



COVID-19 AND ITS FIRST WAVE: A RETROSPECTIVE ANALYSIS OF EARLY CASES IN A BORDER CITY OF BRAZIL

COVID-19 E SUA PRIMEIRA ONDA: UMA ANÁLISE RETROSPECTIVA DOS PRIMEIROS CASOS EM UMA CIDADE FRONTEIRIÇA DO BRASIL

COVID-19 Y SU PRIMERA OLA: UN ANÁLISIS RETROSPECTIVO DE CASOS TEMPRANOS EN UNA CIUDAD FRONTERIZA DE BRASIL

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ABSTRACT

In this retrospective, single-center study, we included all the cases of the first wave of nCoV 2019 at Hospital Padre Germano Lauck, Foz do Iguaçu - PR, Brazil, from April to July 2020, confirmed by real-time RT-PCR and analyzed epidemiologic and clinical features. We aim to retrospectively describe and analyze the clinical and epidemiological characteristics of the cases in the first wave of COVID-19 in the city of Foz do Iguaçu, in Brazil. Categorical data are described by frequency and proportions, while numerical data were described by standard deviation (SD) and median interquartile range (IQR). The mean age of patients was 39 years, including 415 men (44%) and 535 women (56%). The prevalent comorbidities were diabetes, hypertension, and cardiovascular disease. Cough, headache, and myalgia were the common symptoms associated with COVID-19. Age was the main risk factor for death, as was Hypertension and Diabetes. This study found that the first wave of COVID-19 in Foz do Iguaçu had similar characteristics as studies conducted during the same epidemiological period. When compared to later analyses of different strains of the COVID-19 virus, it was seen that there was a predominance of different symptoms and ages of severe cases among infections caused by the Ómicron and Delta variants.

KEYWORDS: COVID-19. Clinical picture. Epidemiological features.

RESUMO

O objetivo deste estudo retrospectivo, de centro único, é incluir todos os casos da primeira onda de casos de COVID-19 no Hospital Padre Germano Lauck, em Foz do Iguaçu - PR, Brasil, de abril a julho de 2020, confirmados por RT-PCR em tempo real e analisar as características epidemiológicas e clínicas. Descrevemos e analisamos, retrospectivamente, as características clínicas e epidemiológicas dos casos da primeira onda de COVID-19 na cidade de Foz do Iguaçu, no Brasil. Os dados categóricos são descritos por frequência e proporções, enquanto os dados numéricos são descritos pelo desvio padrão (DP) e pelo intervalo interquartil mediano (IQM). A idade média dos pacientes foi de 39 anos, incluindo 415 homens (44%) e 535 mulheres (56%). As comorbidades prevalentes foram diabetes, hipertensão e doença cardiovascular. Tosse, cefaleia e mialgia foram os sintomas comuns associados à COVID-19. A idade foi o principal fator de risco para a morte, assim como a hipertensão e o diabetes. Este estudo encontrou que a primeira onda de COVID-19 em Foz do Iguaçu apresentou características semelhantes aos estudos realizados durante o mesmo período epidemiológico. Quando comparadas com análises posteriores de diferentes cepas do vírus COVID-

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19, foi observado que houve uma predominância de diferentes sintomas e idades de casos graves entre as infecções causadas pelas variantes Ômicron e Delta.

PALAVRAS-CHAVE: COVID-19. Quadro clínico. Características epidemiológicas.

RESUMEN

En este estudio retrospectivo de un solo centro, incluimos todos los casos de la primera ola de nCoV 2019 en el Hospital Padre Germano Lauck, Foz do Iguaçu - PR, Brasil, de abril a julio de 2020, confirmados por RT-PCR en tiempo real y analizamos las características epidemiológicas y clínicas. Nuestro objetivo es describir y analizar retrospectivamente las características clínicas y epidemiológicas de los casos en la primera ola de COVID-19 en la ciudad de Foz do Iguaçu, en Brasil. Los datos categóricos se describen por frecuencia y proporciones, mientras que los datos numéricos se describen por desviación estándar (DE) y mediana del rango intercuartil (IQR). La edad media de los pacientes fue de 39 años, incluidos 415 hombres (44%) y 535 mujeres (56%). Las comorbilidades prevalentes fueron diabetes, hipertensión y enfermedad cardiovascular. La tos, el dolor de cabeza y la mialgia fueron los síntomas comunes asociados con COVID-19. La edad fue el principal factor de riesgo de muerte, al igual que la hipertensión y la diabetes. Este estudio encontró que la primera ola de COVID-19 en Foz do Iguaçu tuvo características similares a los estudios realizados durante el mismo período epidemiológico. Cuando se comparó con análisis posteriores de diferentes cepas del virus COVID-19, se observó que había un predominio de diferentes síntomas y edades de casos graves entre las infecciones causadas por las variantes Ômicron y Delta.

PALABRAS CLAVE: COVID-19. Cuadro clínico. Características epidemiológicas.

1. INTRODUCTION

Coronaviruses are RNA viruses related in general to bowel disease and respiratory tract. Some of those are responsible for light respiratory disease, such as hCoV-229E, OC43, NL63 and HKU1. Although, two other types, known as severe acute respiratory syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-COV) got the world's attention due to their high lethality rate in humans (1).

COVID-19 is classified into four groups according to the severity of symptoms: mild, moderate, severe, and critical. The moderate group presents respiratory symptoms, fever, and imaging features of COVID 19. Differently, the severe group can present one of the following features: dyspnea, oxygen saturation lower than 93%, and PaO₂/FiO₂ less than 300mmHg, among others. Furthermore, a critical patient may also show one of the following situations: acute respiratory distress, septic shock, or multiple organ failure (2).

COVID-19 diagnosis can be done by clinical, laboratory, and imaging features. Among laboratories methods employed there is the serological profile, (e.g., ELISA - Enzyme-linked immunosorbent assay and RST - Rapid serology test), which it's used to analyze the presence of antibodies anti-SARS-CoV-2 proteins (antigens), even after the infection has passed. Furthermore, real-time RT-PCR is a molecular approach by viral RNA detection, increasing the accuracy of detection in the initial stages of infection (2,3).

Although initial classifications were established for the first strain of SARS-CoV-2, it has been observed that successive waves of the pandemic, characterized by several other viral strains such as Delta and Omega, have presented variations in clinical and epidemiological characteristics, including



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increased mortality and transmissibility, as well as the emergence of severe cases in younger patients compared to the first viral variants. In this sense, different strategies around the world have been adopted to combat the infection and reduce transmission rates (4).

In Foz do Iguaçu, a city in the south of Brazil located on the triple border between Argentina, Brazil and Paraguay, special procedures were implemented to manage suspected or infected patients. It is possible to highlight strategies that were decisive in facing the coronavirus disease, such as partnerships between municipal and federal institutions, and adequate allocation of financial resources, with an emphasis on expanding the number of infirmaries and ICU beds, implementation of telemedicine and intensive testing and contact tracing (5,6).

Foz do Iguaçu has 258.248 inhabitants within a 618.057km² territory area (7). As January 30th, 2023, more than 85.640 positive cases have been confirmed in the city, resulting in 1.306 deaths (8).

Several studies have sought to examine the various clinical and epidemiological profiles associated with variations on each viral strain (9,10). It has been observed that the profile of severity, comorbidity, and age may differ depending on the strain, and strategies for controlling each one should be consistently updated and discussed.

With the goal of understanding the impact of COVID-19 in Foz do Iguaçu, Paraná, Brazil, we aimed to thoroughly analyze the clinical and epidemiological characteristics of initial cases and investigate the potential risk factors related to disease severity. Additionally, we aimed to compare the epidemiological profiles of different variants and waves of COVID-19 infections.

2 METHODS

The epidemiological, clinical, and a retrospective study of a descriptive and ecological matter, which was conducted with data collected from September to December 2020.

The corresponding positive cases diagnosed were obtained through information provided by the Medical Sciences Research Laboratory from *Universidade Federal da Integração Latino-Americana* (UNILA), in partnership with Hospital Municipal Padre Germano Lauck (HMPGL).

It was considered all the positive cases from RT-qPCR analysis. Clinical data and epidemiological information were acquired manually from an electronic medical record (*Tasy* platform - software).

The system is loaded using anamnesis as a reference. Symptom's selection criteria were based on a record named *NOTIFICA COVID* (developed on behalf of Federal/State Government/Ministry of Health) and fully used in Brazilian states.

2.1 Data analysis

Categorical data are described by frequency and proportions, whereas numeric data were described by standard deviation (SD) and median interquartile range (MIR).



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In this study, we stratified the sampling according to the following variables collected: age, sex, number of comorbidity (cardiovascular, renal, neurological, hematological or hepatic comorbidity, diabetes, chronic respiratory diseases, obesity, immunosuppression), as described in RANZANI (11). Self-declared skin type (white, black, Asian, indigenous), period of presentation of symptoms and diagnosis, lifestyle (smoking and alcoholism), admission to ward or ICU and the outcome were also analyzed.

The descriptive analysis and raw data processing were conducted in the software RStudio (R 4.0.4 version).

The code, dictionary, and raw data are available in the GitHub repository (https://github.com/chagas98/1000COVID_IGU).

2.2 Ethical committee

This study was approved by the Research Ethics Committee (CEP) under the number CAAE 36189220.3.0000.8527.

It was used secondary data base extracted from electronic medical record, as recommended at the Resolution n°. 510 (April 07 - 2016), National Health Council of Health Ministry. Although, ethical aspects were followed regarding on the Resolution n°. 466 (National Health Council of Health Ministry).

3 RESULTS

Between March 21 and July 04 of 2020, there were 1117 RT-qPCR confirmed cases of COVID-19 at the Hospital Padre Germano Lauck. This study comprehended 958 final patients (aged ≥ 10 years old) included on electronic medical database – *Tasy*, as shown in Table 1 above.

Tabel 1: Clinical and demographic characteristics of patients.

Characteristic	Sample	Overall, N = 958	Admission, N = 241	Death, N = 16	No admission, N = 701.
Symptoms Appearance	884				
<i>Mean</i>		4.30 (2.66)	4.55 (2.90)	8.50 (9.70)	4.16 (2.34)
<i>Median (25 to 75%)</i>		4.00 (3.00-6.00)	4.00 (3.00-6.00)	4.50 (3.50-9.00)	4.00 (3.00-6.00)
<i>Range</i>		0.00, 30.00	0.00, 21.00	1.00, 30.00	0.00, 17.00
Sex	950				
<i>Female</i>		535 (56%)	132 (55%)	9 (60%)	394 (57%)
<i>Male</i>		415 (44%)	107 (45%)	6 (40%)	302 (43%)
Age	958				
<i>Mean (SD)</i>		39 (16)	45 (17)	72 (12)	36 (13)



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<i>Median (25%-75%)</i>	36 (26-49)	44 (31-57)	72 (66-81)	33 (25-45)
<i>Range</i>	11, 1	13, 8	49, 8	11, 1
Age bin	958			
<i>10 to 19</i>	80 (8.4%)	8 (3.3%)	0 (0%)	72 (10%)
<i>20 to 29</i>	262 (27%)	49 (20%)	0 (0%)	213 (30%)
<i>30 to 39</i>	232 (24%)	48 (20%)	0 (0%)	184 (26%)
<i>40 to 49</i>	175 (18%)	49 (20%)	1 (6.2%)	125 (18%)
<i>50 to 59</i>	111 (12%)	36 (15%)	1 (6.2%)	74 (11%)
<i>60 to 69</i>	63 (6.6%)	33 (14%)	4 (25%)	26 (3.7%)
<i>70 to 79</i>	22 (2.3%)	13 (5.4%)	4 (25%)	5 (0.7%)
<i>80 to 89</i>	12 (1.3%)	5 (2.1%)	6 (38%)	1 (0.1%)
<i>90+</i>	1 (0.1%)	0 (0%)	0 (0%)	1 (0.1%)
Self-reported race	758			
<i>White</i>	304 (40%)	89 (41%)	3 (20%)	212 (40%)
<i>Brown</i>	428 (56%)	119 (55%)	12 (80%)	297 (56%)
<i>Indigenous</i>	2 (0.3%)	1 (0.5%)	0 (0%)	1 (0.2%)
<i>Asian</i>	5 (0.7%)	1 (0.5%)	0 (0%)	4 (0.8%)
Number of Comorbidityes	958			
<i>No comorbidityes</i>	648 (68%)	116 (48%)	3 (19%)	529 (75%)
<i>1 comorbidity</i>	191 (20%)	60 (25%)	4 (25%)	127 (18%)
<i>2 comorbidityes</i>	71 (7.4%)	37 (15%)	3 (19%)	31 (4.4%)
<i>≥3 comorbidityes</i>	48 (5.0%)	28 (12%)	6 (38%)	14 (2.0%)
<i>Diabetes</i>	74 (7.7%)	32 (13%)	7 (44%)	35 (5.0%)
<i>Systemic Arterial Hypertension</i>	151 (16%)	67 (28%)	9 (56%)	75 (11%)
<i>Cardiovascular Disease</i>	35 (3.7%)	17 (7.1%)	5 (31%)	13 (1.9%)
<i>Renal Disease</i>	12 (1.3%)	9 (3.7%)	1 (6.2%)	2 (0.3%)
<i>Lung Disease</i>	54 (5.6%)	23 (9.5%)	1 (6.2%)	30 (4.3%)
<i>Neoplasm</i>	3 (0.3%)	3 (1.2%)	0 (0%)	0 (0%)
<i>Immunosuppression</i>	4 (0.4%)	1 (0.4%)	0 (0%)	3 (0.4%)
<i>HIV</i>	6 (0.6%)	2 (0.8%)	0 (0%)	4 (0.6%)
<i>Neurological Disease</i>	14 (1.5%)	10 (4.1%)	2 (12%)	2 (0.3%)



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During this range of time, we observed that 73.1% (701) of the patients were sent home to fulfil the isolation. In the meantime, 29.9% (241) needed some type of hospitalization. Of those, 17.22% (139) needed a less complex initial care through the Respiratory Emergency Care (PS) and 9.61% (102) needed hospitalization, such as Infirmery or ICU.

Among these who needed hospitalization, it was observed that 5.67% were placed in a less complex unit when compared with ICU, such as Infirmery or Infectious Disease Therapy Unit while 2.3% needed an Intensive Care Unit (ICU), the most complex and specialized care level. The overall mortality rate was 1.67% (16).

The mean age of the patients was 39 years old. Nonetheless, predominantly age ranges from 10-19 [80]; 20-29 [262]; 30-39 [232]; 40-49 [175] to 50-59 [111] were higher in number compared to the oldest. Also, we can see that most of them were female (56%) whereas the rest were male (44%).

Considering those all who needed hospitalization, the median age was 45 years old. Considering the Infirmery and ICU, the median age was 49 and 55 years old, respectively. Though, the mortality median was 72 years old. As described above, the mortality seen in here increased with age (1 [6%] aged 40-49 years; 1 [6%] aged 50-59 years; 4 [25%] aged 60-69 years; 4 [25%] aged 70-79 years and 6 [38%] aged 80-89 years).

As demonstrated in Figure 1 above, we can associate age and level of specialized care needed once the median age increases according to the higher level of care. Also, the death was higher as the age increases.

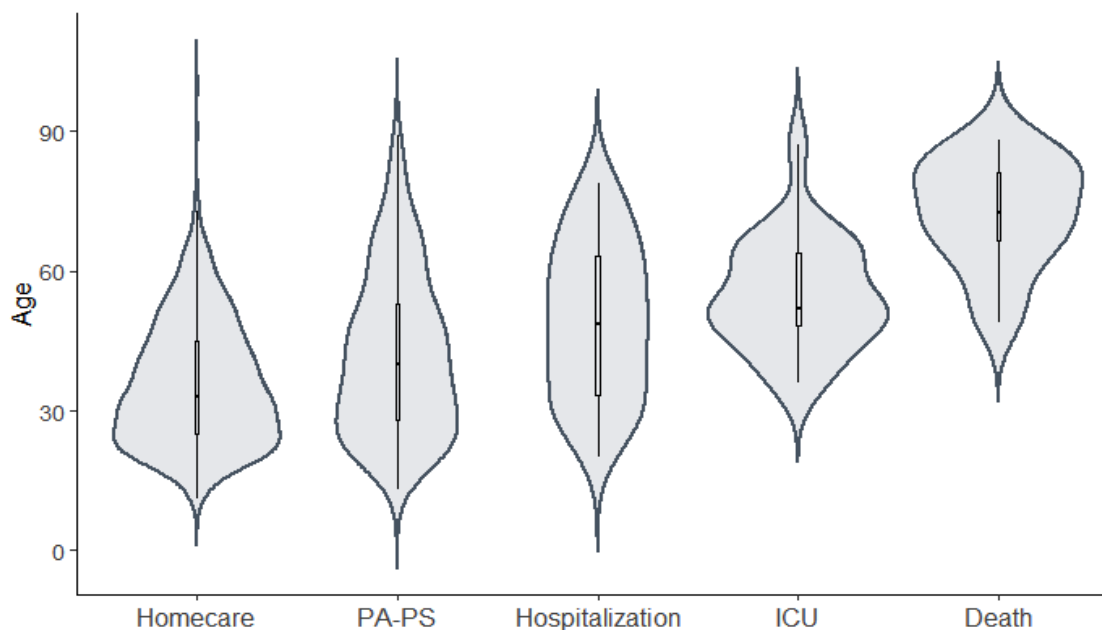


Figure 1: Violin Graphic showing the density of patients admitted to each hospital unit.
PA-PS: Respiratory Emergency Department.
ICU: Intensive care unit.



RECIMA21 - REVISTA CIENTÍFICA MULTIDISCIPLINAR ISSN 2675-6218

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In addition, skin color/race were considered. They were classified as yellow (Asian), white, indigenous, brown or black. From 758 patients, brown people were predominant (56%). Besides, white people represented 40%, black people 2.5% and Yellow [Asian] 0.7%. Only 0.3% were classified as Indigenous. Comparing hospitalized (241 patients) and non-hospitalized (741 patients), it was observed similar proportion between Brown (56%) and White (41%) people. The deaths presented a proportion of 80% brown patients.

Another topic we collected data was comorbidities (Table 1 and Figure 2 – section B). It was registered Diabetes, cardiovascular diseases, renal diseases, pulmonary diseases, neoplasia, immunodeficiencies, HIV, neurologic diseases, Down syndrome, obesity and others.

Considering the hospitalized and non-hospitalized patients, 575 (65%) of 885 studied patients had no comorbidities, 191 (19,9%) had 1 comorbidity and 119 (12%) related having 2 or more comorbidities. Analyzing patients who had at least one comorbidity, we found that 310 presented Systemic Arterial Hypertension (16%) and/or Diabetes (7.7%).

Among the hospitalized patients, 54% had at least one comorbidity, which Systemic Arterial Hypertension (28%) was most common. Between the deaths, 43% had 3 or more comorbidities (Table 1).

As we can see in the A section of Figure 2, mainly initial symptoms pointed by the patient in the anamnesis were headache (68%), cough dry (68%), myalgia (50.1%), coryza (48.8%), odynophagy (44%) dyspnea (34.9%), adynamia (16.1%) and nasal congestion (12.5%).

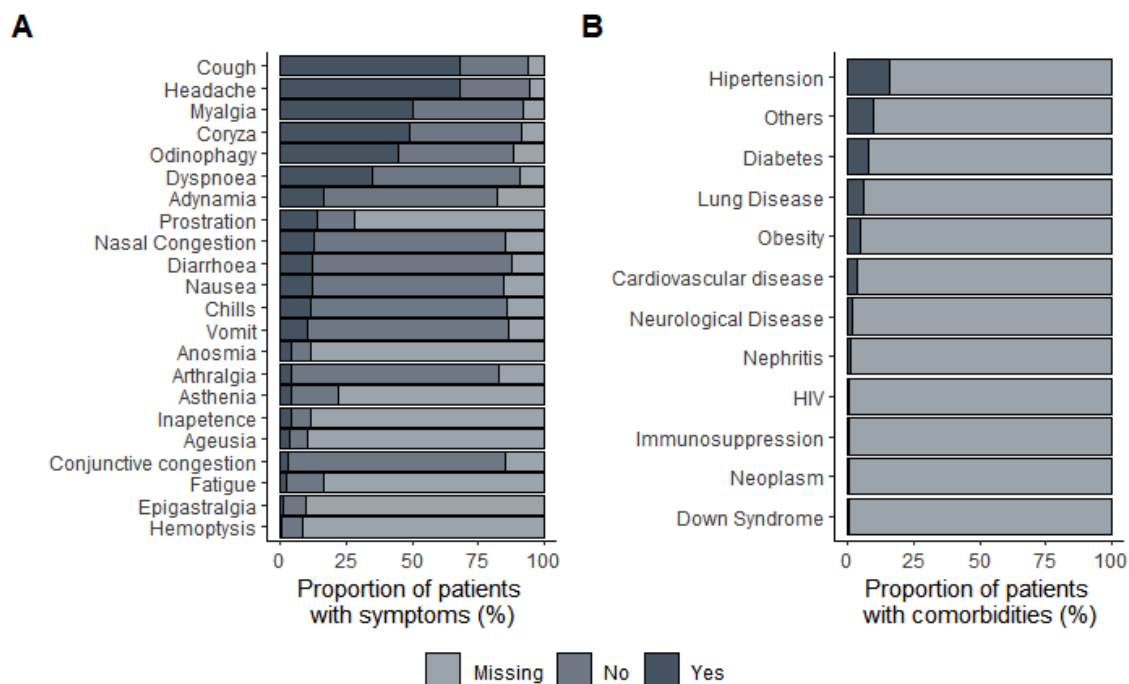


Figure 2: Proportion of symptoms and comorbidities between all studied patients.



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Although, diarrhea (12.3%), nausea (11.9%), chill (11.1%), vomit (9.9%), sputum (6%) and arthralgia (4.2%) were less listed among patients. Only 1.25% were classified as asymptomatic.

Anosmia and ageusia were ignored in medical records profile software due to no insertion at that moment or previously in the notification form used for COVID19. As a result, their complaint depended only on the patient's subjective report because absence of previous questioning in the anamnesis.

It was noticed that 9.2% were smoker. In the other hand, 2.7% informed to be an ex-smoker. Community spread is the major source (45.2%) of transmission of COVID-19 observed in our patients. Along the list, 32.6% reported contact primary with COVID-19 positive person before symptom onset. Travels in the last 14 days were confirmed by 5% of the patients, and nonetheless 3.7% were health professionals who worked in the front line of COVID-19.

4 DISCUSSIONS

This study analyzed retrospectively the first thousand patients tested for SARS-COV-2/COVID-19 in the Hospital Municipal Padre Germano Lauck.

Positive patients for COVID-19 were diagnosed and confirmed by Real Time RT-PCR during April to July of 2020. Electronic medical record data were collected manually which allowed a full description of the patient enhancing a better overview of this new outbreak disease.

Initially, this study showed a predominance of females among positive cases (56%), which goes in the other way of most studies published so far. For instance, other analysis on the similar date of demonstrated that there is a male prevalence among infected patient, from the mildest cases to the most severe cases, which required hospital care in New York, NY – USA (12).

Likewise, other two Brazilian studies that analyzed the whole of Brazil and São Paulo - Hospital Israelita Albert Einstein, respectively, demonstrated a male predominance, with rates of approximately 56% (11,13). A study also realized in Paraná obtained the highest proportion of women among the cases of COVID-19, which is probably because there are more women than man in this State (14).

Concerning on the disease outcome, most of our patients were instructed to comply home isolation and only 2.3% were more severe cases with admission to the ICU. It was also observed that the need for hospitalization increased with age and death was higher between the patients with higher number of comorbidities.

Recent research has revealed that age plays a significant role in the mortality rate of COVID-19. Specifically, for adults, the infection fatality rate (IFR) has been found to increase in an exponential manner with age, doubling the risk of death every 6–7 years (15).

The physiological changes associated with aging create a favorable environment for the replication of the virus. Immunologically, altered signaling of IFN- γ , neutrophilic infiltration, reduction of CD4+ or CD8+ T cell levels and activation of alveolar macrophages with increased release of pro-



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inflammatory cytokines are cited. Additionally, both age and the presence of chronic comorbidities have been found to be associated with higher levels of angiotensin converting enzyme 2 (ACE2) receptors in the lungs, which may explain the increased severity of the disease in these high-risk groups (10).

The median age found in the present study among patients who required hospitalization was 45 years, while 71% of the patients who required hospitalization were between the ages of 20 and 69. An analysis conducted in another Brazilian hospital during the same period as our study demonstrated the median age of 51 years among such patients (13). Another research with similar date conducted in Paraná demonstrated that deaths were primarily concentrated among individuals between the ages of 70 and 79 years (14), while the present analysis demonstrated that the age range most affected was between 80 and 89 years, with a mean age of 72 years.

Recent analyses of the impact of the Delta variants reveal that younger patients, specifically those under 20 years old, have been hospitalized at a higher rate and have presented with more severe cases of the disease compared to previous periods. This phenomenon is believed to be due to the increased transmissibility among this age group, as well as a lower vaccination rate when compared with other age ranges (16).

It was observed diabetes and hypertension were the most prevalent comorbidities among patients who died, accounting for 44% and 56%, respectively. On the other hand, patients who were not hospitalized had a significantly lower prevalence of diabetes and hypertension, 5% and 11% respectively. Additionally, 31% of the patients who died had some form of cardiovascular disease.

According to Zsichka and Muller (10) the association of these diseases has all been consistently shown to considerably increase the risk of severe COVID-19 outcomes. This is possibly explained by the fact that risk factors such as genetic background, insulin resistance, dyslipidemia, and obesity can lead to hyperglycemia, dysregulation of the renin-angiotensin system, increased immune activation, oxidative stress, and chronic inflammation (IL-1 β , IL-6, and TNF- α), which are conditions related to diabetes and hypertension.

These conditions are also associated with the severity of COVID-19 independently of pre-existing diabetes. These complex changes give rise to chronic cardiovascular diseases. During COVID-19, pulmonary distress puts an increasing burden on the previously weakened cardiovascular system with damaged pulmonary endothelial barrier, fluid extravasation, hypoxia, heightened inflammation (possibly through the decreased airway ACE2 levels in CVD patients), and hypercoagulability, which can lead to acute consequences such as myocardial injury, infarction, heart failure, thrombosis, or arrhythmias (17).

Regarding symptoms, our study noticed mostly dry cough, headache, myalgia, runny nose, fever and odynophagia. Anosmia and ageusia had low prevalence in our analysis, which contrasts with other studies that indicate these symptoms were the main ones in the early pre-Delta waves. This can be explained by the fact that the notification form used for collecting medical history does not



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directly include these symptoms, requiring spontaneous reports from patients. However, the symptoms of the patients in the current study align with other studies (12,13,18).

Anosmia and ageusia are frequently linked to nasal congestion in other types of respiratory infections, which is caused by mucosal edema. This is typically the case with the flu or viral upper respiratory tract infections, where changes in smell are a result of secondary nasal congestion. However, this does not appear to be the case with COVID-19 first wave cases, as these symptoms are not commonly associated with nasal obstruction (19). A study conducted in Italy found that 33.9% of patients experienced changes in taste or smell, and 91% of these patients were later hospitalized (20). In contrast, a report from Germany found that more than 65% of individuals had anosmia, while in South Korea, the number was 30% (21).

In February 2021, the Health Secretary of Foz do Iguaçu changed the criteria for defining a positive case, and now automatically considers patients who reported anosmia or ageusia as confirmed cases, in order to avoid the need for RT-PCR exams (21).

An examination of the variations in the clinical course of Covid-19 during different variants has uncovered that symptom such as coughing, fever, headaches, and fatigue were more frequently reported in the time frame before the emergence of Delta and Omicron variants. Additionally, a higher incidence of gastrointestinal symptoms, like nausea and diarrhea, were attributed to the Omicron variant. This study confirms these recent findings, once only 9.9% of our patients reported vomiting during their infection.

In this sense, the variations in clinical, epidemiological, and genomic presentations of this virus open up opportunities to develop strategies so that future waves can have mechanisms for identification (clinical, epidemiological, etc.), targeted and specific diagnosis and treatment.

5 CONSIDERATIONS

The findings of this study indicate that the first wave of COVID-19 in Foz do Iguaçu had similar clinical and epidemiological characteristics to the period studied in other places, mainly affecting the elderly and patients with various comorbidities among the most severe cases. The classic symptoms of the first wave were cough, headache, runny nose, and myalgia, differing from the affections by the viral variant Ômicron, which mainly ran with vomiting and predominated in younger age groups. The age group with the highest hospitalization was between 30 and 69 years, while the average age of deaths was 72 years. Hypertension and diabetes were the most prevalent comorbidities among the most severe cases and deaths.

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