVID-19 outbreak to observe the temporal behavior of the variable of interest in a non-pandemic situation, thus improving the interpretation of the results of this study.

Material and Methods

Study Design

A time-series study was conducted using secondary data extracted from the Brazilian SUS Information Technology Department (*Departamento de Informática do Sistema Único de Saúde*, DATASUS). The data was collected from the digital platform called PAINEL-Oncology, which unifies data from three national information systems: the Outpatient Information System (*Sistema de Informação Ambulatorial*, SIA), the Hospital Information System (*Sistema de Informação Hospitalar*, SIH), and the Cancer Information System (*Sistema de Informações de Câncer*, SISCAN). The DATASUS platform was accessed to build the database used in this study.

Data Collection

Data was collected from patients diagnosed with oral cavity and oropharynx cancer between January 2019 and December 2021. The information was reported to the Ministry of Health through the State Health Departments. The study analyzed patients who were categorized into two groups based on their respective codes

from the tenth edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10): oral cavity cancer (ICD-10: C02, C03, C04, C05, and C06) and oropharyngeal cancer (ICD-10: C01, C09, and C10). The analysis excluded data from patients who did not have a record of the interval between diagnosis and the start of cancer treatment. The data was grouped temporally based on the month and year of the start of treatment during the three-year period from 2019 to 2021, which represents the onset and peak of COVID-19 cases worldwide.

The study analyzed the interval between the date of histopathological diagnosis and the date treatment began. The time between diagnosis and the start of treatment was classified into three categories: up to 30 days (early), 31 to 60 days (intermediate), and more than 60 days (late). The independent variables included the anatomical location of the lesion according to ICD-10, the month/year of the start of treatment, and the modality of the first treatment (surgery, chemotherapy, radiotherapy, and radiochemotherapy).

Statistical Analysis

Analysis was performed using GraphPad Prism version 9.1.1 (GraphPad Software Inc., San Diego, CA, USA) and Joinpoint Regression Program version 4.9.1 (National Cancer Institute, Bethesda, MD, USA). Descriptive statistics were calculated using absolute and relative frequency measures. The Joinpoint Regression Program evaluated trends over time based on significant changes in their patterns of evolution. Monthly Percentage Change (MPC) and 95% Confidence Interval (95% CI) were used to characterize trends over time on a logarithmic scale. Significance tests were performed using a Monte Carlo permutation method to identify the best-fitting joinpoints. The best-fitting points were joined as log-linear segments marking an increase or decrease in the percentage of treatment initiation delays (more than 60 days), providing a flexible and efficient method for detecting change over time series. A 5% significance level ($p<0.05$) was used for all analyses.

Results

This study analyzed data from 13,915 cases of oral cavity cancer and 17,232 cases of oropharyngeal cancer (Table 1). The data collection revealed that the percentage of cases with information on the time between diagnosis and treatment was higher in the oropharyngeal cancer group than in the oral cavity cancer group (85.3% *versus* 58.6%). During the analyzed period, the total number of oral cavity cancer cases peaked from July to November 2019. For the oropharynx group, the highest reported cases were in May and October 2019 (Figure 1).

Table 1. Frequency distribution of oral cavity and oropharyngeal cancers according to the interval between diagnosis and initiation of treatment.

Type of Cancer	Overall		Data on Interval between Diagnosis and Start of Treatment			
			Yes (Study Sample)		No Data	
	N	%	N	%	N	%
Oral Cavity	23,725	100.0	13,915	58.6	9,809	41.3
Oropharyngeal	20,205	100.0	17,232	85.3	3,068	14.7

Figure 2 illustrates the analysis of the time series of the percentage of delays in treatment initiation (interval greater than 60 days), which is the main objective of this study. The general analysis (Figures 2a and 2b) shows that the category greater than 60 days had the highest frequencies throughout the evaluated period (56.62% for oral cavity cancer and 57.98% for oropharyngeal cancer).

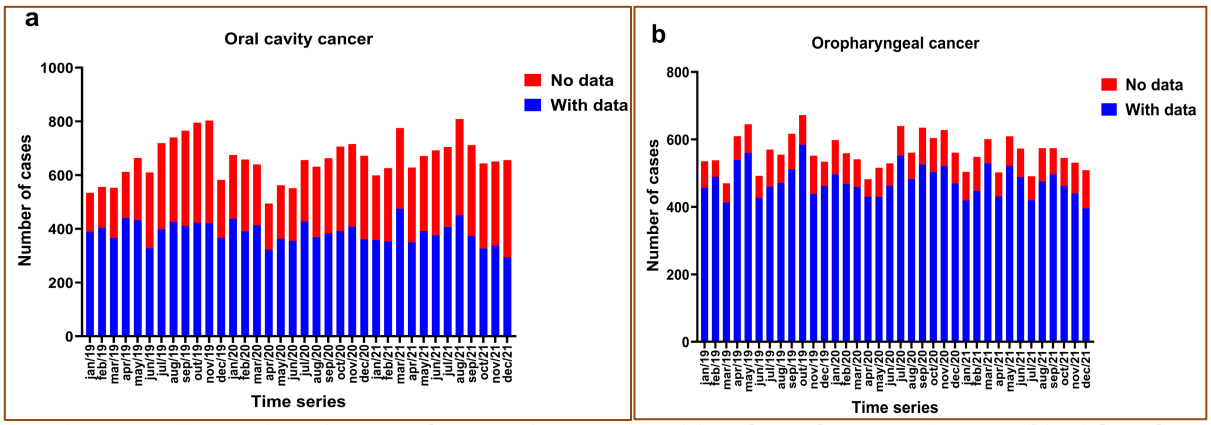
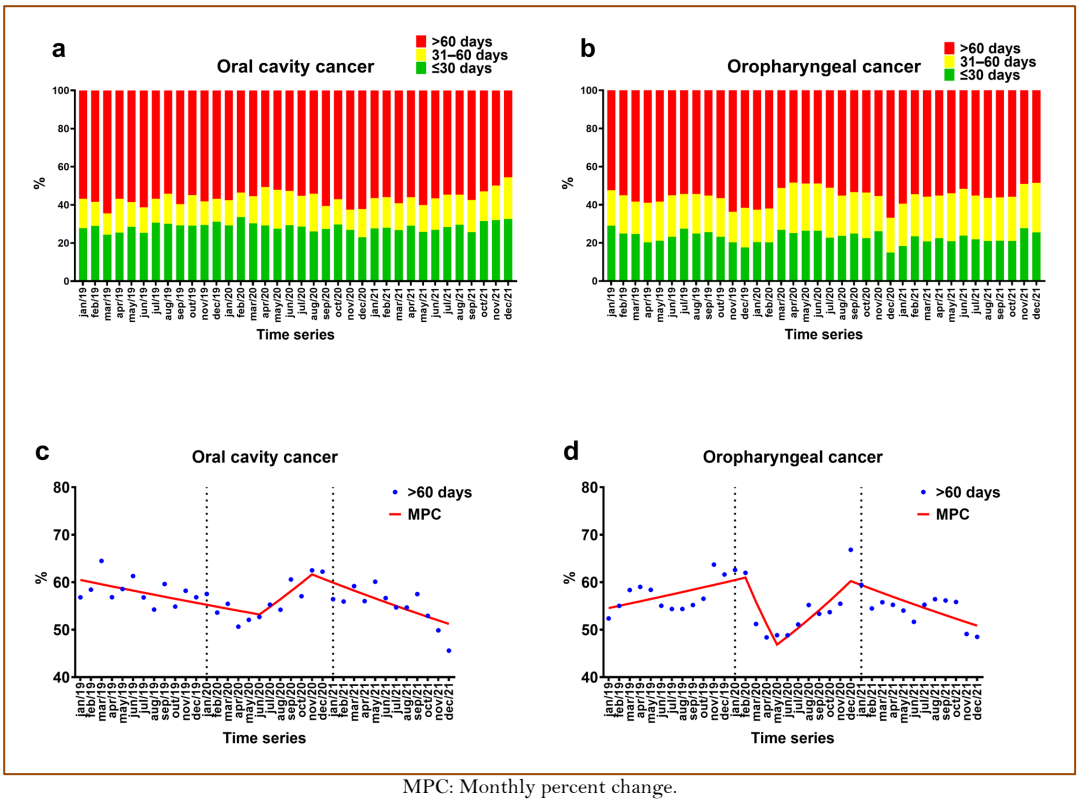


Figure 1. Time series of reported cases of oral cancer (a) and oropharyngeal cancer (b) with and without data on time from diagnosis to treatment initiation.

Figures 2c and 2d display the time series behavior of two types of cancer. Table 2 provides more detailed information, indicating two periods of reduction in cases of delay in starting treatment (>60 days) for oral cavity cancers. The first period was from January 2019 to June 2020 (MPC = -0.75, 95% CI = -1.2 to -0.3, p = 0.004), and the second period was from November 2020 to December 2021 (MPC = -1.41, 95% CI = -2.2 to -0.6, p < 0.001). There was an increase in cases of delays of more than 60 days for oropharyngeal cancers from January 2019 to February 2020 (MPC = 0.86, 95% CI = 0.2 to 1.5, p = 0.014) and from May 2020 to December 2020 (MPC = 3.66, 95% CI = 1.2 to 6.2, p = 0.005). However, there was a reduction at the end of the period evaluated, from December 2020 to December 2021 (MPC = -1.40, 95% CI = -2.3 to -0.5, p = 0.003).



MPC: Monthly percent change.

Figure 2. Time series of the distribution of oral cavity cancer (a) and oropharyngeal cancer (b) cases according to the categories of time interval for the start of treatment and regression model by joinpoints of the time series to identify the pattern of growth or reduction for the oral cavity cancer (c) and oropharyngeal cancer (d).

Table 2. Parameters of the regression for the time series analysis of the percentage of oral cavity and oropharyngeal cancer cases that started treatment more than 60 days apart.

Variables	Month		MPC	95% CI		t	p-value
	Start	End		Lower	Upper		
Oral Cavity							
Segment 1	Jan/19	Jun/20	-0.75	-1.2	-0.3	-3.2	0.004*
Segment 2	Jun/20	Nov/20	2.99	-1.3	7.5	1.4	0.169
Segment 3	Nov/20	Dec/21	-1.41	-2.2	-0.6	-3.7	0.001*
Oropharyngeal							
Segment 1	Jan/19	Feb/20	0.86	0.2	1.5	2.6	0.014*
Segment 2	Feb/20	May/20	-8.41	-22.0	7.5	1.1	0.265
Segment 3	May/20	Dec/20	3.66	1.2	6.2	3.1	0.005*
Segment 4	Dec/20	Dec/21	-1.40	-2.3	-0.5	-3.4	0.003*

MPC: Monthly Percent Change; 95% CI: 95% Confidence Interval; *Statistically Significant.

As shown in Figure 3, chemotherapy was the treatment of choice for 46.1% of oropharyngeal cancers during the study period. Radiotherapy was the most frequent treatment modality for oral cavity cancers, representing 39.6% of cases.

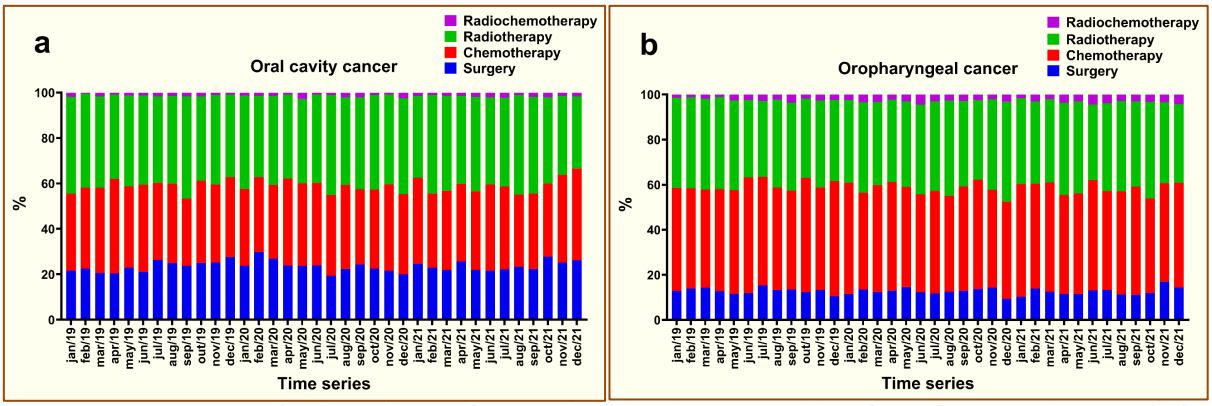


Figure 3. Distribution of treated cases of oral cavity cancer (a) and oropharyngeal cancer (b) by initial treatment modality in Brazil between 2019 and 2021.

Discussion

The main findings of this study suggest that the percentage of delay in starting treatment for oral cavity cancer was falling in Brazil, however, there was an increase in this delay, particularly for oropharynx cancer cases in the period from May to December 2020. Health service managers should consider these findings, as prolonging the interval between histopathologic diagnosis and initiation of treatment for oral cavity and oropharyngeal cancers may contribute to increased mortality [11] and recurrence of these diseases [12], promote tumor growth [13,14], decrease survival [15], and increase the likelihood of progression to more advanced stages of disease [16].

The incidence of oral and oropharyngeal cancers has tended to progress at a faster rate in countries with low or medium HDI [17]. In Brazil, a country in transition, most of the reported cases of these cancers are in advanced stages. This leads to a worse prognosis and minimizes the survival rate of these patients [18]. Findings from a study in Brazil suggest that the delay in diagnosis may be related to socioeconomic, demographic, and cultural indicators on the part of patients, a lack of knowledge on how to diagnose and refer patients on the part of professionals, and the obstacles of the health system itself related to the precariousness of services in terms of meeting the demands of patients [19]. In addition, these authors report that geographical barriers can hinder access for some users of the public health system in Brazil.

The peaks of the notifications of delays in treatment for the two groups of cancers analyzed indicate that the pandemic may have had an impact on the increase in the percentage of delays in starting treatment, especially in the period from May to December 2020, with a decrease again in 2021. These results reinforce that distancing and precautionary measures may have reduced consultations and procedures in outpatient and hospital settings in Brazil [5,20]. These data are also observed in a previous study that found a reduction in hospitalization rates for oral and oropharyngeal cancer in Brazil in 2020 and 2021 [21].

The delay in the initiation of treatment for oropharyngeal cancer from May to December 2020 can be explained by the impact of the overload of health services due to the COVID-19 pandemic. Studies conducted in Brazil have shown that the COVID-19 pandemic has reduced the population's access to treatment and prevention of several diseases [22-24]. Nationwide Brazilian studies showed a decrease in breast cancer screening and early diagnosis and its direct costs [25,26]. These authors also emphasize that the decrease in direct costs of mammography and breast biopsies during the COVID-19 pandemic was likely related to reduced demand rather than a decrease in the value of the test.

A German study has shown a longer treatment delay for surgically treated oral squamous cell carcinoma and that patients presented with more advanced disease in 2020 compared to data from 2010-2019. These findings may indicate that the COVID-19 pandemic may have caused both a reduction in demand for diagnostic services and a delay in treatment initiation [27]. In addition, a national database study in France has shown that there was a reduction in the number of cancer patients attending cancer centers was observed in the country from January to July 2020, this reduction was more pronounced for breast and prostate cancer, and for patients without metastases [28]. Data from the Public Health England National Cancer Registration Service have shown that delays in diagnosis and treatment during the COVID-19 pandemic may be associated with an increase in the burden of attributable cancer mortality [29].

In this sense, a study in Latin America and the Caribbean showed that approximately 67% of cancer patients experienced delays in treatment or medical care, while 15% were unable to receive any type of treatment during the COVID-19 pandemic [30]. Another study of children with cancer and COVID-19 in northeastern Brazil from April to July 2020 showed that 66.6% of them experienced delays in their cancer treatments, as well as an increased need for intensive care and a higher number of deaths [31].

The data from this study showed that the distribution pattern of treatment modality remained stable for oral cavity and oropharyngeal cancer cases in Brazil from 2019 to 2021. Chemotherapy was the most common modality for the initial treatment of oropharyngeal cancer, while radiotherapy was the most common initial treatment for oral cavity cancer. Chemotherapy, in addition to radiotherapy and surgery, is associated with improved overall survival in patients with oral cavity and oropharyngeal cancers [32]. Nevertheless, it is important to note that the COVID-19 pandemic may have affected the different types of therapeutic modalities. There is evidence that surgical capacity for cancer therapy has been reduced, as a large number of ventilators have been required to meet the growing demand for intensive care for COVID-19 patients [33]. In addition, therapeutic modalities such as chemotherapy may expose patients to a greater risk of infection and lead to worse outcomes if they develop COVID-19 [34]. Some studies have recommended the increased use of radiotherapy or chemoradiotherapy instead of surgery for certain cancer patient populations, such as head and neck cancer, to reduce COVID-19 transmission [35,36]. These authors have suggested that the surgical environment may be associated with an increased risk of contamination from aerosol-generating procedures.

This study has limitations inherent to the use of secondary data from the SUS information systems, from the Oncology Panel. Another limiting factor may be the possibility of underreporting. According to Borges

et al. [37], under-registration and under-reporting can still be observed in more remote regions of Brazil. The pandemic period may have worsened the projection of these data, due to the overload in the health departments, in a way that affected the entry of outpatient production in the systems that make up the Oncology Panel.

Despite these limitations, this study demonstrates the need to monitor the stages of oral cavity and oropharynx cancer care line through the SUS, in order to reduce delays in starting cancer treatments in Brazil. Thus, highlighting the need for attention on the part of public managers to the care inherent in patients with oral cavity and oropharynx cancer. Seeking to resume compliance with Law no. 12.732/2012 [2], which, incidentally, has always been at odds with the reality demonstrated by the records of the SUS Information System. Future studies are needed to identify possible factors associated with delays in cancer care. These findings could help managers and health workers develop strategies and policies to improve health network deficiencies.

Conclusion

The COVID-19 pandemic had a greater impact on treatment delays for oropharyngeal cancer than for oral cancer. However, the temporal behavior of the percentage of treatment initiation delay for oropharyngeal cancer showed fluctuation, with an increase in the pre-pandemic period and a decrease after December 2020. Furthermore, the reported data showed that from 2019 to 2021, more than half of the cases of oral and oropharyngeal cancer in Brazil started treatment more than 60 days after diagnosis. Thus, it can be seen that it is still very difficult to enforce Law No. 12.732/2012 in Brazil.

Authors' Contributions

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All authors declare that they contributed to critical review of intellectual content and approval of the final version to be published.

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Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

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