IJCIM
International Journal of Complementary and Internal Medicine

RESEARCH ARTICLE

Factors associated with mortality in patients affected by COVID-19

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Received: July 22, 2025 **Published:** August 18, 2025

Citation: Cindhy SM. Factors associated with mortality in patients affected by COVID-19. Int J Complement Intern Med. 2025;6(4):418–426. DOI: 10.58349/IJCIM.4.6.2025.00157

Abstract

Objective: To investigate the clinical conditions and sociodemographic characteristics associated with mortality due to COVID-19 during the first year of the pandemic in an intensive care unit in a capital city in northeastern Brazil.

Method: This was an exploratory, retrospective documentary study based on secondary data obtained from medical records of patients admitted to an intensive care unit of a public hospital in northeastern Brazil. Data collection occurred between July and September 2021. The data were analyzed via descriptive and inferential statistics. The chi-square test, Fisher's exact test, Student's t test, and binary logistic regression modeling were employed. The study was approved by the Research Ethics Committee.

Results: A total of 274 patients, predominantly male, mixed-race, and aged over 65 years, were included. The variables male sex, age 65 years or older, marital status (married), and length of hospital stay were significantly associated with clinical outcomes. Logistic regression analysis revealed that male individuals, those aged 65 years or older,

those requiring invasive mechanical ventilation, and patients in the prone position had higher odds of mortality as an outcome.

Conclusions: Observing the factors associated with mortality outcomes in patients affected by novel coronavirus infection can aid healthcare professionals and public health managers in decision-making.

Keywords: Coronavirus infections; mortality; public health; critical care; epidemiology

Introduction

The novel coronavirus is an insidious virus with high transmissibility that is capable of causing conditions ranging from mild colds to severe respiratory symptoms. In 2020, the SARS-CoV-2 pandemic was declared, with transmission occurring primarily through direct contact via droplets or aerosols.[1]

Some patients affected by COVID-19 develop severe complications, potentially progressing to acute respiratory distress syndrome (ARDS), kidney injury, cardiopathies, and secondary infections, among other conditions. Consequently, these patients require life-support therapies, such as invasive mechanical ventilation (IMV), renal replacement therapy, and prolonged hospitalizations in intensive care units (ICUs). Nearly four years later, significant questions have been answered, and mechanisms to combat the disease, such as the adoption of vaccination protocols, have been developed. However, despite these efforts, the virus still accounts for high rates of transmission in various regions worldwide.[2,3]

Importantly, the high mortality rate associated with SARS-CoV-2 is due primarily to progressive respiratory failure resulting from lung damage.[4] Although the clinical manifestations are predominantly related to the respiratory system, there is evidence indicating the involvement of the cardiovascular system, leading to various complications, such as heart failure, myocardial injury, arrhythmias, myocarditis, and shock. These complications can result in multiple organ failure and, consequently, death.[5]

Additionally, a high number of COVID-19 cases have been reported among males, who appear to be more susceptible to developing the disease, including its severe form.[6] With respect to age groups, individuals aged 60–69 years are the most affected. Studies have also revealed that compared with older females, older males exhibit significantly abnormal laboratory results, with higher levels of inflammatory biomarkers. Furthermore, comorbidities can exacerbate the clinical condition of infected patients.[7,8]

The most frequent comorbidities include respiratory problems, cardiopathies, diabetes mellitus (DM), systemic arterial hypertension (SAH), and obesity. Cardiopathies are more common and have a poorer prognosis for patients affected by the novel coronavirus. In this context, chronic pulmonary diseases and smoking habits are also associated with more severe prognoses. Moreover, the literature highlights obesity as the third most common comorbidity among deaths in individuals under 60 years of age.[8,9]

Thus, it is crucial to understand the clinical and sociodemographic aspects that can predict mortality in patients affected by COVID-19. This understanding enhances healthcare professionals' knowledge regarding the causes of death caused by SARS-CoV-2, allowing for improved care practices for these patients. Therefore, the present study aimed to answer the following question: What are the factors that can act as predictors of mortality in patients affected by SARS-CoV-2? Consequently, the objective of this study was to investigate the clinical conditions and sociodemographic characteristics associated with mortality from COVID-19 during the first year of the pandemic in an intensive care unit in a capital city in northeastern Brazil.

Method

This was an exploratory, descriptive, retrospective documentary study based on secondary data obtained through the analysis of medical records from an ICU in a public hospital in a capital city in northeastern Brazil, a referral center for treating patients affected by COVID-19. The study followed the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

The study population consisted of all patients who tested positive for SARS-CoV-2 and were admitted between May 2020 and May 2021 to the aforementioned health unit, totaling 903 patients. The sample was determined probabilistically via a simple random sampling technique. The sample size was calculated via the following formula: $n = Z^2PQ/d^2$, where n = minimum sample size, Z = standard score, P = probability of observing the phenomenon studied, Q = 1-P, and d = desired precision. A value of p = 50% was used for the multidimensional evaluation, with a sampling error parameter of 5%. The final sample consisted of 274 patients.

The study included individuals of both genders, aged 18 years or older, with a confirmed diagnosis of COVID-19. The exclusion criteria included medical records of patients who arrived at the destination unit in cardiopulmonary arrest, as well as records with incomplete or illegible information.

Data collection was conducted between July and September 2021 by analyzing medical records provided by the Medical and Statistical Records Service of the investigated unit. A structured instrument was used to include questions relevant to the study's objectives, such as sociodemographic data and associated clinical conditions. Additionally, clinical outcomes and laboratory test results were assessed to identify factors contributing to the outcomes.

The collected data were compiled and stored via Microsoft Office Excel® and later imported into the Statistical Package for the Social Sciences (SPSS®), version 25.0, which was chosen for its suitability in achieving the study objectives and for ensuring result precision and generalization. Data analysis was performed quantitatively via univariate descriptive statistics. Categorical data were analyzed via absolute and relative frequency distributions, whereas continuous variables were summarized via means, ranges, and standard deviations.

To evaluate associations between categorical variables, the chi-square test was used, with a statistical significance level of $p<0.05$ and a 95% confidence interval (CI). When the chi-square test could not be performed, Fisher's exact test was employed. Subgroups were further analyzed via the Shapiro–Wilk normality test. For normally distributed dependent variables, such as age, length of hospital stay, number of complaints, duration of symptoms, and number of comorbidities, Student's t test was applied, with statistical significance set at $p<0.05$.

Multivariate analysis was then conducted via a binary logistic regression model to evaluate factors associated with COVID-19 mortality. The backward stepwise method was used to select all independent variables with $p<0.20$. Model adequacy was assessed through randomized quantile residual analysis and testing for multicollinearity via the variance inflation factor (VIF). Statistically significant variables were defined as those with $p<0.05$. The magnitude of associations was estimated via odds ratios (ORs), with a 95% CI used as the measure of accuracy and precision. The final model adjustments were evaluated via the deviance Homer–Lemeshow test.

Notably, throughout the research process, particularly during data collection, ethical principles governing research involving human subjects, as outlined in Resolution 466/2012 of the Brazilian National Health Council (CNS/MS/BRAZIL), were strictly observed, especially with respect to confidentiality and data privacy. The study was reviewed and approved by the Research Ethics Committee (CEP) under approval number 4.077.113.

Results

A total of 274 patients were included in the study, the majority of whom were male (57.7%), aged 65 years or older (51.5%), married (45.2%), mixed-race (75.6%), and had completed elementary education (34.0%). The associations between sociodemographic characteristics and clinical outcomes revealed that the variables male sex (p=0.02) and marital status (married) (p=0.02) were statistically significant (Table 1).

Discussion

The SARS-CoV-2 virus has significant infectivity and potential for clinical deterioration. With respect to individual characteristics, this study revealed a greater incidence of death among male patients, corroborating the findings of a cohort study conducted in Italy involving 3,988 critically ill patients with SARS-CoV-2 admitted to ICUs, where 700 (50.1%) male patients died.[10]

In this context, epidemiological data show that male individuals have a greater probability of developing COVID-19, as well as higher rates of disease severity and mortality.[11] A study conducted in Italy revealed that the mortality rate of men is up to 1.74 times higher than that of women.[12]

Table 1. Association between sociodemographic characteristics and clinical outcomes in patients affected by COVID-19. Northeast Brazil, 2021

Variables	Discharge n (%)	Death n (%)	p value
Sex			0,02*
Female	27 (32,1)	89 (46,8)	
Male	57 (67,9)	101 (53,2)	
Total	84 (100)	190 (100)	
Marital Status			0,02*
Married	40 (57,1)	63 (39,9)	
Widowed	09 (12,9)	42 (26,6)	
Single	18 (25,7)	38 (24,0)	
Divorced	03 (04,3)	15 (09,5)	
Total	70 (100)	158 (100)	
Cor			0,13†
Brown	44 (74,5)	102 (76,1)	
White	15 (25,4)	25 (18,7)	
Black	-	07 (05,2)	
Total	59 (100)	134 (100)	
Education			0,22†
Illiterate	04 (15,4)	18 (25,3)	
Incomplete Primary	06 (23,0)	17 (24,0)	
Completed Primary	07 (27,0)	26 (36,6)	
Incomplete Secondary	01(03,8)	01 (01,4)	
Higher Education	08 (30,8)	09 (12,7)	
Total	26 (100)	71 (100)	

Source: Research data, 2021. *Chi-square test; †Fisher's exact test.
Note: Not all patients had complete demographic and clinical data collected at admission. Therefore, the number of patients is indicated for each variable.

With respect to the associations between clinical characteristics, hospital stay, and patient outcomes, age (p=0.00) and length of hospital stay (p=0.03) were statistically significant (Table 2).

Table 2. Association between clinical characteristics, length of hospital stay, and outcomes of patients affected by COVID-19. Northeast Brazil, 2021

Variables	Clinical outcome		p value
	Discharge	Death	
	Média ± DP†	Média ± DP†	
Age	57,93±15,55	65,87±14,47	0,00*
Length of hospital stay	16,37±8,50	13,73±9,90	0,03*
Number of complaints	2,67±0,98	2,70±1,1	0,84*
Days with complaints	7,61±3,76	6,75±3,49	0,07*
Number of comorbidities	1,26±0,94	1,35±1,01	0,48*

Source: Research data, 2021. *Student's t test; †SD = standard deviation.

The logistic regression analysis revealed that male individuals (OR: 1.86, p=0.00), those aged 65 years or older (OR: 2.66, p=0.00), those under invasive mechanical ventilation (OR: 7.47, p=0.000), and those subjected to the prone positioning technique (OR: 4.17, p=0.00) had greater odds of death.

Table 3. Variables associated with COVID-19 mortality in patients admitted to the ICU through binary logistic regression. Northeast Brazil, 2021

Variables	OR*	95% CI†	p value
Sex			0,00
Male	1,86	1,08 -3,19	
Female	1,00	-	
Age group			0,00
18 to 64 years	1,00	-	
65 anos or older	2,66	1,55 -4,57	
Invasive mechanical ventilation			0,00
Yes	7,47	3,09 -18,0	
No	1,00	-	
Prone positioning technique			0,00
Yes	4,17	2,36 –7,35	
No	1,00	-	

Source: Research data, 2021. *OR: odds ratio; †95% CI: 95% confidence interval.

This phenomenon may be associated with differences between males and females, such as sexual dimorphism; hormonal, genetic, social, and behavioral factors; and immune responses.[11–14] In addition to the social roles that increase male exposure to the virus, women tend to develop more robust innate and adaptive immune responses, as estrogen stimulates B-cell growth and antibody production, thereby enhancing immunity in women.[12,14,15]

Furthermore, the biochemical signaling mediated by estrogen regulates anti-inflammatory action, reducing the production of proinflammatory substances and thus preventing the cytokine storm. As a result, a more balanced immune response occurs in female individuals than in male individuals, providing superior antiviral defense.[12,14,15]

SARS-CoV-2 is an enveloped virus with a single RNA strand that enters host cells via a transmembrane protein called angiotensin-converting enzyme 2 (ACE2), which is expressed on the surface of various body cells, such as those in the respiratory epithelium. Sex hormones genetically influence the expression of this receptor, which is more prominent in male tissues.[13,15]

Studies have shown that male plasma has a greater concentration of ACE2 than female plasma does, which implies significant tissue expression, particularly in pulmonary tissues. In differentiated epithelial cells of the airways, estrogen may inhibit ACE2, whereas testosterone increases receptor expression, thereby increasing the probability of infection by the virus responsible for COVID-19. Additionally, tobacco use and alcohol consumption, which are significantly associated with male sex, are linked to the development of noncommunicable chronic diseases such as hypertension, diabetes, renal diseases, and cardiovascular conditions, all of which contribute to increased mortality risk.[12,15]

The mean age of the patients who died was 65.87 years, according to the data presented in this study. In this context, binary logistic regression revealed that individuals aged 65 years or older were 2.66 times more likely to die than other age groups were. Research conducted in China has shown that mortality increases with age, with individuals aged 40 years or younger having a case fatality rate of 0.4%, 3.6% among those aged 60 years, 8% among those aged 70 years, and approximately 14.8% among people aged 80 years or older.[16]

Although the incidence of COVID-19 is greater among adults, lethality is more significant in the elderly population because of the presence of comorbidities, which constitute an important risk factor for mortality. Additionally, physiological changes associated with aging, such as immunosenescence, increase the risk of developing infections.[17]

With respect to the length of hospitalization, a study conducted in Brazil reported an average duration of 12–14 days from admission to death, corroborating the data obtained in the present study.[18] Conversely, a retrospective study conducted in Wuhan, China, reported lower figures, with an average hospitalization duration until death of seven days.[19]

In this context, a strong relationship has been observed between the number of days hospitalized and mortality in patients, particularly among those with a prior history of hypertension, diabetes mellitus, cardiac diseases, respiratory conditions, and neoplasms.[20] Additionally, this patient profile is predisposed to complications that lead to prolonged hospitalization and a higher risk of mortality, especially when patients are subjected to the use of invasive devices, such as orotracheal tubes.[3]

During the pandemic, high mortality rates were observed among patients affected by the novel coronavirus who required invasive ventilatory support. Like other pneumonias, lung injury caused by SARS-CoV-2 leads to destruction of the lung parenchyma, resulting in extensive consolidation and interstitial inflammation.[21] For this reason, invasive mechanical ventilation (IMV) is a therapeutic modality of choice for patients who develop respiratory complications, as the use of the device allows the pulmonary musculature to rest and ensures appropriate oxygenation.[22]

Although recognized as one of the main options for maintaining respiratory function in critically ill patients, the use of IMV in patients affected by COVID-19 is associated with a significant mortality rate, which can range from 30% to 97%, even after the adoption of protective parameters.[23]

A study conducted with individuals admitted to Italian hospitals revealed that, among the 350 patients receiving oxygen therapy through nasal cannulas or reservoir masks, 127 patients (7.4%) died; however, among the 2,929 patients receiving IMV via orotracheal intubation, 1,514 (13.0%) died.[24]

The prolonged use of IMV can lead to significant complications, which can be classified as pulmonary or nonpulmonary. Among these, ventilator-associated pneumonia (VAP) stands out as the most frequent complication in patients with COVID-19 because of the associations between viral infection and other etiologies, microaspiration from the oropharyngeal cavity, mucociliary impairment, and reduced cough efficiency caused by excessive sedation and prolonged ventilation.[24] The choice of care method should be based on clinical criteria, as patients affected by COVID-19 are more likely to develop barotrauma—a condition in which alveolar rupture occurs, resulting in the entry of air into the extra-alveolar space. A study conducted in 38 hospitals in Italy revealed a higher incidence of barotrauma following the use of IMV in patients diagnosed with the disease.[24,25]

In this context, a study conducted with 601 coronavirus-infected patients undergoing invasive mechanical ventilation (IMV) revealed that approximately 15% developed barotrauma following the use of this therapy. Notably, the high mortality rate can be partially explained by multiple organ failure and other complications inherent to SARS-CoV-2 infection, as well as prolonged stays in the intensive care unit (ICU).[26]

Among the procedures adopted for patient treatment, the prone position (PP) stands out. With the aim of improving oxygenation, PP enhances pulmonary homogeneity, compliance, and redistribution, in addition to increasing the proportion recruited for infiltration and pulmonary function.[27–29] Regarding the pronation technique, a study analyzing the medical records of 170 patients diagnosed with the novel coronavirus demonstrated that a significant percentage of those subjected to the prone position progressed to death. In the mentioned study, of the 119 patients who required orotracheal intubation (OTI), 60 (50.42%) needed PP, 38 (63.3%) of whom died.[29]

Although it yields good results, PP requires continuous nursing care, as one of its main complications is the risk of developing pressure injuries (PIs). Prolonged ventral decubitus, combined with the use of vasoactive drugs, sedation, and invasive mechanical ventilation, can result in the deterioration of skin integrity within hours. This is aggravated by the body's natural pressure points and the multiple medical devices used.[28]

Therefore, it is the nursing team's responsibility to establish measures to prevent such complications, such as evaluating the patient's skin before placing them in the prone position to determine the need for devices that redistribute and relieve pressure on bony prominences. Additionally, it is essential to perform small repositioning maneuvers every two to four hours, alternating the position of the arms and head, and to keep the skin clean and hydrated, as moisture can cause tissue maceration, increasing the risk of PIs and infections.[30]

Notably, COVID-19, an infectious disease, has been responsible for thousands of deaths worldwide. Although the World Health Organization declared the end of the Public Health Emergency on May 5, 2023, the virus continues to circulate and infect populations, with the potential for clinical worsening. Thus, this study provides evidence on mortality predictors in COVID-19 patients admitted to ICUs. Recognizing these factors is crucial for nursing teams, as prevention and early detection of complications support patient-centered care, enhancing safety and quality of care.

Although the study achieved its proposed objective, its limitations must be highlighted. One notable limitation is its cross-sectional design, which makes it impossible to establish cause–effect relationships between variables. Furthermore, as a documentary study, it was not possible to collect all the information from all the sample participants because of the reliance on records made by the attending professionals. However, despite these limitations, this study provides important findings on variables associated with COVID-19 morbidity and mortality. Further research in other regions of the country is suggested to broaden the knowledge on this topic.

Conclusion

A detailed analysis of the data presented in this study and from the literature review indicated that mortality from the novel coronavirus was significantly associated with male sex, marital status, and being in the 65 years or older age group. Additionally, increased odds of death were identified among patients undergoing pronation techniques and IMV during hospitalization.

This research contributes to understanding the phenomena related to death and the factors influencing mortality rates due to coronavirus infection. These findings also shed light on the risk factors for the development of complications and mortality in COVID-19 patients.

In this sense, observing the factors associated with mortality outcomes in patients affected by SARS-CoV-2 infection can aid public health decision-makers. Moreover, it highlights the importance of developing institutional protocols and providing ongoing education in healthcare services to ensure that preventive measures are adopted by the care team.

Acknowledgement

None.

Funding

None.

Conflicts of Interest

The author declares no conflict of interest.

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