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Risk factors associated with COVID-19-induced death in patients hospitalized in intensive care units (ICUs) in a city in Southern Brazil

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ABSTRACT

Objectives: The aim of this research was to address risk factors associated with death after hospitalization in intensive care units (ICUs) in 728 COVID-19 patients in Londrina, the second most populated city in the State of Paraná – Brazil, between March and December 2020.
Methods: Statistical analysis, including multiple logistic regression was performed to identify risk factors associated with death in these patients.
Results: The results showed that age (60 years or more, O.R. = 3.13, C.I. 95% [2.02; 4.84]), days in the ICU (11 days or more, O.R. = 1.76, C.I. 95% [1.16; 2.66]), neurological diseases (O.R. = 2.15, C.I. 95% [1.07; 4.31]), pneumopathy (O.R = 2.19, C.I. 95% [1.01; 4.82]), diabetes (O.R. = 1.55, C.I. 95% [1.03; 2.32]), and kidney disease (O.R. = 2.27, C.I. 95% [1.18; 4.70]) were associated with increased risk for death from COVID-19.
Conclusion: Knowing the risk factors associated with death after ICUs hospitalization is useful for identifying the most vulnerable groups, as well as for defining vaccination priorities, considering its scarcity in many parts of the world, mainly in underdeveloped countries, including Brazil.

1. Introduction

The COVID-19 started in Wuhan, Hubei, China, in December 2019 [1], spread rapidly to other locations around the world, and was classified as global pandemic by the World Health Organization (WHO) as of March 11, 2020 [2]. The rapid spread of COVID-19 is associated with the high transmissibility of the virus SARS-CoV2 [3], and the person-to-person transmission that occurs from asymptomatic COVID-19 subjects to others [4], increasing transmission.

Most people infected with COVID-19 are asymptomatic or with few symptoms such as anosmia, hyposmia, dysgeusia, shortness of breath, fever and fatigue [5–7]. More severe symptoms of COVID-19 include mild to severe acute respiratory distress, gastrointestinal, liver, cardiac, renal and pancreatic dysfunction, as well as central and peripheral neurological manifestations [8,9].

Brazil, with a population approximating 212,000,000 inhabitants had the first COVID-19 case confirmed on February 25, 2020, representing the first reported case of COVID-19 in South America [10]. On March 2021, Brazil was designated as the epicenter of COVID-19 with more than 2,000 deaths daily, more than 12 million cases overall, and over 300,000 deaths, globally ranking second in both cases and deaths in absolute numbers, second only to the United States [11].

The Brazilian Unified Health System ("Sistema Unico de Saude" - SUS) provides universal and free-of-charge access to a comprehensive set of healthcare services for the population [12]. According to Correa-Galendi et al. [13], about 70% of the population is exclusively insured with SUS and private insurance companies offer supplementary coverage.

The city of Londrina, located in northern State of Parana (one of the 26 Brazilian States, located in Southern Brazil), has an estimated population of 575,377 inhabitants according to IBGE [14], and it is the second most populous city in Parana. The first COVID-19 case in Londrina was confirmed on March 18, 2020, and immediately thereafter, the City Hall and the Paraná State Government established restrictive

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measures to contain the spread of the virus [15].

COVID-19 is novel disease, and its characteristics are recognized as the disease progresses. Indeed, issues related to mortality and risk factors are fluid, being updated in the course of the pandemic [16]. Even among newly reported studies, most COVID-19 prediction models still lack validation [17]. Taken together, and considering that further studies are needed to better understand the disease, the aim of this research was to describe the comorbidity profile of COVID-19 patients hospitalized in intensive care units (ICUs) in Londrina, and risk factors associated to death after hospitalization in ICUs.

2. Materials and methods

The Parana Health Administration is divided in 22 "Health-Regions" (HR). The city of Londrina is the headquarters of the second most authoritative HR in the State (shown as 17th HR in Fig. 1).

Data provided by the City Health Secretary of Londrina identified 728 patients admitted to ICUs with COVID-19 diagnosis. Additional information such as age, comorbidities and number of days in the ICUs was obtained. Data collection was carried out from the first case of COVID-19 identified in Londrina, March 18, 2020, through December 31, 2020. This research was approved by the Ethical Committee of the State University of Londrina, protocol nº 36044520.5.0000.5231.

To identify risk factors associated with death from COVID-19 after hospitalization in the ICUs, we performed univariate and multiple logistic regression, considering death (yes/no) as a response variable, and age, comorbidities and days in ICU as explanatory variables. All analyses were conducted with software R [18].

3. Results

The first three patients diagnosed with COVID-19 in Londrina presented symptoms on March 9, 2020, upon return from international travel; two of them from the USA and one from Italy. COVID-19 was confirmed in these patients on March 18. The first ICU hospitalization from COVID-19 in Londrina took place March 21, 2020. The patient was a 33-year-old woman who was hospitalized for 15 days and recovered and discharged. The first death by COVID-19 after ICU hospitalization was a 69-year-old male patient who was admitted to the ICU on March 22, 2020, and died on April 6, 2020. By the end of December 2020, Londrina had registered 21,873 COVID-19 cases. Of those 20,908 recovered and the remainder (436) died.

From the 728 COVID-19 patients that were admitted to the ICU between March and December 2020, 363 recovered from the disease and 365 died. Most patients in both groups were male, i.e. 56.5% in the recovered group and 61.6% in the group of patients that died. In the latter group, the majority (82.7%) were elderly (60-years or older), while in the recovered group 49.6% were in this age range (Table 1). For the analysis of associated factors related to death by COVID-19 after ICU hospitalization, the following variables were considered: gender, age, days in ICU, neurological disease, pneumopathy, diabetes, kidney disease, obesity and heart disease. Hematological disease, Down's syndrome, liver disease, asthma and immune depressive variables were also available, but were not included in the analysis, given that greater than 95% of COVID-19 patients in both groups did not clinically present with these comorbidities. The results of the univariate and multiple logistic regression with the respective unadjusted O.R. and adjusted O.R. are presented in Table 1.

In the univariate analysis, the associated factors with death after ICU hospitalization were age (60 years or greater, O.R. = 4.87, C.I. 95% [3.47; 6.85]), days in ICU (11 days or more, O.R. = 1.97, C.I. 95% [1.38; 2.81]), neurological diseases (O.R. = 2.07, C.I. 95% [1.22; 3.51]), pneumopathy (O.R = 2.70, C.I. 95% [1.44; 5.06]), diabetes (O.R. = 1.85, C.I. 95% [1.33; 2.58]) and kidney diseases (O.R. = 2.22, C.I. 95% [1.34; 3.67]). The variables gender (p-value = 0.16), obesity (p-value = 0.87) and heart disease (p-value = 0.12) were not associated to death after ICU hospitalization in the univariate analysis (Table 1).

Multiple logistic regression was performed to identify confounding variables. The variables included in the model were the associated variables in the univariate analysis (p-value < 0.05). In the multiple logistic regression the associated variables remained the same as in the univariate analysis: age (60 years or greater, O.R. = 3.13, C.I. 95% [2.02; 4.84]), days in ICU (11 days or more, O.R. = 1.76, C.I. 95% [1.16; 2.66]), neurological diseases (O.R. = 2.15, C.I. 95% [1.07; 4.31]), pneumopathy (O.R = 2.19, C.I. 95% [1.01; 4.82]), diabetes (O.R. = 1.55, C.I. 95% [1.03; 2.32]) and kidney diseases (O.R. = 2.27, C.I. 95% [1.18; 4.70]), establishing these as risk factors for death in ICU hospitalized COVID-19 patients.

4. Discussion

Our results corroborated the previously described association between risk of death from COVID-19 and age greater than 60 [16,19–23] or 65 years [17,24].

Kidney disease was also previously associated with deaths and/or higher risk of severe cases [17,21]. A past history of chronic kidney disease can be one possible explanation, considering that it may lead to a proinflammatory state with functional defects in innate and adaptive immune cell populations and consequently may result in a higher risk

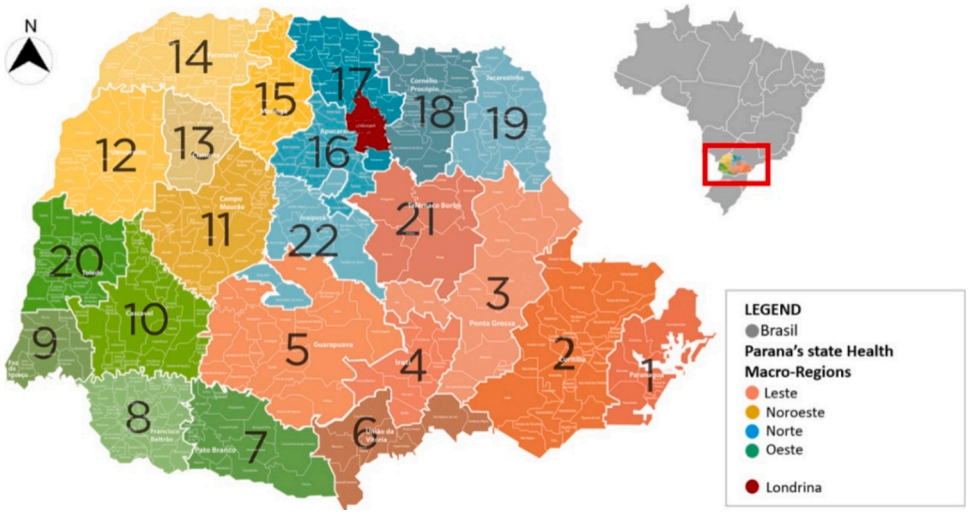

Fig. 1. Location of Londrina city situated in the north of the State of Parana (divided in 22 "Health- Regions") – Brazil.

Table 1
Summary of the variables and results of the univariate and multiple logistic regression.

Variables	Recovered (n = 363)	Died (n = 365)	Unadjusted O.R.	C.I. (95 %)	p-value*	Adjusted O.R.	C.I. (95 %)	p-value**
Gender					0.16			
Female	43.5%	38.4%	1					
Male	56.5%	61.6%	1.24	0.92; 1.67				
Age					< 0.01			< 0.01
Until 59 years	50.4%	17.3%	1			1		
60 years or more	49.6%	82.7%	4.87	3.47; 6.85		3.13	2.02; 4.84	
Days in ITU					< 0.01			< 0.01
Up to 10 days	26.3%	41.2%	1			1		
11 days or more	73.7%	58.8%	1.97	1.38; 2.81		1.76	1.16; 2.66	
Neurological disease					< 0.01			0.03
No	92.0%	84.7%	1			1		
Yes	8.0%	15.3%	2.07	1.22; 3.51		2.15	1.07; 4.31	
Pneumopathy					< 0.01			0.05
No	94.9%	87.3%	1			1		
Yes	5.1%	12.7%	2.7	1.44; 5.06		2.19	1.01; 4.82	
Diabetes					< 0.01			0.03
No	67.5%	52.9%	1			1		
Yes	32.5%	47.1%	1.85	1.33; 2.58		1.55	1.03; 2.32	
Kidney disease					< 0.01			0.01
No	91.4%	82.7%	1					
Yes	8.6%	17.3%	2.22	1.34; 3.67		2.27	1.18; 4.40	
Obesity					0.87			
No	86.3%	86.8%	1					
Yes	13.7%	13.2%	0.96	0.60; 1.53				
Heart disease					0.12			
No	41.5%	35.3%	1					
Yes	58.5%	64.7%	1.3	0.94; 1.80				

* p-value obtained in the univariate logistic regression.
** p-value obtained in the multiple logistic regression.

for upper respiratory tract infection and pneumonia [22]. Additionally, patients with COVID-19 that develop acute kidney injury with an abrupt loss of kidney function, may also be at increased risk of mortality and morbidity [22].

We observed lack of evidence for an association between gender and death after ICU hospitalization, unlike other studies where being a male was a predictor for hospital death [23–25].

Moreover, fewer than 10% of the population in Brazil and particularly in Londrina have been exposed to the virus until the end of December 2020, and therefore, the results may vary over time as additional cases are identified.

As long as the population is not immunized against the virus, it is hard to predict when the COVID-19 pandemic will end, especially considering the rising number of novel viral variants. Therefore, greater knowledge of risk factors associated with death upon ICU admission of COVID-19 patients is essential, not only for overcoming the disease, but also for future challenges, including group prioritization for immunization and preventive campaigns given the shortage of vaccines and the lack of global vaccine strategy [26].

5. Conclusions

This research addressed risk factors associated to death from COVID-19 in ICU hospitalized patients in Londrina, Brazil, between March and December of 2020. Both univariate and multivariate analysis showed similar results, validating the variables as being relevant. Age greater than 60 years, neurological disease, pneumopathy, diabetes and kidney disease were associated with increased death among ICU hospitalized patients.

Although there are several publications on this topic, gaps to be better characterized remain; the differences obtained in the surveys indicate that social, economic, and political contexts, to name a few, can influence the health status of a population. This study contributes to the identification of risk factors associated with COVID-19, in addition to corroborating earlier research.

Author statement

A.S. Olak: Conceptualization, statistics, original draft preparation; A. M. Susuki: conceptualization, original draft preparation; M. Kanashiro: original draft preparation; M.M.B. Paoliello: conceptualization, reviewing and editing; M. Aschner: conceptualization, reviewing and editing; M.R. Urbano: Conceptualization, statistics, original draft preparation, reviewing.

Declaration of Competing Interest

The authors declare no conflict of interest.

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