Original Article

Risk Factors for Death among Hospitalized and Nonhospitalized Patients due to COVID-19 in a Triple International Border Municipality

Erica Alves Ferreira Gordillo, Rubia Laine de Paula Andrade[1], Ismael Hoare[2], Ricardo Izurieta[2,3], Adriana Zilly, Laiz Mangini Cicchelero, Merielly Kunkel, Ernesto Valdes Gordillo[4], Reinaldo Antonio Silva-Sobrinho, Regiane Bezerra Campos, Rosane Meire Munhak Silva

CELS- Center for Education, Literature and Health- Western Paraná State University, Foz do Iguaçu, Paraná, [1]Public Health Nursing -School of Nursing, University of São Paulo, [2]Global Communicable Diseases, College of Public Health Nursing -School of Nursing, University of São Paulo, São Paulo, Brazil, [3]One Health Research Group, University of the Americas, Quito, Ecuador, [4]University of Medical Sciences of Pinar del Rio, Pinar del Rio, Cuba

Abstract

Introduction: The severity of COVID-19 in the general population ranges from minimally symptomatic disease to critical illness, which may require hospitalization and progress to death. **Methods:** A retrospective cohort study carried out with all positive cases of COVID-19 reported in the municipality of Foz do Iguaçu (PR) between the period from March 2020 to December 2021. Data were collected from Bank Notifies COVID-19 is the name of the information system that provides notifications by professionals of suspected and confirmed cases of the disease. Data were analyzed using descriptive statistical techniques and calculation of relative risk. **Results:** 24,647 confirmed cases were identified in the study; among these, 22,211 (90.1%) were not hospitalized and 2436 (9.9%) were hospitalized. Among the 2436 patients hospitalized for COVID-19, 947 (38.9%) died and 1489 (61.1%) recovered. Among the 22,211 outpatients, 93 (0.4%) died and 22,118 (99.6%) recovered. An association between death and the following characteristics was identified among the cases that were hospitalized: male gender, all age groups over 40 years, indigenous race/color, hospital staylength of more than 10 days,hospitalization in a Unified Health System (SUS) bed and in an Intensive Care Unit (ICU). According to the clinical characteristics of symptoms and comorbidities, the following prevailed:ities dyspnea, intercostal retraction, cyanosis, hypertension, diabetes, obesity, cardiovascular disease, smoking, lung disease, kidneydisease, neurological disease, neoplasia, and immunodeficiency. Among the cases that were not hospitalized, death was associated with: malegender, all age groups over 50 years, dyspnea, cyanosis, hypertension, diabetes, obesity, cardiovascular disease, kidney disease, neurological disease, neoplasia, and liver disease. **Conclusions:** Older adults, male, and Caucasian people are commonly affected by COVID-19 and can evolve with aggravation when they have modifiable risk factors such as obesity and smoking, as well as nonmodifiable risk factors such as: cardiovascular disease, neurological disease, renal, hypertension, diabetes, and immunosuppression.

Keywords: Border areas Brazil, COVID-19, death, epidemiology, pandemic, public health

Introduction

Due to the accelerated spread of COVID-19 in late 2019 and early 2020, the World Health Organization declared a pandemic situation for the disease in March 2020, which was associated with intense interaction between humans.[1]

The severe form of the disease was more frequent in older adults with comorbidities, such as hypertension, diabetes, neurological, respiratory/cardiovascular diseases, constituting risk factors for the emergence of complications and unfavorable clinical outcomes such as hospitalization, need for intensive care unit (ICU), and death.[1-3] In the above context, understanding the epidemiology and identifying the characteristics of the affected population and the factors associated with greater severity and lethality of the disease in

Access this article online

Quick Response Code:

Website: www.jgid.org

DOI: 10.4103/jgid.jgid_72_23

Address for correspondence: Ms. Erica Alves Ferreira Gordillo, Luiz Zanivan, 579, CEP: 88816-720, Criciuma, Santa Catarina, Brazil.
E-mail: ericagordillo1981@gmail.com

How to cite this article: Gordillo EA, Andrade RL, Hoare I, Izurieta R, Zilly A, Cicchelero LM, *et al*. Risk factors for death among hospitalized and nonhospitalized patients due to COVID-19 in a triple international border municipality. J Global Infect Dis 2024;16:19-26.

Received: 18 April 2023 **Revised:** 03 September 2023
Accepted: 01 November 2023 **Published:** 18 March 2024

critically ill patients is important to guide decision-making in the public health.[4]

Border regions suffer a greater impact from the disease due to the virus transmission characteristics between humans, emergence of new variants, and the intense cross-border mobility, making new studies important with the objective of elucidating the epidemiological characteristics to determine which factors contribute to mortality.[4] Therefore, the objective of this study was to analyze the risk factors for death among hospitalized and nonhospitalized patients affected by COVID-19 in a triple international border municipality.

Methods

Design-setting

This is a retrospective cohort study conducted in Foz do Iguaçu, Brazil, which is part of a triple international border region (Brazil–Paraguay–Argentina). It is the main triple international border in South America given its position as an international tourism hub. The municipality was the first in this cross-border arrangement to register cases of severe acute respiratory syndrome (SARS)-CoV-2 infection.[5] Foz do Iguaçu recorded 80,635 cases of COVID-19 from March 2020 to October 2022, with an incidence of 31,257 cases/100,000 inhabitants and a lethality rate of 0.6%.[6]

The municipality has 589 hospital beds, 71% of which are provided by the Unified Health System (Sistema Único de Saúde [SUS]). Both SUS and the municipality's private services serve the local and regional population, as well as visitors and Argentine and Paraguayan citizens seeking access to the health system.[7]

Study participants and data collection

The study population consisted of all patients who were notified and confirmed for COVID-19 in Foz do Iguaçu, PR, from March 2020 to December 2021 from the Banco Notifica COVID-19 of the Municipal Epidemiological Surveillance Department.

Exclusion criteria

Cases without outcome information or death from other causes were excluded, as well as cases without information about hospitalization.

Outcome variables

The study variables included: hospitalization characteristics (length of stay, type of bed, and admission place); sociodemographic characteristics (gender, age, race/color, education, and occupation); clinical characteristics, which involve symptoms (cough, dyspnea, fever, intercostal retractions, and cyanosis) and comorbidities/risk factor (hypertension, diabetes, obesity, cardiovascular disease, smoking, lung disease, kidney disease, neurological disease, neoplasm, liver disease, immunodeficiency, and HIV infection); and outcome of cases.

Statistical analysis

Data were initially analyzed using descriptive statistical techniques such as absolute and relative frequency distribution for qualitative variables and central tendency (mean and median) and variability measures (standard deviation [SD] and Interquartile range [IIQ]) for quantitative variables, in order to evaluate the degree of data spread (dispersion) around the centrality measure. Finally, the existing strength of association between the presence of risk factors for death from COVID-19 between hospitalized and nonhospitalized patients was quantified by calculating the relative risk (RR). All analyzes were performed using the Software XlStat Version 2014 program- Statistical software for excel-By mail: 40, rue Damrémont, 75018 Paris.

Results

It was possible to identify 200,213 suspected cases of the disease through Banco Notifica COVID-19 notified in Foz do Iguaçu, Paraná, Brazil from March 2020 to December 2021. Of these, 34,955 (17.5%) were confirmed for COVID-19, of which 7491 (21.4%) cases without outcome information or which had death from other causes were excluded, as well as 2817 (8.1%) cases without information on hospitalization, leaving 24,647 cases remaining in the study. Among these, 22,211 (90.1%) were not hospitalized and 2436 (9.9%) were hospitalized.

The average length of stay of the cases that were hospitalized was 15 days (SD 20 days) and the median of this time was 9 days (interquartile range 4–20). The cases were hospitalized in SUS beds (1869, 89.2%) and private beds (226, 10.8%), being distributed in wards (1123, 52.1%) and ICU (1034, 47.9%). Among the cases that were hospitalized, 975 did not have information on the length of stay, 341 on the type of bed and 279 on the place of admission.

Sociodemographic profile of the COVID-19 cases notified in Foz do Iguaçu, hospitalized or not

Most patients who were hospitalized with COVID-19 were male (59.0%) and were aged between 40 and 79 years (76.4%), with a mean age of 57.1 years (SD 17.3). The most frequent race/color was white (48.9%), followed by brown (43.8%). Elementary school I (40.4%) and high school (27.2%) were the most frequent education levels achieved. Most cases (98.7%) had an occupation other than being a health or public safety professional [Table 1].

The majority of the reported cases of COVID-19 that were not hospitalized were female (55.3%) and were aged between 20 and 59 years (78.4%), with the average age being 37.1 years (SD 16.2). The most frequent race/color was white (53.9%). Most of the nonhospitalized cases had high school (28.6%) or higher (28.6%) education levels. The majority (97.7%) had another occupation in addition to health professional/student or laboratory or public safety professional [Table 1].

Clinical and risk factor profile of the COVID-19 cases notified in Foz do Iguaçu, hospitalized or not

Regarding the most frequent symptoms of hospitalized COVID-19 cases, 75.2% had cough, 70.3% dyspnea, and 58.3% fever. The most frequent comorbidities were: 59.0% hypertension, 37.2% diabetes, 28.6% obesity,

Table 1: Distribution of COVID-19 cases reported in Foz do Iguaçu, Paraná, Brazil, according to sociodemographic characteristics (2020–2021)

Variables	Categories	Hospitalization	
		Yes, *n* (%)	No, *n* (%)
Gender	Male	1438 (59.0)	9926 (44.7)
	Female	998 (41.0)	12,285 (55.3)
Age range*	0–2	21 (0.9)	291 (1.3)
	3–12	15 (0.6)	857 (3.9)
	13–19	16 (0.7)	1504 (6.8)
	20–29	97 (4.0)	5156 (23.2)
	30–39	212 (8.7)	5202 (23.4)
	40–49	393 (16.1)	4225 (19.0)
	50–59	549 (22.5)	2836 (12.8)
	60–69	512 (21.0)	1476 (6.6)
	70–79	409 (16.8)	502 (2.3)
	80–89	176 (7.2)	127 (0.6)
	90 or older	36 (1.5)	22 (0.1)
Race/skin color**	White	1023 (48.9)	10,761 (53.9)
	Brown	916 (43.8)	7206 (36.1)
	Yellow	93 (4.4)	1371 (6.9)
	Black	58 (2.8)	614 (3.1)
	Indigenous	2 (0.1)	26 (0.1)
Education**	Preschool/ kindergarten	5 (2.0)	4 (14.3)
	Elementary I	101 (40.4)	7 (25.0)
	Elementary II	45 (18.0)	1 (3.6)
	High School	68 (27.2)	8 (28.6)
	University	31 (12.4)	8 (28.6)
Occupation**	Worker/health professional	15 (1.0)	290 (1.7)
	Public safety professional	5 (0.3)	65 (0.4)
	Health-care student	-	24 (0.1)
	Laboratory worker/ professional	-	15 (0.1)
	Other	1537 (98.7)	16,463 (97.7)

**n* differs from the previously reported for nonhospitalized cases due to the absence of records in the database, ***n* differs from the previously reported for hospitalized and nonhospitalized cases due to the absence of records in the database. Source: This study, 2022

Table 2: Distribution of reported COVID-19 cases in Foz do Iguaçu, Paraná, Brazil, according to clinical characteristics and hospitalization (2020–2021)

Variables	Hospitalization	
	Yes, *n*/*N** (%)	No, *n*/*N** (%)
Symptoms		
Cough	1633/2171 (75.2)	2348/6346 (37.0)
Dyspnoea	1516/2156 (70.3)	1049/6224 (16.9)
Fever	1242/2130 (58.3)	2549/6300 (40.5)
Intercostal retraction	71/1973 (3.6)	102/6142 (1.7)
Cyanosis	58/2080 (2.8)	115/20,144 (0.6)
Comorbidities		
Hypertension	994/1685 (59.0)	721/3105 (23.2)
Diabetes	570/1532 (37.2)	284/2893 (9.8)
Obesity	411/1435 (28.6)	273/2868 (9.5)
Cardiovascular disease	338/1403 (24.1)	133/2806 (4.7)
Smoking	206/1357 (15.2)	327/2902 (11.3)
Lung disease	203/1359 (14.9)	196/2831 (6.9)
Kidney disease	136/1353 (10.1)	46/2778 (1.7)
Neurological disease	128/1345 (9.5)	39/2746 (1.4)
Neoplasm	67/1294 (5.2)	21/2731 (0.8)
Liver disease	41/1294 (3.2)	26/2738 (0.9)
Immunodeficiency	38/1296 (2.9)	27/2733 (1.0)
HIV infection	14/1290 (1.1)	14/2725 (0.5)

**N* differs from the previously reported for hospitalized and nonhospitalized cases due to blank data in the database. Source: This study, 2022

24.1% cardiovascular disease, 15.2% smoking, 14.9% lung disease, and 10.1% kidney disease. For the nonhospitalized COVID-19 cases, 40.5% had fever, 37.0% cough, and 16.9% dyspnea, while the most frequent comorbidities/risk factor were 23.2% hypertension and 11.3% smoking [Table 2].

Among the 2436 patients hospitalized for COVID-19, 947 (38.9%) died and 1489 (61.1%) recovered. Among the 22,211 outpatients, 93 (0.4%) died and 22,118 (99.6%) recovered.

Risk factors associated with death from COVID-19 cases among patients reported in Foz do Iguaçu who were hospitalized or not

An association between death from COVID-19 and the following sociodemographic characteristics was identified among the cases that were hospitalized: male gender; all age groups over 40 compared to the 30–39 age group; indigenous race/skin color in relation to white. Yellow race/skin color was considered a protective factor for death from COVID-19 among hospitalized cases. Occupation was not a factor associated with death among cases that were hospitalized. An association between death from COVID-19 and the following sociodemographic characteristics was identified among the cases that were not hospitalized: all age groups over 50 years old compared to the age group 30–39 years old. Race/color and occupation were not factors associated with death among cases that were not hospitalized [Table 3].

In addition, an association between death from COVID-19 and the following hospitalization characteristics was identified among the cases that were hospitalized: length of stay for more than 10 days, hospitalization in a private bed and in an ICU [Table 4].

An association between death from COVID-19 and the following symptoms was identified among the cases that were hospitalized: dyspnea, intercostal retraction, and cyanosis. Cough and fever were considered protective factors for death from COVID-19 among hospitalized cases. Furthermore, the following comorbidities/risk factor stand out as being associated with death among the cases that were hospitalized: hypertension, diabetes, obesity, cardiovascular disease, smoking, lung disease, kidney disease, neurological disease, neoplasia, and immunodeficiency. Finally, an association between death from COVID-19 and the following symptoms was identified among the cases that were not hospitalized: dyspnea and cyanosis; while the following

Table 3: Analysis of sociodemographic factors associated with death from COVID-19 according to hospitalization

Variables	Categories	Hospitalized cases			Nonhospitalized cases		
		Death, *n* (%)	Recovered, *n* (%)	RR (95% CI)	Death, *n* (%)	Recovered, *n* (%)	RR (95% CI)
Gender	Male	594 (62.7)	844 (56.7)	1.17 (1.05–1.30)	50 (53.8)	9876 (44.7)	1.44 (0.96–2.16)
	Female	353 (37.3)	645 (43.3)	1	43 (46.2)	12,242 (55.3)	1
Age range*	0–2	-	21 (1.4)	0.20 (0.01–3.28)	-	291 (1.3)	1.37 (0.08–24.27)
	3–12	1 (0.11)	14 (0.9)	0.61 (0.09–4.24)	-	857 (3.9)	0.47 (0.03–8.27)
	13–19	2 (0.21)	14 (0.9)	1.15 (0.30–4.46)	-	1.504 (6.8)	0.27 (0.02–4.72)
	20–29	11 (1.2)	86 (5.8)	1.05 (0.53–2.06)	1 (1.1)	5.155 (23.3)	0.17 (0.02–1.40)
	30–39	23 (2.4)	189 (12.7)	1	6 (6.5)	5.196 (23.5)	1
	40–49	82 (8.7)	311 (20.9)	1.92 (1.25–2.96)	6 (6.5)	4.219 (19.1)	1.23 (0.40–3.81)
	50–59	186 (19.6)	353 (24.4)	3.18 (2.13–4.76)	24 (25.8)	2.812 (12.7)	7.34 (3.00–17.93)
	60–69	238 (25.1)	274 (18.4)	4.28 (2.88–6.37)	19 (20.4)	1.457 (6.6)	11.16 (4.47–27.89)
	70–79	259 (27.4)	150 (10.1)	5.84 (3.94–8.65)	22 (23.7)	480 (2.2)	38.00 (15.48–93.27)
	80–89	115 (12.1)	61 (4.1)	6.02 (4.03–8.99)	11 (11.8)	116 (0.5)	75.09 (28.21–199.89)
	90 or older	30 (3.2)	6 (0.4)	7.68 (5.08–11.60)	4 (4.3)	18 (0.1)	157.64 (47.77–520.17)
Race/skin color**	White	399 (48.5)	624 (49.2)	1	51 (58.6)	10.710 (53.8)	1
	Brown	381 (46.3)	535 (42.2)	1.07 (0.96–1.19)	33 (37.9)	7.173 (36.1)	0.97 (0.62–1.50)
	Yellow	15 (1.8)	78 (6.2)	0.41 (0.26–0.66)	2 (2.3)	1.369 (6.9)	0.31 (0.08–1.26)
	Black	26 (3.2)	32 (2.5)	1.15 (0.86–1.54)	1 (1.2)	613 (3.1)	0.34 (0.05–2.48)
	Indigenous	2 (0.2)	-	2.56 (2.37–2.77)	-	26 (0.1)	3.87 (0.25–61.12)
Education**	Preschool/ kindergarten	4 (1.6)	1 (100.0)	-***	4 (25.0)	-	-***
	Elementary I	101 (40.6)	-		5 (31.3)	2 (16.7)	
	Elementary II	45 (18.1)	-		-	1 (8.3)	
	High school	68 (27.3)	-		5 (31.3)	3 (25.0)	
	University	31 (12.5)	-		2 (12.5)	6 (50.0)	
Occupation**	Worker/health professional	5 (0.8)	10 (1.1)	0.83 (0.41–1.71)	2 (2.9)	288 (1.7)	1.69 (0.42–6.88)
	Public safety professional	3 (0.5)	2 (0.2)	1.50 (0.73–3.07)	-	65 (0.4)	1.85 (0.12–29.54)
	Health-care student	-	-	–	-	24 (0.1)	4.88 (0.31–76.64)
	Laboratory worker/ professional	-	-	–	-	15 (0.1)	7.62 (0.49–117.88)
	Other	616 (98.7)	921 (98.7)	1	67 (97.1)	16,396 (97.7)	1

Foz do Iguacu, Paraná, Brazil. 2020–2021. **n* differs from the information previously reported for nonhospitalized cases due to the absence of records in the database, ***n* differs from the previously reported for hospitalized and nonhospitalized cases due to the absence of records in the database, ***RR was not calculated due to the precariousness of filling this variable in the database. Source: This study, 2022. CI: Confidence interval, RR: Relative risk

stand out among the comorbidities associated with death among cases that were not hospitalized: hypertension, diabetes, obesity, cardiovascular disease, kidney disease, neurological disease, neoplasia, and liver disease [Table 5].

Discussion

The present study identified several risk factors for death in patients hospitalized with COVID-19 in Foz do Iguaçu, Brazil, in particular male gender and age over 40 years. This is in line with studies carried out in countries on different continents, which also showed advanced age and male gender as risk factors for unfavorable outcomes from COVID-19.[2,3]

It is known that men have more behavioral risk factors such as smoking, present more comorbidities, and take less care of their health often arriving at the health service with a more advanced clinical condition than women.[8] Thus, a study suggests the need for care to be planned according to the patient's gender, since COVID-19 in men is associated with severe cases which require hospitalization and have worse prognoses.[8] In addition, people in more advanced age groups are more likely to develop SARS due to changes in immune functions and in the production of type 2 cytokines, leading to deficiencies in the control of SARS-CoV2 replication and pro-inflammatory response with a less rigorous immune response,[3] reinforcing the need to increase protective measures against COVID-19 proportionately as people age.[9] This recommendation is also valid for people who did not require hospitalization, since death was associated with age groups over 50 years.

An association of death from COVID-19 was identified for the indigenous race/skin color in relation to white patients among

Table 4: Analysis of hospitalization characteristics associated with death from COVID-19

Variables	Categories	Hospitalized cases		
		Death, *n* (%)	Recovered, *n* (%)	RR (95% CI)
Hospitalization time (days)*	0–10	194 (42.1)	625 (62.5)	1
	11–20	129 (28.0)	168 (16.8)	1.83 (1.53–2.19)
	21–30	72 (15.6)	78 (7.8)	2.03 (1.65–2.49)
	31 or more	66 (14.3)	129 (12.9)	1.43 (1.13–1.80)
Bed type*	SUS	730 (87.6)	1.139 (90.2)	1
	Private	103 (12.4)	123 (9.8)	1.17 (1.01–1.36)
Hospitalization location*	Ward	257 (28.6)	866 (68.8)	1
	ICU	641 (71.4)	393 (31.2)	2.71 (2.41–3.05)

Foz do Iguacu, Paraná, Brazil. 2020–2021. **n* differs from the previously reported for hospitalized cases due to the absence of records in the database. Source: This study, 2022. CI: Confidence interval, RR: Relative risk, SUS: Sistema Único De Saúde, ICU: Intensive care unit

Table 5: Analysis of clinical factors associated with death from COVID-19 according to hospitalization

Variables*	Categories	Hospitalized cases			Nonhospitalized cases		
		Death, *n* (%)	Recovered, *n* (%)	RR (95% CI)	Death, *n* (%)	Recovered, *n* (%)	RR (95% CI)
Symptoms							
Cough	Yes	620 (72.4)	1.013 (77.1)	0.86 (0.77–0.97)	41 (69.5)	3957 (62.9)	1.34 (0.77–2.32)
	No	237 (27.6)	301 (22.9)	1	18 (30.5)	2330 (37.1)	1
Dyspnoea	Yes	634 (74.4)	882 (67.6)	1.23 (1.09–1.39)	32 (56.1)	1017 (16.5)	6.31 (3.76–10.61)
	No	218 (25.6)	422 (32.4)	1	25 (43.9)	5150 (83.5)	1
Fever	Yes	449 (54.3)	793 (60.9)	0.85 (0.76–0.94)	23 (40.4)	2526 (40.5)	1.00 (0.59–1.69)
	No	378 (45.7)	510 (39.1)	1	34 (59.6)	3717 (59.5)	1
Intercostal retraction	Yes	46 (6.0)	25 (2.1)	1.70 (1.42–2.04)	3 (5.7)	99 (1.6)	2.97 (0.95–9.30)
	No	723 (94.0)	1.179 (97.9)	1	60 (94.3)	5990 (98.4)	1
Cyanosis	Yes	33 (4.2)	25 (1.9)	1.51 (1.20–1.90)	7 (9.2)	108 (0.5)	17.67 (8.30–37.61)
	No	762 (95.8)	1.260 (98.1)	1	69 (90.8)	19,960 (99.5)	1
Comorbidities							
Hypertension	Yes	541 (71.8)	453 (48.7)	1.77 (1.56–2.00)	37 (77.1)	684 (22.4)	11.12 (5.70–21.69)
	No	213 (28.2)	478 (51.3)	1	11 (22.9)	2373 (77.6)	1
Diabetes	Yes	307 (45.7)	263 (30.6)	1.42 (1.27–1.59)	22 (50.0)	262 (9.2)	9.19 (5.15–16.38)
	No	365 (54.3)	597 (69.4)	1	22 (50.0)	2587 (90.8)	1
Obesity	Yes	214 (33.9)	197 (24.5)	1.28 (1.14–1.44)	11 (26.2)	262 (9.3)	3.37 (1.71–6.63)
	No	417 (66.1)	607 (75.5)	1	31 (73.8)	2564 (90.7)	1
Cardiovascular disease	Yes	229 (36.8)	109 (14.0)	1.84 (1.65–2.04)	17 (39.5)	116 (4.2)	13.14 (7.31–23.61)
	No	393 (63.2)	672 (86.0)	1	26 (60.5)	2647 (95.8)	1
Smoking	Yes	105 (18.0)	101 (13.1)	1.22 (1.05–1.42)	4 (10.0)	323 (11.3)	0.88 (0.31–2.44)
	No	480 (82.0)	671 (86.9)	1	36 (90.0)	2539 (88.7)	1
Lung disease	Yes	139 (23.1)	64 (8.5)	1.71 (1.52–1.92)	3 (7.5)	193 (6.9)	1.09 (0.34–3.50)
	No	464 (76.9)	692 (91.5)	1	37 (92.5)	2598 (93.1)	1
Kidney disease	Yes	100 (16.6)	36 (4.8)	1.78 (1.57–2.00)	5 (12.2)	41 (1.5)	8.25 (3.39–20.06)
	No	504 (83.4)	713 (95.2)	1	36 (87.8)	2696 (98.5)	1
Neurological disease	Yes	77 (13.2)	51 (6.7)	1.45 (1.24–1.69)	11 (25.6)	28 (1.0)	23.86 (12.99–43.81)
	No	506 (86.8)	711 (93.3)	1	32 (74.4)	2675 (99.0)	1
Neoplasm	Yes	60 (10.5)	7 (1.0)	2.16 (1.94–2.40)	3 (7.3)	18 (0.7)	10.19 (3.41–30.43)
	No	509 (89.5)	718 (99.0)	1	38 (92.7)	2672 (99.3)	1
Liver disease	Yes	23 (4.1)	18 (2.5)	1.31 (0.99–1.73)	2 (5.3)	24 (0.9)	5.79 (1.47–22.82)
	No	537 (95.9)	716 (97.5)	1	36 (94.7)	2676 (99.1)	1
Immunodeficiency	Yes	24 (4.3)	14 (1.9)	1.47 (1.14–1.89)	1 (2.5)	26 (1.0)	2.57 (0.37–18.03)
	No	540 (95.7)	718 (98.1)	1	39 (97.5)	2667 (99.0)	1
HIV infection**	Yes	8 (1.4)	6 (0.8)	1.33 (0.84–2.11)	-	14 (0.5)	2.35 (0.15–36.48)
	No	547 (98.6)	729 (99.2)	1	38 (100.0)	2673 (99.5)	1

Foz do Iguacu, Paraná, Brazil. 2020–2021. **n* differs from the information previously reported for hospitalized and nonhospitalized cases due to the absence of records in the database, **RR was not calculated due to the precariousness of filling this variable in the database. Source: This study, 2022. CI: Confidence interval, RR: Relative risk

the cases that were hospitalized. The severity of the exposure of indigenous peoples to the new coronavirus is potentiated in the multiple adversities related to socioeconomic and health vulnerability with interethnic contact with high potential for spreading, resulting in high hospitalization rates and deaths.[10] As shown in this study, yellow ethnicity/skin color was considered a protective factor for death from COVID-19 among hospitalized cases. In contrast, Mascarello *et al*. study[11] found higher prevalence of negative outcomes among yellow skin color individuals.

Regarding sociodemographic characteristics, it was found that having an occupation focused on health or safety was not a risk factor for death, neither among people who required hospitalization nor among those who did not. This was an unexpected finding, as health professionals are at the forefront of dealing with COVID-19 cases, which can increase the chance of contagion and death compared to other professional activities; this result is possibly related to the fact that the category is composed of younger age people who have less comorbidities.[12]

Regarding the hospitalization characteristics, a length of stay longer than 10 days constituted a risk factor for death, showing that such time may reflect the severity of these cases, as well as those that required admission to the ICU. There was a slightly higher risk of death for hospitalization in a private bed compared to those hospitalized in SUS beds. This shows the potential of the performance of SUS health professionals due to the institutional learning of public services for the care of cases and for the provision of intensive and complex care. This result may also be a reflection of the large concentration of hospital beds (general and ICU) in the municipality in SUS hospitals for care of coronavirus victims, especially the most serious ones.[13]

The results also showed the clinical symptoms which indicated greater severity of the cases, including dyspnea, intercostal retraction, and cyanosis, which constituted risk factors for death. Other symptoms such as coughing and fever were protective factors for death, despite being very common among COVID-19 cases. Thus, the importance of risk stratification for the disease severity is emphasized, which, according to the Ministry of Health, should be carried out in a medical consultation through anamnesis and clinical diagnosis, as the signs and symptoms could indicate potentially serious cases and prone to respiratory syndrome, and consequently to death, especially in the period when there was a lack of laboratory tests.[14]

A study in Lombardy (Italy) showed that the most common comorbidity among hospitalized patients with COVID-19 was hypertension, affecting 49% of patients, followed by cardiovascular disease (21%).[15] The same occurred in New York in a study with 5700 individuals hospitalized for the disease, which revealed the most prevalent comorbidities to be arterial hypertension (56.6%), followed by obesity (41.7%) and diabetes mellitus (33.8%).[2] Thus, the results of these studies are in line with what was identified in this study carried out in Foz do Iguaçu, showing the importance that chronic conditions have when a patient is infected by COVID-19 and its consequences, highlighting the importance of establishing and strengthening health-care networks. This is similar to what is advocated by Mendes,[16] as health-care networks should also provide care according to the care model for such conditions, integrating health actions and services for health promotion and disease prevention, as well as for their recovery and rehabilitation. In turn, COVID-19 came to show the importance of the need for services to act in such a way which go beyond only reactive and focused action in acute conditions.

Hypertension constitutes the most common comorbidity in middle-aged and older adults globally, and comprises the group with the highest frequency of fatal COVID-19 cases.[17] A possible explanation for the severe conditions of COVID-19 in people affected by diabetes is due to the constant recognition of glucose by type C lectin receptors, generating greater inflammation in these individuals.[18] Furthermore, clinical data have shown that SARS-CoV-2 infection in these patients can trigger a stress condition and increased secretion of hyperglycemic hormones, causing an inflammatory and immune response with a propensity to rapidly develop acute respiratory distress syndrome, septic shock and multiple organ failure.[19] Scientific evidence has shown that patients with diabetes mellitus hospitalized with COVID-19 in fact have a long hospital stay, severe complications of the disease and higher mortality when compared to nondiabetic patients with COVID-19.[20]

An association was also identified between death from COVID-19 and obesity, both among hospitalized and nonhospitalized individuals. This finding is in line with other studies that show that such severity is evidenced by the combination of impaired cardiorespiratory reserve and compromised immune response to infection in individuals with obesity, which in turn results in a greater probability of death.[21] This risk is particularly pronounced in the USA, where obesity affects approximately 40% of the population, in Spain 24%, in Italy 20%, while in China it is 6.2%.[22] Thus, the COVID-19 pandemic seems to be more problematic in western countries and in Brazil, whose obesity affects 20.3% of the population,[23] further justifying the implementation of public health measures to prevent SARS-CoV2 infection and reduce the incidence of severe COVID-19.

Hospitalized smokers with COVID-19 had a greater chance of death compared to nonsmokers, which was also observed in other studies.[24] Since the onset of the COVID-19 pandemic, it has been identified that smokers are more vulnerable to infection by SARS-CoV-2 and its consequences, since it compromises lung capacity, which is the target organ of SARS-CoV-2, and the immune response. Another aspect is mechanical given the need to bring the hand to the face and lips for the act of smoking, not to mention sharing cigarettes or smoking equipment, which is also a source of air contamination due to the release of aerosols, affecting passive smokers.[25]

The association between death from COVID-19 and cardiovascular, pulmonary, renal and neurological diseases can be partly explained by the virus behavior, which can use the converting enzyme of the renin-angiotensin II system[26] as a receptor entry point of SARS-CoV2 by binding to its spike protein, facilitating viral entry into target cells,[18] and reaching the lung and various other tissues, such as the brain, kidney, gastrointestinal tract, and adipose tissue. Thus, these pathologies worsen when associated with COVID-19, with a sharp increase in pro-inflammatory cytokines[26] and consequently the occurrence of unfavorable outcomes such as death.

As in our study, neoplasms were reported by other studies as risk factors for death from COVID-19.[2,3,15] A Chinese study reports that cases with some type of malignancy are 3.5 times more likely to be admitted to the ICU, use invasive ventilation or evolve to death.[26] Another factor which has been described as associated with a worse prognosis in cases hospitalized for COVID-19 are immunodeficient patients. According to Matsura *et al*.,[27] it is possible that primary immunodeficiency causes more severe COVID-19 conditions by both direct action of the virus and by an inadequate inflammatory response, meaning that any type of immunodeficiency, whether genetic or extrinsic, has a higher risk of developing complications when infected by the SARS-CoV-2.

There was a statistical association for death among cases which were not hospitalized in the case of patients with liver disease. Liver injury is an important marker of worsening infection in individuals affected by the new coronavirus infection; an exacerbated increase in inflammatory cytokines has been described as a cytokine storm, and together with lymphopenia and decreased levels of CD4 + T-cells are associated with disease intensity and mortality.[28]

The presence of HIV was not associated with death from COVID-19 in the present analysis; in this case, it should be noted that the use of antiretroviral medication could be a protective factor against viral replication and preventing the release of mediators associated with the cytokine storm.[28]

In view of the above, the municipality's response to organize an emergency plan to face COVID-19 included training health teams, structuring the care network such as expanding hospital beds in wards and ICUs, hiring and training human resources, acquiring consumables and equipment, and accreditation of hospitals and laboratories.

Thus, this study can contribute to identifying potential risk markers for death from COVID-19 among hospitalized and nonhospitalized people, as well as to define strategies and tools for the care of the population affected by this disease according to the identified risk factors.

Limitation

This study may present an information bias due to the collection of secondary data, as some variables had a high rate of incompleteness. In addition, it is worth highlighting the difficulty in controlling confounding variables due to the type of analysis performed in the study. We chose to calculate the RR, since the option for a multivariate analysis would lead to an even greater sample loss than that presented in the study for certain variables.

Conclusions

This study showed that the risk of death from COVID-19 increased as people's age increased for both people who needed hospitalization and for those who did not, as well as among those who had signs and symptoms suggestive of the severity of the disease such as dyspnea and cyanosis. Risk factors for death regarding comorbidities were identified as hypertension, diabetes, obesity, and cardiovascular, kidney, and neurological diseases, as well as neoplasms. Male gender, indigenous race/skin color, hospitalizations for more than 10 days, in private beds and in the ICU were also associated with death from COVID-19 among people who required hospitalization, as well as the presence of intercostal retraction, smoking, lung disease, and immunodeficiency. Among those who did not require hospitalization, liver disease was also identified as a risk factor for death from COVID-19.

Thus, identifying factors associated with death from COVID-19 showed weaknesses which could have been better addressed by health-care networks in the period prior to the pandemic, especially modifiable risk factors such as obesity and smoking, as well as some preventable ones by better life habits such as hypertension and diabetes. It is also important to identify nonmodifiable risk factors for death from COVID-19 in the anamnesis and clinical evaluation to stratify the population regarding the risk of disease worsening and consequently death, in such a way as to provide care that is adequate and directed toward the identified risks. Finally, it is worth highlighting the vocation of the SUS for the care of complex cases that in many cases required intensive treatment, such as those studied herein.

Research quality and ethics statement

This study was approved by the Ethics Committee in Research Involving Human Beings at Human Beings of the Unioeste university, the project was approved (CAAE 49785121.6.0000.0107), according to consolidated opinion number 4.894.155 of August 9, 2021. The authors followed applicable EQUATOR Network (https://www.equator-network.org/) guidelines during the conduct of this research project.

Acknowledgment

The present work was performed with support from the Level Personnel Improvement Coordination Higher – Brasil (CAPES) PROAP.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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