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Clinical profile and factors associated with the death of COVID-19 patients in the first months of the pandemic

Perfil clínico e fatores associados ao óbito de pacientes COVID-19 nos primeiros meses da pandemia

Perfil clínico y factores asociados a la muerte de pacientes COVID-19 en los primeros meses de la pandemia

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ABSTRACT

Objective: to analyze the individual and clinical characteristics and the factors associated with mortality in patients with COVID-19, in a public hospital in the state of Paraná, Brazil. **Methods:** a cross-sectional, retrospective, documentary study (n= 86), with adult inpatients, from March to June 2020. **Results:** mortality was 12.8%, the highest risk group was the elderly with comorbidities, especially cardiovascular ones. The chance of death was 58 times higher in the elderly compared to adults, and eight times higher in those with comorbidities compared to the healthy ones. Most patients presented with respiratory symptoms, fever, and myalgia. Treatment was based on antibiotics, anticoagulants and antivirals, associated with ventilatory support. The main complications were hypoxia, acute renal failure, and secondary infection. **Conclusion and implications for practice:** elderly people with cardiovascular comorbidities who required intensive care had a higher chance of death. The results from one of the reference centers in the pandemic make it possible to discuss epidemiological measures adopted, with emphasis on restrictive concepts in the first months.

Keywords: COVID-19; Cross-Sectional Studies; Morbidity; Mortality; SARS-COV-2

RESUMEN

Objetivo: analizar las características individuales, clínicas y los factores asociados a la mortalidad en pacientes con COVID-19 en un hospital público del estado de Paraná. **Métodos:** estudio transversal, retrospectivo, documental (n = 86), con pacientes adultos hospitalizados, de marzo a junio de 2020. **Resultados:** la mortalidad fue del 12,8%, grupo de mayor riesgo para los ancianos con comorbilidades, especialmente enfermedades cardiovasculares. La probabilidad de muerte fue 58 veces mayor en los ancianos en comparación con los adultos y ocho veces mayor en aquellos con comorbilidades en comparación con los sanos. La mayoría de los pacientes presentaban síntomas respiratorios, fiebre y mialgia. Tratamiento a base de antibióticos, anticoagulantes y antivirales, asociado al soporte ventilatorio. Las principales complicaciones fueron hipoxia, insuficiencia renal aguda e infección secundaria. **Conclusión e implicaciones para la práctica:** los ancianos con comorbilidades cardiovasculares que requirieron cuidados intensivos tenían una mayor probabilidad de muerte. Los resultados de uno de los centros de referencia pandémica permiten discutir las medidas epidemiológicas adoptadas, con énfasis en conceptos restrictivos en los primeros meses.

Palabras clave: COVID-19; Estudios Transversales; Morbilidad; Mortalidad; SARS-COV-2.

RESUMO

Objetivo: analisar as características individuais, clínicas e os fatores associados à mortalidade de pacientes com COVID-19, em hospital público do estado do Paraná, Brasil. **Métodos:** estudo seccional, retrospectivo, documental (n= 86), com pacientes adultos internados, de março a junho de 2020. **Resultados:** a mortalidade foi de 12,8%, o grupo de maior risco foi de idosos com comorbidades, especialmente, cardiovasculares. A chance de óbito foi 58 vezes maior em idosos, comparada aos adultos, e oito vezes maior naqueles com comorbidades, comparadas aos hígidos. A maioria dos pacientes apresentou sintomatologia respiratória, febre e mialgia. Tratamento à base de antibióticos, anticoagulantes e antivirais, associado ao suporte ventilatório. As principais complicações foram hipóxia, insuficiência renal aguda e infecção secundária. **Conclusão e implicações para a prática:** idosos com comorbidades cardiovasculares que necessitaram de cuidados intensivos apresentaram maior chance de óbito. Os resultados de um dos centros de referência na pandemia possibilitam discutir medidas epidemiológicas adotadas, com ênfase em conceitos restritivos nos primeiros meses.

Palavras-chave: COVID-19; Estudos Transversais; Morbidade; Mortalidade; SARS-CoV-2.

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INTRODUCTION

The pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) revealed the importance of global health. This virus emerged in one country and spread rapidly to others, causing a crisis in the world health system[1].

In Brazil, the first case occurred in February 2020 and, initially, the cases were concentrated in the large metropolises, spreading from the capital cities to the municipalities[2]. Since the beginning of the disease in Brazil, until July 28, 2021, there have been more than 19 million cases and 551,835 deaths[3], being considered the country with the second highest number of deaths in the world.[4] In Curitiba, there are 258,679 cases and 6,642 deaths[5].

With the numbers of those infected and killed by SARS-CoV-2 growing exponentially, scientists are sparing no effort to learn more about the virus and Coronavirus Disease 2019 (COVID-19). Understanding how the virus affects people who are sick and knowing the proper treatment are challenges for all countries affected by the pandemic.

With the growth of cases, one of the public policies used to support people with COVID-19 was to increase the number of beds, both in wards and Intensive Care Units (ICU), although this increase was insufficient for the population's demand for hospital services.[6]

For an effective health action plan to combat the pandemic, a national health system is needed with data collection, quantifying the effect of the disease on the health care sector, data regarding the number of cases and deaths by age, gender, ethnicity, and care setting, stratified by health care area, such as ward and ICU[7].

Knowing the characteristics of patients who were hospitalized for COVID-19 offers subsidies to health professionals and managers to develop strategies for the population at higher risk of becoming ill, due to the probabilities of complications related to the disease and demand for a hospital bed[8].

The objective of this study was to analyze the individual and clinical characteristics and the factors associated with mortality in patients with COVID-19 in a public hospital in the state of Paraná, Brazil.

METHOD

This is a sectional, retrospective, analytical study that included a population of 86 adult patients with COVID-19 and admitted to a public hospital in the Southern Region of the country from March 26, 2020 to June 31, 2020.

The research was developed in a reference hospital for treatment of patients with COVID-19, in the capital. On March 23, 2020, the Institution was accredited, for the first time, in a center dedicated to this disease and, with the increase in demand, the hospital made specific units available for the treatment of those patients.

Adults who were hospitalized during the data collection period and met the established selection criteria participated in the study. Inclusion criteria were: hospitalized adult patients aged 18 years or older, confirmed diagnosis for COVID-19, clinical criteria, and positive result for real-time reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 in respiratory samples (nasopharyngeal and/or oropharyngeal swabs)[9].

Six medical records were excluded from the study because it was not possible to locate the record after five attempts, making data collection impossible. From a total of 92 eligible medical records for the study, six were excluded, totaling a sample of 86 records.

At the time of this research, there were two respiratory wards, I and II, located on the seventh and ninth floors, respectively, of the central building, with a total of 52 beds, and five COVID ICUs: COVID I and II which were located on the sixth floor; III, located on the 12th floor; IV, on the 13th floor; and V, on the third floor of the annex building, totaling 63 beds.

The units had a multidisciplinary team, including approximately 71 nurses, 182 technicians and 23 nursing assistants, respecting the dimensions recommended by the Federal Council of Nursing (COFEN).

The participants' data was obtained from paper records available at the Medical Archives and Statistics Service (MASS) and consolidated using an instrument designed by the researchers and developed with the support of an information technology specialist. The Visual Basic® (VBA) language was used in the Microsoft Excel 97® program. The data from the medical records were filled in by the health professionals of the institution that directly assisted the patient. This information was collected from the medical records and registered in the instrument previously tested by the research team, composed of two doctoral students, a nursing master's student and a nurse from the institution. Data collection occurred from September to November 2020.

The instrument comprised some variables, namely: individual and clinical conditions such as previous symptoms, comorbidities (by human body systems), complications during hospitalization, treatments instated during hospitalization, i.e., medications (antibiotics, anticoagulants, corticosteroids, antiretroviral therapy), and respiratory support (nasal catheter, high concentration mask with reservoir, mechanical ventilation, macro nebulization). The hospital discharge and death condition, defined in the medical record, was used as the outcome of the hospitalization.

The independent variables of social characterization were: sex (female and male), age (age groups), race (white, brown and black), origin (place of residence), marital status (married, single, widowed).

Categorical variables were presented as absolute numbers (n) and percentages (%) and analyzed by the Chi-square test for comparison of frequency and odds ratio, and Fisher's exact test. Continuous variables were represented by mean (M_e) and standard deviation (± SD). Statistical Package for the Social Sciences (SPSS 22.0) for Windows® software was used for data analysis. The variables age (< 65 years, ≥ 65 years), race (white, brown/black), comorbidity (yes, no) and number of comorbidities (one, two or more) were categorized for the statistical analyses. Values of $p<0.05$ were considered significant.

Because this was a retrospective analysis, informed consent was waived by the Research Ethics Committee, considering that the data was obtained directly from the clinical records, without using other collection techniques, such as interviews or physical examination. The study was approved by the Research Ethics Committee of the institution where the study was conducted, in accordance with Resolution 466/2012, according to opinion 4,183,502, in 2020.

RESULTS

Between March and June 2020, 92 patients diagnosed with COVID-19 were admitted to the study site; however, six medical records were excluded. The individual and demographic characteristics of the 86 patients analyzed in the period are described in Table 1.

It is possible to highlight a higher prevalence of death in people older than 65 years, white, from municipalities outside the state of Paraná (visitors), widowers and married. When evaluating the characteristics with the outcome, the analyses showed that there was no significant difference between males and females (p>0.05).

In ten medical records, there was information that the patient had not traveled outside the country; in the others, there was no data on recent international trips (n=76). About 17 had a history of close contact with a positive SARS-CoV-2 case, of which 16 were with a family member and one with another person. Nine had contact with suspected cases, of which eight were family members and one was a co-worker; the remaining 60 medical records had no information on contact with a suspected or confirmed case.

Of the total number of inpatients, 62 (72%) were admitted to the wards and 24 (28%) to the ICU, but five patients who were in the ward at some point required intensive care and were referred to the ICU, totaling 29 patients admitted to the ICU. The

Table 1. Individual and demographic characteristics (n=86). Curitiba, Paraná, Brazil, 2021.

Variables	Outcomes		*p-value**	n (%)
	Discharge	Death		
Sex				
Male	44(89.8)	5(10.2)	0.402	49 (57.0)
Female	31(83.8)	6(16.2)		37 (43.0)
Age group (years)				
18-29	7(87.5)	1(12.5)		8 (9.3)
30-49	30(100)	0		30 (34.9)
50-64	27(100)	0		27 (31.4)
≥65	11(52.4)	10(47.6)		21 (24.4)
White	53(85.5)	9(14.5)		62 (72.1)
Brown	13(100)	0		13 (15.1)
Black	7(100)	0		7 (8.1)
Not informed	2(50)	2(50.0)		4 (4.7)
Origin				
They live in the municipality of the hospital (Curitiba)	50(90.9)	5(9.1)		55 (64.0)
Metropolitan Region of Curitiba	19(86.4)	3(13.6)		22 (25.6)
Other municipality in Paraná	4(100)	0		4 (4.6)
Municipality outside of Paraná	1(50.0)	1(50.0)		2 (2.3)
Not informed	1(100)	0		3 (3.5)
Marital status				
Married/Stable Union	29(80.6)	7(19.4)		36 (41.9)
Single	16(94.1)	1(5.9)		17 (19.8)
Widow/er	4(80.0)	1(20.0)		5 (5.8)
Not informed	24(92.3)	2(7.7)		26 (30.2)
Total	**75(87.2)**	**11(12.8)**		**86 (100)**

SOURCE: research data, 2020.* Chi-square test.

minimum length of stay in both sectors was one day, in the wards the maximum was 33 days (M_e=7.6 and SD=(±)5.6) and in the ICU 28 days (M_e=9.5; SD=(±)8.4).

The previous symptoms, the complications developed during the hospitalization period, and the drugs used in the treatment are shown in Table 2.

The main symptoms described in the medical records were respiratory, such as cough and difficulty breathing, followed by fever and myalgia. The most prevalent complications were hypoxia, renal failure and secondary infection, and treatment was based on antibiotics, anticoagulants and antiretroviral drugs.

Regarding ventilatory support, approximately 85% (n=73) of patients required oxygenation. Most used nasal catheter (n=70), high concentration mask with reservoir (n=21) and invasive mechanical ventilation (IMV) (n=12). Only one patient required macronebulization and another required tracheostomy.

Of the total number of patients assisted in the hospital investigated, about 58.1% (n=50) had some type of prior comorbidity. It is noteworthy that 36 people had two or more comorbidities, and the main diseases were: 76%(n=38) cardiovascular, 22% (n=11) neurological, 12%(n=6) pulmonary, 2% (n=1) hepatic and 2% (n=1) nephrological.

Table 2. Clinical and drug treatment variables. Curitiba, Paraná, Brazil, 2021.

Variables	Yes (%)	No (%)
Symptoms		
Cough	66 (76.7)	22 (23.3)
Difficulty breathing	64 (74.4)	22 (25.6)
Fever	56 (65.1)	30 (34.9)
Muscle pain	40 (46.5)	46 (53.5)
Headache	24 (27.9)	62 (72.1)
Ageusia (absence or reduction in taste)	18 (20.9)	68 (79.1)
Diarrhea	18 (20.9)	68 (79.1)
Coryza	14 (16.3)	72 (83.7)
Fatigue	14 (16.3)	72 (83.7)
Anosmia (diminished or lost sense of smell)	13 (15.1)	73 (84.9)
Nausea	10 (11.6)	76 (88.4)
Sore throat	9 (10.5)	77 (89.5)
Emesis (vomiting)	9 (10.5)	77 (89.5)
Abdominal pain	4 (4.7)	82 (95.3)
Chills	1 (1.2)	85 (98.8)
Nasal Congestion	1 (1.2)	85 (98.8)
Complications		
Hypoxia	27 (31.4)	59 (68.6)
Acute Renal Failure	10 (11.6)	76 (88.4)
Secondary infection	8 (9.3)	78 (90.7)
Thromboembolic event	3 (3.5)	83 (96.5)
Apnea	2 (2.3)	84 (97.7)
Medication		
Azithromycin	78 (90.7)	8 (9.3)
Anticoagulants	74 (86.0)	12 (14.0)
Dexamethasone	46 (53.6)	40 (46.5)
Other antibiotics and antiviral (n=81)	56 (69.1)	25 (30.9)
Other Antibiotics (n=81)	19 (23.5)	62 (76.5)
Antiviral (n=81)	6 (7.4)	75 (92.6)

SOURCE: Research data, 2020.

Regarding the variables age, race and previous health conditions, Table 3 shows the analysis of the factors associated with the outcome.

During the first 128 days of the pandemic, 11 of 86 patients died, resulting in a mortality rate of 12.8%. Of these, 82% (n=9) died in the ICU and 18% (n=2) in the ward. Regarding gender, 54.5% (n=6) were women and 45.5% (n=5) were men.

The only young patient who died, aged between 18 and 29 years, was diagnosed with spinal cord tumor in the cervical region, after surgery for tumor resection. The chance of death in the population over 65 years of age was 58 times greater when compared to those under 65. Another factor to be highlighted in the analysis is the presence of comorbidities, since the chance of death for those with comorbidities was eight times higher when compared to the previously healthy population. Cardiovascular diseases stand out as those with the worst outcome.

DISCUSSION

This is one of the first studies exploring the characteristics of patients diagnosed with COVID-19, in a referral hospital, in the first months of the pandemic, in Curitiba, Brazil. The pandemic continues with no signs of remission, requiring systematic solutions.

With the appearance of the first cases in Curitiba, on March 12, 2020, the municipal government declared a public health emergency situation, on March 16, and declared the implementation

Table 3. Association of factors to the outcome discharge and death in patients with COVID-19 (n=86). Curitiba, Paraná, Brazil, 2021.

Variables	Outcomes		p-value*	*OR* (95%CI)
	Discharge	Death		
Age (years)			<0.001	
< 65	64(98.5)	1(1.5)		1
≥ 65	11(52.4)	10(47.6)		58.182 (6.756-500.918)
Race				
White	54(85.7)	9(14.3)	0.720	1.750 (0.349-8.781)
Brown/Black	21(91.3)	2(8.7)		1
Presence of comorbidity				
Yes	40(80.0)	10(20.0)	0.018	8.750 (1.066-71.818)
No	35(97.2)	1(2.8)		1
Number of comorbidities				
One	22(91.7)	2(8.3)		1
Two or more	27(75.0)	9(25.0)	0.095	3.667 (0.717-18.758)
Type of comorbidity				
Neurological				
Yes	8(72.7)	3(27.3)	0.145	3.141 (0.690-14.302)
No	67(89.3)	8(10.7)		1
Cardiovascular				
Yes	29(76.3)	9(23.7)	0.009	7.138 (1.440-35.393)
No	46(95.8)	2(4.2)		1
Pulmonary				
Yes	5(83.3)	1(16.7)	0.572	1.400 (0.148-13.242)
No	70(87.5)	10(12.5)		1

SOURCE: survey data, 2020. * Fisher's Exact Test.

of preventive and restrictive measures, such as suspension of events open to the public, of any nature, with agglomeration above fifty people, institution of telework, cancellation of the circulation of interstate passenger road transportation originating from all the federative units of the country and the Federal District, closing of shopping centers, galleries and similar establishments, gyms or fitness centers, schools and universities, among others. In addition to social distancing measures, hand hygiene, cough etiquette, and the use of masks[10]. The incidence rate of infection in Curitiba residents was the lowest among the ten most populated capitals in Brazil in the first two months of the pandemic[11].

During the first 128 days of the pandemic, 11 of 86 patients died, resulting in a mortality rate of 12.8%, of which 82% died in the ICU and 18% in the ward. This indicator denotes low prevalence, when compared to general hospital mortality in Brazil, which was 38% in the same period.[12] Results show that hospitalized patients with SARS-CoV-2 infection demand clinical and intensive nursing care.

The individual and demographic profile showed that most patients were male, white, married, under 65 years old and from Curitiba and the metropolitan region. International studies show a predominance of males and a median age of higher hospitalization in patients under 65 years of age[12-14]. A cohort carried out in Brazil showed a higher proportion of white people in the South Region, representing 88% of this population[12].

Most patients were admitted to the ward, but 33.7% required intensive care at some point. The average length of stay was seven days in the ward and nine days in the ICU.

In a study of 2,215 ICU cases in the United States of America (USA), the mean time from onset to ICU admission was seven days[15]. In a cohort conducted in Brazil, there was the same mean number of days for ICU admission[12]. According to a cohort study, almost 80% of all ICU admissions occurred within the first five days of admission. For all severe cases, about 40% were admitted to ICU, with 29% requiring IMV[13].

The survey showed a prevalence of respiratory symptoms, fever (65%), followed by myalgia (46%). According to the Ministry of Health (MH), the main symptoms related to COVID-19 are: fever (83%), cough (82%), shortness of breath (31%), and muscle pain (11%)[16]. A symptom survey smartphone application with more than 2 million participants in the USA and London showed that the main symptoms reported by patients were: anosmia and ageusia, adding up to 64.76%, cough (56.73%), chest pain (42.73%), lack of appetite (42.03%), and fever (34.34%)[1].

Symptoms of COVID-19 can appear as early as two to 14 days after exposure. The average incubation period is approximately 5.2 days. The transmissibility of infected patients is on average seven days after the onset of symptoms. However, transmission can occur even without the appearance of signs and symptoms[17,18].

The results of this study showed that 42% of the patients had two or more comorbidities, especially cardiovascular, neurological, and pulmonary. Patients with comorbidities, especially cardiovascular, had a higher chance of death.

The Health Surveillance Secretariat of the Brazilian Ministry of Health warns that the main comorbidities identified in patients diagnosed with COVID-19 are: heart disease, diabetes, neurological disease, kidney disease, and pneumopathy[19].

Another study also points out that people with cardiovascular disease are more likely to develop severe complications of COVID-19, including hospitalization and death[20].

In the USA, the Centers for Disease Control and Prevention (CDC), by monitoring in 14 states, through COVID-NET, a tool for monitoring the demographics of patients with COVID-19, shows that the main comorbidities related to hospitalization are cardiovascular disease (56.3%), obesity (48.2%), and diabetes (42%)[21].

The most prevalent complications were hypoxia, renal failure and secondary infection. Most required ventilatory support and 14% required IMV. In a cohort study, 36% of patients had renal failure, most of them being patients with IMV and comorbidities[22].

In critical respiratory diseases, IMV is an essential and effective treatment method to create an artificial airway, maintaining good ventilation and helping to control lung infections[23]. In a study conducted in Brazil, of those who required IMV, the rate was also 14% among the population studied[12].

As for the treatment used, the most used medication was azithromycin, followed by the use of anticoagulants and antiviral drugs in association with antibiotics.

Azithromycin is an antibiotic used mainly in bacterial lung infections, but in studies it has also been shown to have antiviral activity in vitro, acting against the SARS-CoV-2 virus, in addition to playing an immunomodulatory role, which can interrupt intense inflammatory responses that can potentially cause progression to organ failure and death from COVID-19[24]. In a study conducted in New York, this medication was the second most used in the treatment[14].

Another study points out that a high rate of D-dimer was associated with a worse outcome, increasing the need for intubation and thrombotic complications.[25] However, when using anticoagulants, it is essential that the professional be aware of the risk of bleeding that can be increased by the use of medication.

The mortality rate in this study was 12.8%. Elderly with cardiovascular comorbidities were associated with the worst outcome. The elderly, who are a vulnerable population, and patients with chronic conditions, such as diabetes and cardiovascular or pulmonary diseases, are not only at greater risk of developing serious diseases, but also of dying from the disease[18].

The CDC warns that the elderly are at greater risk of needing hospitalization or dying from a diagnosis of COVID-19. It also points out that people over 65 years old have a mortality rate that is 90 times higher compared to people 18 to 29 years old. When the age is over 85, this risk increases to 630 times higher[26].

The physiological changes of aging and age-related comorbidities, such as heart and lung disease, diabetes, dementia, and polypharmacy, are associated with unfavorable outcomes in older patients[27]. According to a study, in populations over 60 years of age, comorbidities present themselves as a risk factor[28].

Therefore, the profile of the population most associated with deaths, according to this study, comprises white men, aged over 65 years, with the presence of comorbidity, mainly cardiovascular disease.

This study examined the pandemic of COVID-19 from the point of view of a single center. However, it is emphasized that the municipal strategy led by the immediate epidemiologic measures in Curitiba during the pandemic resulted in relatively few severe patients and deaths compared to the rest of Brazil in the first months of the pandemic. Another limitation was the quality of the selected medical records, since many of them had incomplete data, which made it difficult to collect and analyze the data. Therefore, it is evident the relevance of planning measures to improve the quality of the records in the patient's medical record, as well as the development of actions towards a more adequate filling out, in order to provide improvement in the development of future research. One can also mention the type of study, since the cross-sectional design does not allow the establishment of the risk relationship. As a limitation, one can also mention the period and the restricted population, which directly influences the results and confidence intervals.

CONCLUSION AND IMPLICATIONS FOR PRACTICE

Mortality was 12.8%, and elderly patients with cardiovascular comorbidities had a higher chance of death. The main symptoms were cough, dyspnea, fever and myalgia, and one third of the patients required intensive care, as well as antibiotics, anticoagulants and antiviral drugs associated with ventilatory support. The main complications were hypoxia, renal failure, and secondary infection. The results of one of the reference centers in the pandemic make it possible to discuss epidemiological measures adopted, with emphasis on restrictive concepts in the first months of the pandemic.

AUTHOR'S CONTRIBUTIONS

Study design. Leticia Pontes. Mitzy Tannia Reichembach Danski. Jéssica de Fátima Gomes Pereira. Letícia Bettega Costa. Andrea Moreira Arrué.

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