UNESP - Universidade Estadual Paulista
"Júlio de Mesquita Filho"
Faculdade de Odontologia de Araraquara

Emily Ricelly da Silva Oliveira

Avaliação dos impactos da pandemia de Covid-19 sobre o diagnóstico do câncer de cabeça e pescoço

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Orientador: Cleverton Roberto de Andrade

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Avaliação dos impactos da pandemia de Covid-19 sobre o diagnóstico do câncer de cabeça e pescoço

Comissão julgadora

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Dedico este trabalho a todos aqueles que vivem com câncer. Que estes registros contribuam para a construção do conhecimento, acerca da desassistência sofrida por estes pacientes, durante a pandemia de Covid-19.

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RESUMO

O câncer de cabeça e pescoço (CCP) é o sétimo tumor maligno mais frequente em humanos e, apesar dos recentes avanços no tratamento, como o uso de terapias-alvo específico, ainda apresentam grande morbidade e reduzidos níveis de sobrevida em estádios avançados. De outra parte, a pandemia de Covid-19 teve grandes impactos sociais e na dinâmica de oferecimento dos serviços de saúde. Analisamos os aspectos que pressionaram o processo diagnóstico e o impacto no estádio dos pacientes durante a pandemia Covid-19. Para tal, coletamos dados em um centro de diagnóstico (Laboratório de Anatomia Patológica da Universidade Federal do Rio Grande do Norte [LAP]) e um hospital de tratamentos de pacientes com CCP (Hospital do Câncer de Barretos [HCB]) em período pré-pandêmico e pandêmico. Nos estudos, estão incluídos os seguintes dados: data de admissão, características clínicas, diagnóstico histopatológico, idade e gênero, tempo entre admissão, diagnóstico e tratamento e classificação TNM. Os dados quantitativos foram analisados por meio de medidas de tendência central e variabilidade; as variáveis qualitativas foram descritas por meio de frequência relativa, expressa por percentual. Os testes estatísticos consideram nível de significância de 5% para todas as análises. Os resultados foram apresentados na forma de dois artigos científicos, o primeiro com dados provenientes do LAP, o segundo com dados do HCB. O LAP sofreu redução de 56,1% nos diagnósticos emitidos durante a pandemia, a maior redução foi verificada nos espécimes provenientes das clínicas odontológicas da UFRN (62,5%), mas o impacto também foi sofrido no setor privado com redução de 47%. O HCB também apresentou queda geral no número de casos admitidos, mas, os estádios iniciais (I/II) sofreram menos impacto durante este período, propiciando relativo aumento proporcional de 24.81% para 33.33%, em contraposição, estádios avançados (III/IV) sofreram redução proporcional de 75.18% para 66.66%. Outro impacto importante foi a redução do número de dias entre admissão e diagnostico, de 70.68 para 40.43 dias, e entre o diagnóstico e tratamento, de 117.48 para 89.27 dias. Nossos dados demonstraram maior impacto na universidade quando comparada aos serviços privados. Além disso, o HBC apresentou rápida adaptação às condições pandêmicas.

Palavras-chave: Neoplasias de cabeça e pescoço. Carcinoma de células escamosas. Neoplasias bucais. COVID-19.

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ABSTRACT

Head and neck cancer (HNC) is the seventh most common malignant tumor in humans and, despite recent advances in treatment, such as the use of specific target therapies, it still has high morbidity and reduced levels of survival in advanced stages. On the other hand, the Covid-19 pandemic had major social impacts and on the dynamics of offering health services. We analyzed the aspects that put pressure on the diagnostic process and the impact on the stage of patients during the Covid-19 pandemic. To this end, we collected data at a diagnostic center (Lab of Pathological Anathomy, Federal University of Rio Grande do Norte [LPA]) and a hospital for the treatment of patients with HNC (Barretos Cancer Hospital [BCH]) in the pre-treatment period. pandemic and pandemic. The studies include the following data: date of admission, clinical characteristics, histopathological diagnosis, age and gender, time between admission, diagnosis and treatment, and clinical and pathological TNM classification. Quantitative data were analyzed using measures of central tendency and variability; qualitative variables were described by means of relative frequency, expressed as a percentage. Statistical tests consider a significance level of 5% for all analyses. The results were presented in the form of two scientific articles, the first with data from the LPA, the second with data from the BCH. The LPA suffered a 56.1% reduction in diagnoses issued during the pandemic, the greatest reduction was seen in specimens from UFRN dental clinics (62.5%), but the impact was also suffered in the private sector with a 47% reduction. BCH also presented a general decrease in the number of admitted cases, but the initial stages (I/II) suffered less impact during this period, providing a relative proportional increase from 24.81% to 33.33%, in contrast, advanced stages (III/IV) suffered a general reduction and relative increase from 75.18% to 66.66%. Another important impact was the reduction in the number of days between admission and diagnosis, from 70.68 to 40.43 days, and between diagnosis and treatment, from 117.48 to 89.27 days. Our data showed a greater impact on the university when compared to private services. In addition, BCH showed rapid adaptation to pandemic conditions.

Keywords: Head and Neck Neoplasms. Carcinoma, squamous Cell. Mouth neoplasms. COVID-19.

SUMÁRIO

1 INTRODUÇÃO

As neoplasias malignas são doenças multifatoriais, que envolvem acúmulo de alterações mutagênicas ao longo do tempo. Essas alterações podem propiciar o surgimento de modificações morfológicas de caráter potencialmente maligno, precedendo o surgimento de lesões, ou levar ao desenvolvimento de tumores *de novo*[1].

Mundialmente, o câncer é a segunda causa de morte em países em desenvolvimento e a terceira em países desenvolvidos. Estima-se que, em 2030, 26 milhões de pessoas serão diagnosticadas com neoplasias malignas e cerca de 17 milhões irão a óbito, sendo, portanto, alvo de grande interesse de saúde no mundo[2,3].

Os cânceres de cabeça e pescoço (CCPs) são um grupo de tumores originários dos tecidos dessa região, incluindo a cavidade oral, orofaringe, nasofaringe e laringe. Ocupando a sétima posição dentre as neoplasias malignas mais frequentes em todo o mundo, estas lesões provocam mais de 325,000 mil óbitos todos os anos. Novos estudos têm proposto aumento na prevalência, mesmo com a redução do consumo de tabaco em países desenvolvidos. Segundo o Instituto Nacional do Câncer –INCA, CCPs foram a causa de 20.722 mortes no Brasil em 2019[4-6].

Em geral, CCPs afetam mais homens que mulheres (2/4 H/M), especialmente os localizados em cavidade oral e lábios. No Brasil, o INPE estimou 15.000 novos casos anuais de carcinomas orais no triênio 2020-2022[7,8].

Aproximadamente 90% dos CCPs são carcinomas espinocelulares (CECs), o restante envolve glândulas, ossos, tecido conjuntivo, vasos, nervos, tecido adiposo, linfático ou outras células sanguíneas, sendo devidamente nomeados de acordo com os critérios estabelecidos pelos *guidelines* da Organização Mundial de Saúde[2,9,10].

De outra parte, tumores semelhantes em origem celular, apresentam etiologias distintas de acordo com a sua localização. É o caso dos CECs da cavidade oral e de lábio. Tumores de lábios são associados a exposição à radiação ultravioleta, já os CECs de cavidade oral são, predominantemente, associados ao tabagismo e etilismo. Em ambos os casos há maior prevalência em homens com mais de sessenta anos de idade. Já na orofaringe, apresentam forte associação com a infecção pelos papilomavírus humanos (HPVs) de alto risco e, geralmente, os pacientes acometidos são mais jovens[10,11].

Quanto ao diagnóstico dos CCPs, o exame clínico, exames de imagem e citologia, auxiliados pela avaliação histológica da biópsia, permanecem como padrão-ouro. O protocolo de tratamento dos CCPs considera a localização, tamanho e gradação histológica, estado de

saúde do paciente, cooperação, condições nutricionais, envolvimento de linfonodos regionais, metástase à distância, dentre outros aspectos tumorais. As abordagens incluem cirurgia, radioterapia e quimioterapia combinadas ou não de acordo com o tipo histológico e estadiamento tumoral[12-17].

De fato, mesmo com as novas terapias ainda se observam significativa morbidade e reduzidas taxas de sobrevida. De fato, os tumores são, com frequência, diagnosticados em estádios avançados e a sobrevida geral em 5 anos permanece próxima dos 40%, contrastando de forma veemente com os índices de sobrevida de 80% nos pacientes diagnosticados nos estádios iniciais (I e II). Portanto, o estadiamento tumoral continua a impactar fortemente o prognóstico dos pacientes [18-23]. Além disso, a detecção tardia exige tratamento mais agressivos com maiores margens de ressecção e associação de diferentes abordagens de tratamento (cirurgia, radioterapia e/ou quimioterapia) com significativos efeitos adversos e consequente redução na qualidade de vida. Portanto, o diagnóstico precoce, associado a consequente estádio considerado inicial, propiciam os melhores prognósticos.

O acompanhamento dos pacientes de risco para o desenvolvimento de câncer de cabeça e pescoço e ações de escaneamento populacionais regulares são essenciais para o diagnóstico precoce, assim como ações educativas. Neste último caso, a população pode se tornar capaz de identificar sintomas relacionados aos CCP e se dirigir para locais especializados, que são capazes não só de realizar o diagnóstico, como também realizar o encaminhamento no menor tempo possível para os centros especializados no tratamento do CCP[24-26].

Em 2020, a pandemia de Covid-19 causou mudanças profundas na sociedade e nos sistemas de saúde de todo o mundo. Muitos países adotaram medidas de isolamento social que foram incorporadas pelas pessoas e pelos serviços de saúde, com o intuito de reduzir a circulação do vírus em ambientes hospitalares ou não. Foram adotados protocolos de estratificação de pacientes baseados no risco da doença, bem como da necessidade de intervenção cirúrgica, priorizando atendimentos de urgência ou emergência. No contexto brasileiro, alguns serviços permaneceram fechados por longos períodos. É o caso das faculdades de odontologia, verdadeiros centros de referência em diagnóstico de COs que, em condições de normalidade, são a principal forma de diagnóstico e encaminhamento dos pacientes com CCP[27-30].

Dados já publicados descreveram redução em intervenções eletivas e procedimentos diagnósticos rotineiros não-urgentes e urgentes. O Ministério da Saúde considera o impacto dessas mudanças sobre os portadores de doenças crônicas. As repercussões envolvem diagnósticos tardios, subnotificações, dificuldade de acesso a medicações e desassistência[27-30].

Diante do exposto, consideramos importante investigar o impacto da pandemia de Covid-19 na dinâmica diagnóstica das neoplasias, buscando identificar possíveis prejuízos, para que se possa minimizar seus impactos no prognóstico destes pacientes no futuro.

2 OBJETIVO

Analisar os dados clínicos e patológicos de CCP dos arquivos do Hospital do Câncer de Barretos (HCB), entre 2018 e 2020, e de carcinomas orais do arquivo do Laboratório de Anatomia Patológica (LAP), do Departamento de Odontologia da Universidade Federal do Rio Grande do Norte (DOD-UFRN), de 2010 a 2021. Os dados foram organizados em período "pré-pandemico" e "pandêmico" considerando a pandemia de Covid-19.

2.1 Objetivos Específicos

- Obter dados clínicopatológicos dos pacientes com diagnóstico de carcinoma oral entre os anos de 2010 e 2021;
- Obter dados clínicopatológicos de carcinomas de cabeça e pescoço dos arquivos do HCB entre e 2018 e 2020;
- Descrever dados clinicopatológicos das amostras obtidas;
- Comparar a média de diagnóstico observadas nos períodos "pré-pandemico" e "pandêmico";
- Verificar o estádio clínico diagnóstico nos períodos "pré-pandemico" e "pandêmico";
- Verificar o tempo decorrido entre admissão, diagnóstico e tratamento.

3 PUBLICAÇÕES

Este trabalho foi executado em uma unidade diagnóstica e uma unidade hospitalar, respectivamente localizadas nos níveis secundário e terciário de atenção ao paciente com CCP. A pesquisa resultou na produção de dois artigos científicos, o primeiro, abrangendo os casos diagnosticados no LAP, do Departamento de Odontologia da UFRN, e o segundo, com dados do HC de Barretos. As publicações foram redigidas em língua inglesa, e normatizadas de acordo com as revistas selecionadas para envio dos trabalhos.

3.1 Publicação 1*

COVID-19 reduced the quantitative diagnosis of oral cancer in private, public, and institutional oral cancer services.

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Abstract

Oral squamous cell carcinoma (OSCC), representing over 90% of oral neoplasms, is a serious health problem worldwide. The pandemic (Covid-19) had the potential to cause delays in cancer diagnosis and treatment, considering the lockdowns and health necessities associated with the treatment of Covid-19 patients. To study how Covid-19 changed the diagnostic pathway of oral cancer, we observed the resistance figures in a lab for pathological anatomy (LPA) located in a school of dentistry in Brazil. The LPA receives biopsies on demand. It remained functional during the lockdown. We compared pre-pandemic, pandemic and post-pandemic age at diagnosis, year of diagnosis, ethnicity, sex, admission date, histological diagnosis, and biopsy origin. A total of 340 patients were included in the study. All statistical analyses were performed at a significance level of <0.05. The pandemic period shows a reduction of 56.1% compared to the pre-pandemic period. Institutional and external services (private and public) showed decreased diagnoses of 62.5% and 47%, respectively. A subsequent increase of cancer diagnosis in pos-pandemic period was also observed, similar to pre-pandemic data. The type of lesion diagnosed in LPA did not change during Covid, with OSCC accounting for 91.2% of all lesions. The data obtained describe a subsequent overload on cancer treatment hospitals when case seizure affects the service.

Keywords: Head and Neck Cancer; Squamous Cell Carcinoma; Oral Carcinoma; COVID-19.

Introduction

The Covid-19 pandemic (March 2020) and its subsequent social restrictions have changed the demand and supply of health services worldwide. In fact, all aspects of healthcare have been affected by the lockdown, mobility restrictions and reallocation of services and equipment to treat the complications associated with Covid-19[1,2].

The impact on patients with chronic diseases remains to be investigated. Data show difficulties in access, late diagnosis, and treatment losses. Specifically for cancer patients, delayed diagnosis and referral has great potential to affect survival and quality of life, as delays may result in late diagnosis [3,4].

In the head and neck (HN) region, squamous cell carcinoma (SCC) accounts for more than 90% of cases. The oral cavity is particularly affected. Oral squamous cell carcinoma (OSCC) is known for its rapid growth, doubling of size and loco-regional metastasis. Previous studies have shown that patients diagnosed at stage I and II have a better prognosis than those diagnosed at stage III and IV[4-6]. In addition, the need for screening campaigns is reinforced by the fact that OSCC often progresses without symptoms or functional impairment in the detection phase.

Investigation of the impact of Covid-19 on the diagnosis of oral cancer (OC) could reduce the consequences of late diagnosis. The Laboratory of Pathological Anatomy (LPA) is a permanent secondary care unit for the examination of biopsies of oral lesions. The LPA is part of the Oral Pathology Department of the School of Dentistry, at the Federal University of Rio Grande do Norte, and receives specimens on demand from the institution's dental clinics and from third parties, both public and private. Our aim was to investigate the influx of OC biopsies during Covid-19 and, considering the role of dental services in OC screening, to observe the impact of restrictions on access to these services in numerical terms. We collected data on admission date, sex, age, ethnicity, tumor sublocation, biopsy origin, clinical diagnosis and histological diagnosis and compared cases diagnosed before, during and after SARS-coV-2.

Materials and Methods

The study adhered to the ethical standards of the Declaration of Helsinki, as well as relevant Brazilian and international legislation and ethical guidelines for research and was

approved by the Research Ethics Committee of the Federal University of Rio Grande do Norte (NO 5.019.302).

Data source and study subjects

We collected data from the LPA database of cases from 2010 to 2021, according to the International Classification for Oncology. We included specimens with a definite histological diagnosis and demographic data including age at diagnosis, year of diagnosis, ethnicity, sex, date of admission, histological diagnosis, and origin of material. In total, 340 patients diagnosed with OSCC, mucoepidermoid carcinoma (MEC) or adenoid cystic carcinoma (ACC) were included.

Analysis

According to the official declaration of public emergency by the World Health Organization in March 2020, cases were classified as pre-pandemic and pandemic. The descriptive data were described by means and standard deviations (n=+/- SD), and the categorical data were expressed as percentages of the descriptive data. All analyses were performed using SPSS Statistics 26. The significance level was set at <0.05.

Results

A total of 340 patients fulfilled the inclusion criteria, with baseline characteristics as shown in Table 1. Male patients, with a mean age of 63 years, represented 56.5% of this sample (192 males and 148 females). The majority of lesions were diagnosed as OSCC, observed in 91.2% (n=310); 6.8% (n=23) were MEC and 2.1% (n=7) were ACC. The tongue was the most commonly involved subsite (n=102). This was followed by the floor of the mouth (n=52) and the lower lip (n=42.8). Most samples (n = 294) were obtained using incisional biopsies.

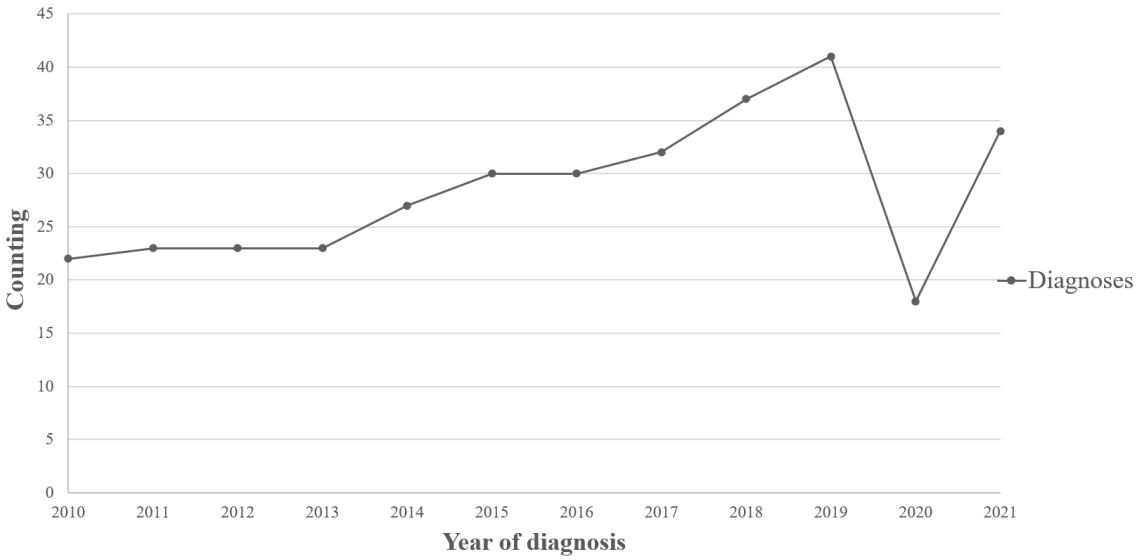
Table 1 - Clinical data

	Mean	*N*	*%*
Age	63 (±15,61)		
Gender	F	148	43,5
	M	192	56,5
Diagnose	SCC	310	91,2
	MEC	23	6,8
	ACC	7	2,1
Subsite	Tongue	102	30
	Floor of mouth	52	15,3
	Lower lip	42,8	12,6
	Others	60	42,1
Biopsy	Incisional	294	86,5
	Excisional	46	13,5
Admission date	Pre-pandemic	288	84,7
	Pandemic	52	15,3

Source: Authors

The average number of diagnoses per year from 2010 to 2021 was 28.3. Diagnosis rates rise slowly but steadily from 2015 to 2020, when they reach their lowest level in eleven years. As shown in Figure 1, due to the increase in Covid-19, only 5.3% of the diagnoses in this sample are made in 2020, a decrease of 56.1% compared to 2019.

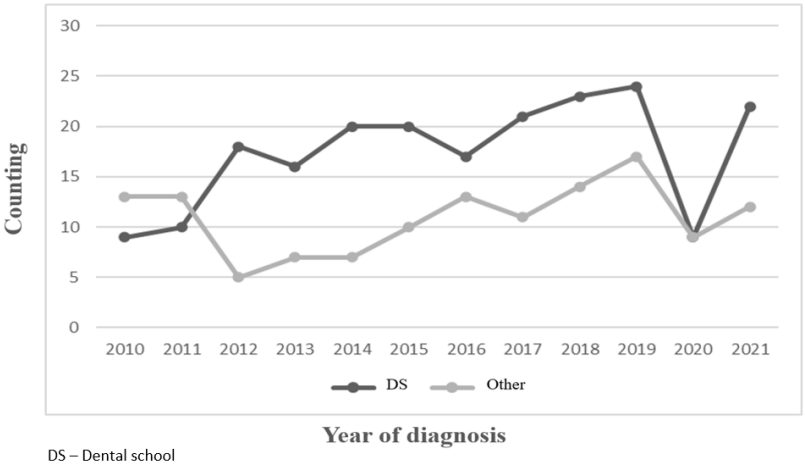
Figure 1 - Frequency of diagnoses issued per year



Source: Authors

The LPA has been receiving samples in response to demand and has remained fully operational throughout the pandemic. The laboratory processes and produces diagnostic biopsies from the University's dental facilities, mainly the Dental and Maxillofacial Service, and from external private and public institutions. Investigating the origin of the biopsies, we observed that in 2012 the Dental School (DS) began to be the main source of samples sent to the LPA. During the pandemic, both internal and external sources decreased significantly, but 2021 showed pre-pandemic levels, as shown in Figure 2. Indeed, our data showed a consistent decrease in 2020, the biggest drop was observed at the institution (62.5%), but also felt by the external sources (47%).

Figure 2 - Distribution of histopathological results for the years 2010 to 2021



DS – Dental school
Other – External Sources

Source: Authors

Discussion

This research brings an insight into the picture of OC diagnosis during the SARS-coV-2 pandemic, by comparing diagnostic data from before, during, and after the health emergency. Our sample had a similar proportion of male and female patients, mostly in their 6[a] decade of life. Although OC has historically affected males in a ratio of 2:1, the gap between the genders has shortened in the last decades, due to the habits of tobacco and alcohol consumption becoming more popular amongst women[7-10].

Subtyping by year of diagnosis was stable, and OSCC accounted for 91.2% of cases. Tumors located in the anterior two thirds of the tongue or floor of the mouth accounted for the majority of patients diagnosed at LPA. These sites have been described as having aggressive biological behavior, a tendency to infiltrate neural and lymphovascular beds, and to cause nodal and distant metastases[11,12].

The number of biopsies in LPA showed a decrease of 56.1% in 2020. Similar data was described with an increase in delayed diagnosis and lack of access to screening services[13-17]. Reductions in screening for other tumors were as high as 77%, 80%, and 90% for cervical, colorectal, and stomach cancers, respectively[18]. A recent international study showed a broad decline in diagnoses, with a higher decline in early stage patients[19]. These findings suggest an increased incidence of late diagnosed OC as a further consequence of the healthcare disruption caused by the pandemic.

Dentists are a crucial part of OC screening and diagnosis, and data demonstrates that these professionals have better conditions to identify potential malignancies, perform oral biopsies and refer patients to cancer hospital[20]. Our results described both an institutional service and an expressive external group of private and public dentists engaged in the diagnosis of oral cancer.

Our results show that the pandemic affected both clinical diagnosis groups. The restrictive measures taken to reduce the spread of COVID-19 may have reduced both the number of patients seen and the services available[21]. Dental services were restricted or suspended in several countries, especially after pandemic declaration, although some urgent and emergency services remained open[22-26].

According to our results, the disruption of dental assistance in the first months of the pandemic was universally suffered. Measures of restriction in mobility, lockdowns and social distancing, are considered to contribute to the alterations in dental care. The postponement of regular examinations and loss in follow-up of patients with pre-cancerous disorders caused the delay in malignant lesion diagnosis [21].

The extent of the restrictions seems to have been worse in countries more affected by the health emergency. An Italian study reports that 95% of all dental services, public and private, were closed in 2020 because of Covid-19[27]. It was a particularly hard time for dentistry and consequently for those who needed care.

The dental clinics of the DS, particularly the maxillofacial and dental services, are the main source of biopsies for the LPA. The DS provides free specialized care and is a reference center for the diagnosis of oral lesions in the region, as are many dental schools around the world[28-30]. Our patients come from rural areas where OC specialists are not always available. However, our university has carried out actions in these communities, which have already shown results as evidenced by the fact that the trend of increasing frequency of diagnosis is correlated with the school's initiative to take specialists to remote areas of the state, to actively search for potential malignancies and OC[31,32]. Unfortunately, with the closure of schools and universities, these essential aspects do not seem to have played a role in the decision-making process.

Nevertheless, the public sector seems to be recovering faster, returning to pre-pandemic levels by 2021. This may represent pent-up demand, especially from those seeking dental examinations in these facilities, motivated by lack of resources to visit private practices and recognition of the services offered by the facility.

These findings suggest that there is a delayed demand for OSCC diagnosis. This could be reflected in late diagnosis and poorer prognosis[33]. The impact of Covid-19 was felt at all levels of support, and those services that remained open have reported a decrease in the number of diagnoses or screening procedures carried out during the crisis. Regarding OC, the main door for early diagnosis - the dentist's chair - was kept closed during the critical pandemic moments, and services linked to educational institutions continued to suffer throughout the crises.

It is time to reach out to those who couldn't get access to screening and avoid losses in treatment, outcome, and survival rates. Nonetheless, it is also crucial to learn from the choices made during the SARS-coV-2 outbreak, allowing screening and diagnosis centers, as essential services, to best prepare for future emergencies.

Conclusion

The COVID-19 pandemic had a quantitative impact on both institutional and private oral diagnostic services, with reductions ranging from 47.2% to 62.5%. However, we did not observe qualitative differences in histological type. Data of subsequent increase of cases in the pos-pandemic period was similar to pre-pandemic levels.

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3.2 Publicação 2*

Head and neck cancer screening in times of Covid-19: profile, trends in diagnose and start of treatment in a tertiary care facility

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Abstract

Head and neck cancer (HNC) has the potential to cause locoregional growth and infiltration, increasing treatment complexity and worsening prognosis. Thus, early detection is of utmost importance to achieve good outcomes and increase survival rates. The Covid-19 pandemic led to changes in virtually all levels of health care worldwide, and investigating the extent of its impact over HNC assistance is the way to identify a possible demand for diagnoses, preventing disease progression and advance of TNM stage. We aimed to verify cases of HNC diagnosed between 2018 and 2020 at Barretos Cancer Hospital (BCH), one of the biggest referral centers for HNC treatment in Brazil. The data included years of diagnosis, age, sex, data of admission, tumor progression, histological diagnosis, course of treatment and TNM staging. All cases containing the specified data were included, resulting in 1.068 patients. All analyses had a significance level of <0.05. No change in the histological profile of lesions was observed at BCH. Decreases in time between admission and diagnosis, from 70.68 to 40.43 days, and diagnosis and start of treatment from 117.48 and 89.27 days were identified. An overall drop in diagnosis was observed during the pandemic. However, there was an increase in early stage patients (24.81% to 33.33%) versus advanced patients (75.18% to 66.66%) during 2020. These findings add to the comprehension of HNC assistance during the biggest health emergency of the century, aiding the assessment of the disruption in cancer care and the discussion of better courses of actions for future pandemics.

Keywords: Head and Neck Cancer; Squamous Cell Carcinoma; Oral Carcinoma; COVID-19.

Introduction

The initial stage of diagnosis and subsequent treatment of head and neck cancer (HNC) is crucial to the assessment of the best prognosis. HNC is ranked as the 7th most common cancer in humans in the world. The clinical/pathological TNM stage is the most relevant factor influencing survival rates. The Covid-19 pandemic and subsequent social isolation had the potential to have an impact on access to oral health services during the global emergency outbreak[1,2].

The pandemic required adjustments at all levels of healthcare as the world mobilized to control the spread of the virus and cope with the flood of infected patients suddenly needing medical care. Global initiatives included the reallocation of human resources and workflows, to prioritize emergency care; such movements were seen on all continents. Naturally, other health care services declined, affecting diagnostic procedures, primary care for chronic diseases, and follow-up care[3-6].

On the other hand, the spread of the virus also has a direct impact on the treatment process in oral health services. In the beginning, only urgent and emergency procedures were maintained. Other interventions were postponed or suspended until a lower level of infection was established[7,8]. The first data regarding cancer diagnosis, described a 90% reduction in procedures for cervical and breast cancer in women, including cytology and screening. The scenario is of an internationally highlighted and warned upcoming delayed process, that could lead to a reduction in survival rates of cancer patients[9,10].

Head and neck cancer (HNC) has the potential for locoregional growth and infiltration, which increases the complexity of treatment[8,11]. Indeed, the 325,000 HNC diagnosed annually, mostly advanced stage (III and IV), have poor prognosis and overall survival[11-13].

Although the Brazilian population represents only 3% of the world population, government data describe 10% of the Covid-19 pandemic deaths[14]. The complexity of the pandemic needs to be understood and the social dynamic process described. In order to identify political decision-making guidelines for future similar pandemic diseases, the possible delay process must be understood. The aim of this research was to study the impact of Covid-19 on the diagnosis and treatment of HNC at the BHC. Data collected included stage, location, time since diagnosis and treatment initiation.

Materials and Methods

Ethical statement

This study was approved by the ethical review board of the Ethics Committee of the Pio XII Foundation - Barretos Cancer Hospital (NO. 5.227.688) and complied with the ethical standards of the Declaration of Helsinki, as well as with relevant Brazilian and international legislation and ethical guidelines in research.

Data source and study subjects

We collected data from the BHC's database of cases from 2018 to 2020. According to the International Classification for Oncology. Data with a confirmed histological diagnosis were included and demographic data, including age at diagnosis, year of diagnosis, ethnicity, sex, admission date, tumor progression, histological diagnosis and TNM staging, were added. The clinicopathological variables, including tumor size, histological grade, Lymph Node Metastasis, tumor invasion extent, average size of metastatic lymph nodes, and TNM/clinical stage were also collected, and analyzed. Treatment modality, surgical, radiotherapy and/or chemotherapy data were obtained. 1.068 patients were included. The clinical stage was redefined as early-stage (stages I and II) or advanced-stage (stages III and IV).

Analysis

The Covid-19 pandemic was declared by the World Health Organization in March 2020, therefore we classified it into pre-pandemic and pandemic periods. The descriptive data were described by means and standard deviations (n=+/- SD), and the categorical data were expressed as percentages of the descriptive data. Student's T-test was used to examine the time between admission date, diagnosis and treatment. Pearson's chi-squared and Fisher's exact test were used to compare the TNM stage of those diagnosed before and during the Covid-19 trial. All analyses were performed using SPSS Statistics 26 at a significance level of <0.05.

Results

The patients' baseline characteristics are shown in Table 1. There were 868 males (81.3%) and 200 females (18.7%) among the 1.068 patients who met the inclusion criteria. In 2018 and 2019 there will be 896 (83.9%) and 448 (16.1%) cases respectively, whereas in 2020

there will be just 172 (16.1%). Figure 1 shows the frequency of patients diagnosed with HNC that continued treatment at HCB per year.

The information on histological diagnoses showed 43 different types of lesions, the tumors were grouped according to their tissue of origin, as shown in Figure 2. 94% of the tumors were carcinomas, which were most commonly represented by the squamous cell carcinoma variant, which was present in 86.4% of the cases.

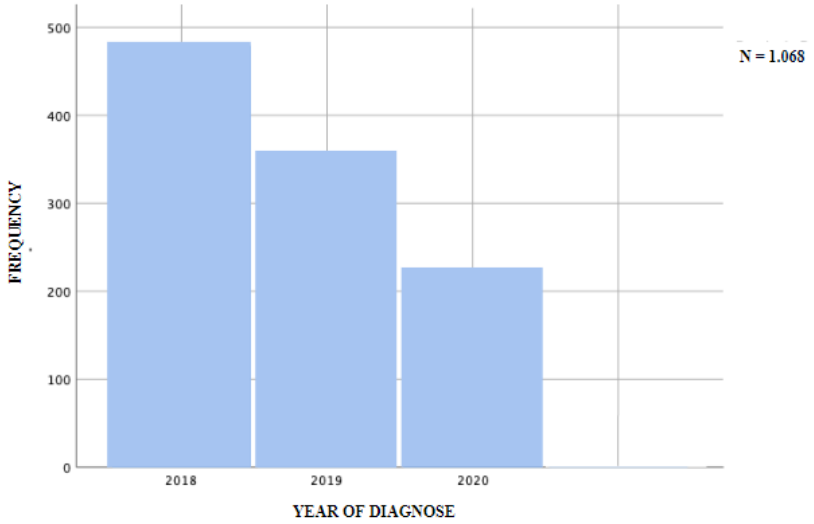
The differences in time between the treatment phases before and after Covid-19 are shown in Table 2. The average number of days between the admission to health services and the issuing of a diagnosis was 71.68 days before the introduction of Covid-19. This was reduced to 40.43 days (p=.000) during the pandemic. After diagnosis, the patients where referred BCH, where the treatment was conducted. The mean time from diagnosis to treatment initiation at HCB was 117.48 days, decreasing to 89.27 days during the pandemic (p=0.001).

Table 1. Clinical data

		N	*%*
Gender	Female	200	18,7%
	Male	868	81,3%
Date of admission	Pré-pandemic	896	83,9%
	Pandemic	172	16, 1%

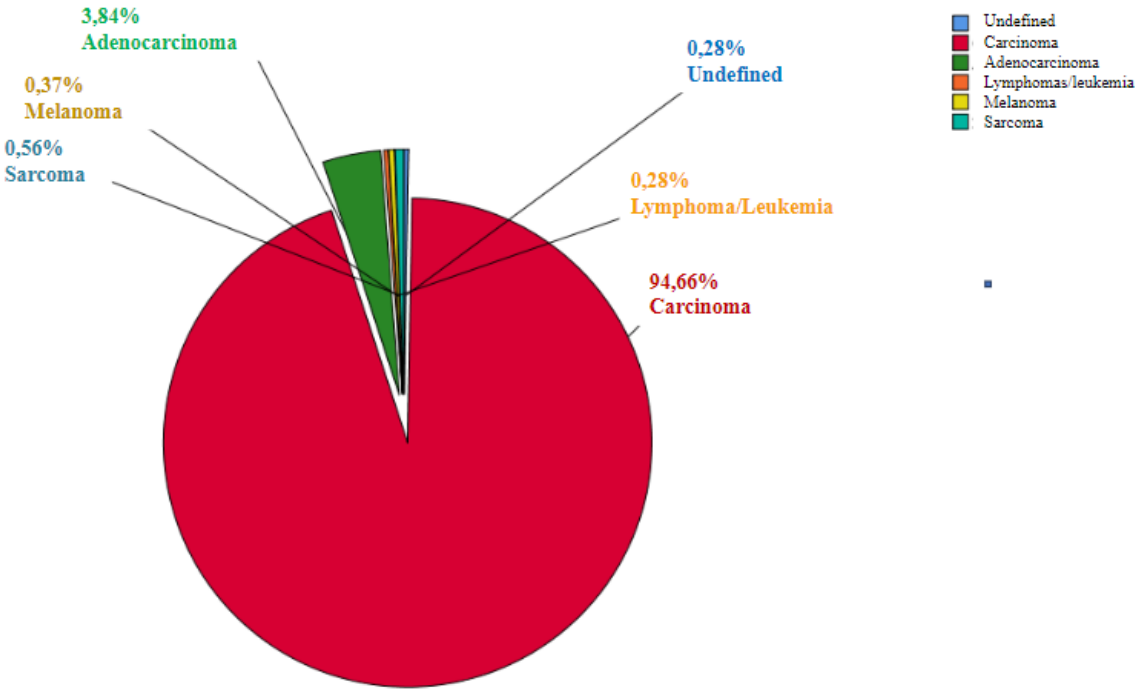
Source: Authors

Figure 1. Year of diagnose of patients that attended treatment at BCH between 2018 and 2020



Source: Authors

Figure 2. HNCs grouped according to histological diagnoses



Source: Authors

Table 2. Time elapsed between admission, diagnosis, and treatment before and after Covid-19.

	Admission	*N*	*%*	*Mean*	*Standard deviation*	*(P<0,05)*
Time elapsed between admission and diagnose (days)	Pre-pandemic	896	18,7%	71,68	105,490	,000
	Pandemic	172	81,3%	40,43	46, 136	
Time elapsed between diagnose and treatment (days)	Pre-pandemic	753	83,9%	117,48	102, 135	0,001
	Pandemic	151	16, 1%	89,27	61, 108	

Source: Authors

A comparison of the proportions of staging for early and advanced cases was performed for both time points. The distribution for both groups was significantly different from expectation during the pandemic (p=0.03), as shown in Table 3. The reduction in the numbers was observed for both early and advanced cases. The number of early stage patients was increased from 24.81% to 33.33% and the advanced stage reduced from 75.18% to 66.66% as illustrated in Figure 3.

BHC is a hospital reference for cancer treatment. We studied the origin of patients participating in this work. There was a general decrease in the number of patients coming all over the country. During the pandemic, patients from 6 different states ceased to be admitted at all. São Paulo State, the hospital's location, suffered the most, with 60% less patients in 2020. Figure 4 illustrates patient distribution by home state.

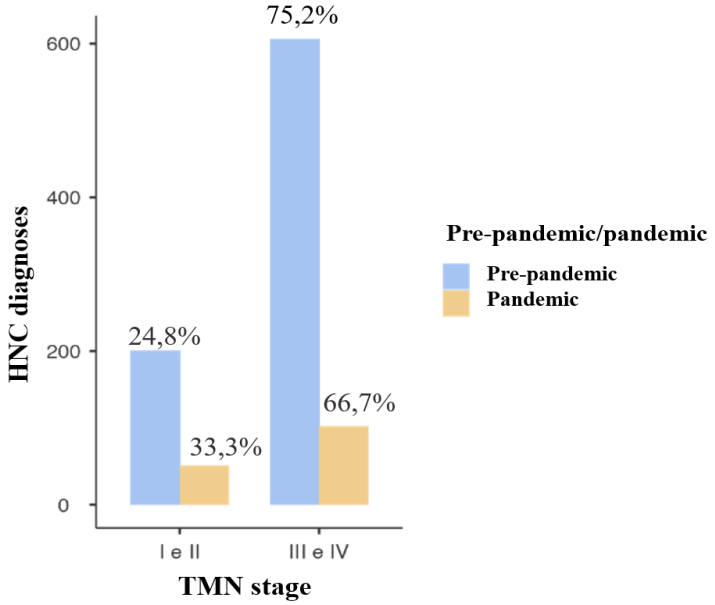
Table 3 – Initial and advanced diagnosis staging for patients treated at BCH before and after Covid-19

			Pre-pandemic	*Pandemic*	*Total*
TMN Stage	I+II	Count	200_a	51_b	251
		Expected Count	211,0	40,0	251,0
		%	24,8%	33,3%	26,2%
	III+IV	Count	606_a	102_b	708
		Expected Count	595,0	113,0	708,0
		%	75,2%	66,7%	73,8%
Total		Count	806	153	959
		Expected Count	806,0	153,0	959,0
		%	100%	100%	100%
			(P<0,05)		
Chi-squared test			,028		
Fisher's exact			,019		

I+II – Initial TNM Stage
III+IV – Advanced TNM stage

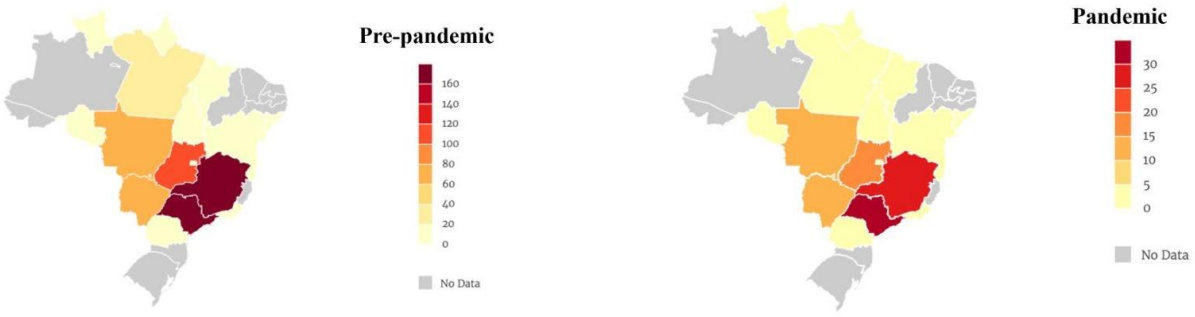
Source: Authors

Figure 3 - Covid-19 observed reduction in early and advanced HNC patients treated at HCB



Source: Authors

Figure 4 - Spatial distribution of HNC patients before and after the pandemic



Source: Authors

Discussion

The data provides a perspective on the complex picture of caring for HNC patients during the Covid-19 pandemic. Our results were similar to other data described worldwide, raising concerns about the gap in assistance for those living with cancer. Consistent with HNC epidemiological studies, our sample was overwhelmingly squamous cell carcinoma in male patients[15,16].

Other countries have also reported a decrease in diagnoses following the outbreak of the pandemic. A report from Scotland showed a 38.6% decrease in HNC referrals, mostly concentrated in the first months after the official global emergency declaration, when stay-at-home measures were emphasised[15].

Although few studies have described the impact of the SARS-coV-2 pandemic over the diagnosis of HNC, important data is coming to light on tumors from other regions. A study conducted in the United States showed that 50% of cancer screening services have stopped completely during the peak of the pandemic[16]. On the other hand, reductions have also been reported for breast cancer (77% to 100%), cervical cancer (90%), colorectal cancer (50% to 86%) and stomach cancer[16-18]. In addition, a study conducted in France, comparing the first quarters of 2019 and 2020, reported a dramatic reduction in all procedures performed in essential oncology services, including consultations (54%) and oncogeriatric assessments (86%)[17].

During the health crises, the average time between admission, diagnosis and treatment decreased significantly in our sample. While some centers have maintained the interval between diagnosis and first oncological approach similar to pre-pandemic rates, other services have reported a decrease in treatment procedures[19-21]. Those findings indicate that individual aspects of each service are also linked to the extent of changes in assistance. In our research, the patients where first diagnosed at other health facilities and then referred to treatment in BCH. A number of factors including prioritization of urgent cases, reduced patient flow and reduced workload, could explain this change, but it is also possible that a decentralized approach to the pandemic, which was coordinated by each State individually, has affected the access and process of referral of HNC patients. It is possible to quantify the implementation and use of services by analyzing the resources and facilities of oncology care and follow-up. Over a two-year follow-up period, 7.452 cancer patients received 85.336 clinical consultations, according to a study conducted in Italy[22].

HNC is frequently detected at an advanced stage. Similarly, our patients were mostly diagnosed at stages III/IV, which was similar in the pre-pandemic period and in the pandemic period (SARS-coV-2). TNM allows clinicians to assess disease status, prognosis, and treatment options; earlier diagnosis is associated with better surgical outcomes. HNC does not usually present with pain or functional impairment, which makes it difficult to diagnose at an early stage. Tumors in this region have a high potential for invasion and locoregional spread, with recurrence rates of 50% in the first 2 years of follow-up in advanced stages (III/IV)[23,24].

The reasons for the general decrease in diagnoses may be related to access to the service. Though BCH has remained functional after a quick period of adaptation, the diagnose services were compromised during 2020, thus, referring less patients to the hospital. Other tertiary referral services reacted in different ways, some even suspending procedures for long periods. Furthermore, the social distancing imposed by Covid-19 encouraged people to seek care only for serious illness, and HNC often lacks early signs or symptoms. The delay in seeking care may be the cause of later, more advanced diagnoses. The British Dental Association warned of a 22.83% increase in late diagnoses in 2020 compared to previous years[24]. Other reports indicate a 48% increase in stage IV patients during the pandemic[25]. Similarly, in lung cancer, there have been declines in new cases and increases in advanced stage cases[26].

Curiously, our data shows a slight increase in the relative percentage of stage I/II cases treated during the health emergency, while other studies show that patients diagnosed at that time were more likely to be stage IV[26]. Further studies analyzing the profile of patients treated

during the months that followed the pandemic outbreak, will help elucidate the trends for different services, as well as the possible increase in post-pandemic late-stage diagnoses.

BHC serves cancer patients from different areas of Brazil. In 2022, 1.673.441 procedures (consultations, returns, investigations, oncological surgeries, radiotherapy, and chemotherapy) were performed on more than 540,000 patients[27]. In 2020, by evaluating the origin of patients, we observed a reduction in the number of regions served by the hospital. In this context, the Brazilian government refrained from central decisions, leading to different responses from each state of the country, which may have affected local care. These data provide important parameters for maintaining a diagnostic process that can be used both for future global epidemics and for improving current diagnostic and referral processes for head and neck cancer. Meanwhile, research has shown the impact of social restrictions on mental health. An increased rate of anxiety has been found, which may have influenced patients' decision to delay diagnosis[28].

A side effect of the Covid-19 pandemic is highlighted by our work. Delays in HNC screening lead to advanced stages, requiring more complex treatment and recovery, and worsening prognosis and survival of patients. Tertiary diagnostic screening centers and cancer treatment hospitals are capable of anticipating and organizing measures to reduce the impact of a new pandemic. In this way, they can prepare, propose measures and protocols to international bodies, such as the World Health Organization, allowing for a more unified and prompt response in health emergencies yet to come.

Conclusion

The pandemic period did not change the histological profile of tumors at Barretos Hospital of Cancer. The time to diagnosis decreased from 70.68 to 40.43 days during the pandemic. Similarly, the median time to start treatment after diagnosis decreased from 117.48 days to 89.27 days. There was an overall decreased number of patients diagnosed and referred to BCH during the pandemic. Interestingly, however, there was an increase in the proportion of patients diagnosed at an early stage (24.81% to 33.33%) compared with an advanced stage (75.18% to 66.66%).

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4 CONCLUSÃO

Ambas as unidades apresentaram redução no número de diagnósticos emitidos em 2020. As fontes internas e externas de biópsia para LAP sofreram redução. A maior queda foi registrada nas clínicas internas (62.5%), do Departamento de Odontologia, entretanto, o setor externo também foi fortemente afetado (47%).

No HCB, a frequência relativa de pacientes em estádios iniciais aumentou durante a pandemia, em relação aos anos anteriores (de 24.81% a 33,33%). A unidade registrou redução no número de dias decorridos entre admissão e emissão de diagnóstico (de 70.68 a 40.43) e entre diagnóstico e início do tratamento (de 117.48 a 89.27).

A pandemia de Covid-19 parece ter afetado todos os níveis de assistência à saúde. Enquanto o HCB, após um breve período de adaptação, permaneceu funcional, o LAP perdeu sua principal fonte de biópsias em 2020, em decorrência do fechamento dos serviços odontológicos, especialmente o Departamento de Odontologia. Estes dados, juntamente com as experiências internacionais compartilhadas neste trabalho, indicam a existência de uma demanda reprimida para diagnóstico de CCP. Com o advento da vacinação e a retomada da vida cotidiana, é hora de endereçar as consequências da pandemia sobre o curso de outras enfermidades, especialmente os pacientes de câncer, que estão sujeitos a progressão da doença, evitando perdas prognósticas e piora da sobrevida.

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