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ORIGINAL ARTICLE

Association of biological factors, social determinants of health, and hospitalization with mortality due to SARS/COVID-19

Associação de fatores biológicos, determinantes sociais de saúde e hospitalização com a mortalidade devido a SRAG/COVID-19

Asociación de factores biológicos, determinantes sociales de la salud y hospitalización con mortalidad por SRAS/COVID-19

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ABSTRACT

Background and Objectives: To study the factors related to mortality in patients with severe acute respiratory syndrome (SARS) in order to understand the dynamics of transmission, health care delivery, and the epidemiological profile of patients upon the demographic, economic and health care diversity found in Brazil. The present study seeks to evaluate the association of sociodemographic, clinical and hospitalization variables with mortality among hospitalized patients with SARS by COVID-19 between the 14th and 39th epidemiological weeks of 2021 in Ituiutaba-MG. **Methods:** Cross-sectional study with on-site review of SARS notifications, diagnostic examinations, and death certificates of SARS-CoV-2 cases. Prevalence ratio was estimated using Poisson regression. **Results:** Out of 8,770 cases confirmed, 592 notifications were evaluated from April 4th to October 2nd, 2021. Fewer years of education, vaccination with two doses and need for invasive ventilation were associated with mortality. The risk of death increased with every year of life (PR=1.03; 95%CI 1.02-1.04), the presence of chronic disease (PR=1.55; 95%CI 1.1-2.18), and ICU hospitalization (PR= 3.49 95%CI 2.7-4.54). C**onclusion:** In addition to age, pre-existing clinical conditions and ICU hospitalization contribute to mortality.

Keywords: *Severe acute respiratory syndrome*. *Mortality registries*. *COVID-19 vaccines. Comorbidity*. *COVID-19 Testing*.

RESUMO

Justificativa e Objetivos: Investigar os fatores relacionados com a mortalidade em pacientes com síndrome respiratória aguda grave (SRAG), a fim de compreender as dinâmicas de transmissão, oferta de serviços de saúde e o perfil epidemiológico dos pacientes mediante a diversidade populacional, econômica e de assistência em saúde encontradas no Brasil. O presente estudo busca avaliar a associação de variáveis sociodemográficas, clínicas e de hospitalização em pacientes com por COVID-19 com a mortalidade entre a 14ª e 39 ª semana epidemiológica de 2021 em Ituiutaba-MG. **Métodos:** Estudo transversal com consulta local de notificações de SRAG, de diagnóstico e certidão de óbito. Razões de prevalência foram estimadas por regressão de Poisson. **Resultados:** Dos 8.770 casos confirmados, 592 notificações foram avaliadas entre 4 de abril a 2 de outubro de 2021. Poucos anos de estudo, vacinados com duas doses e necessidade de ventilação invasiva foram associadas ao óbito. O risco de morte aumentou a cada ano de vida (RP=1,03; IC95% 1,02-1,04), na presença de doença crônica (RP=1,55; IC95% 1,1-2,18), e para os hospitalizados na UTI (RP= 3,49 IC95% 2,7-4,54). **Conclusão:** Além da idade, as condições clínicas preexistentes e a internação em UTI são contributivas para o óbito.

Descritores: *Síndrome respiratória aguda grave. Registros de mortalidade. Vacinas contra COVID-19. Comorbidade. Teste para COVID-19.*

RESUMEN

Justificación y Objetivos: Investigar los factores relacionados con la mortalidad en pacientes con el síndrome respiratorio agudo severo (SRAS), a fin de comprender las dinámicas de transmisión, la oferta de servicios sanitarios y el perfil epidemiológico de los pacientes mediante la diversidad de población, económica y de asistencia en salud encontradas en Brasil. El presente estudio busca evaluar la asociación de variables sociodemográficas, clínicas y de hospitalización de individuos con síndrome respiratorio agudo severo por COVID-19 con la mortalidad entre la semana epidemiológica 14 y 39 del año 2021 em Ituiutaba-MG. **Métodos:** Estudio transversal, con consulta local de notificaciones de SRAS, de diagnóstico y certificado de defunción. Las razones de prevalencia se estimaron mediante regresión de Poisson. **Resultados:** De los 8.770 casos confirmados, se evaluaron 592 notificaciones entre abril y octubre del 2021. Los menores años de escolaridad, la vacunación con dúas doses, y el uso de ventilación invasiva se asociaron con la muerte. El riesgo de muerte aumentó con cada año de vida (RP=1,03; IC95% 1,02-1,04), en presencia de enfermedad crónica (RP=1,55; IC95% 1,1-2,18), y en pacientes hospitalizados en UCI (RP= 3,49; IC95% 2,7-4,54). **Conclusiones:** Además de la edad, las condiciones clínicas preexistentes, el ingreso en UCI contribuyen a la muerte.

Palabras Clave: *Síndrome respiratorio agudo severo*. *Registros de mortalidad*. *Vacunas contra la COVID-19*. *Comorbilidad*. *Prueba de COVID-19.*

INTRODUCTION

SARS-CoV-2 is a respiratory virus that can lead infected patients to develop severe acute respiratory syndrome (SARS).[1] Clinical manifestations include flu syndrome along with other symptoms such as dyspnea or respiratory distress, low oxygen saturation, chest pain, progressive respiratory difficulties, and acute respiratory distress syndrome.[1] The COVID-19 symptomatology varies widely, ranging from asymptomatic cases to those that evolve with severe complications that lead to death.[1]

The first case of corona virus disease (COVID-19) in Brazil was confirmed on February 25, 2020.[2] But the country currently records more than 38 million accumulated cases, approximately 710 thousand deaths,[3] and a monovalent vaccinal coverage of 83% (±169 million) with two doses, and 51% (±103 million) with three doses as of January 29, 2024.[4]

The decline in deaths caused by COVID-19 has been propelled by vaccinating the elderly,[5] which now extends to the administration of booster vaccine doses.[6] Nevertheless, the potential of the disease increasing morbidity and mortality rates is still high.[7]

Since September 15, 2021, the Ministry of Health adopted the administration of a booster dose for elderly people aged 70 and above who had completed their primary vaccination schedule. Other groups have subsequently been included according to their risk of exposure to the virus, risk of complications, and death.[6] Surveillance of COVID-19 remains continuous, especially due to the potential emergence of new variants and outbreaks. Moreover, monitoring the disease is crucial for individuals who are more susceptible to infections and complications, even if they are vaccinated.[7]

In addition to the disease's general clinical characteristics, today the scientific literature discusses post-COVID-19 symptoms, sequels, and comorbidities.[8,9] Previous studies have shown that age,[10,11] being male, and having comorbidities, especially cardiovascular diseases, diabetes, kidney, and chronic respiratory diseases[10,12,13] are some of the risk factors that influence gravity and mortality of SARS-CoV-2 patients.

Therefore, investigations about the factors associated with hospitalization and mortality in SARS-CoV-2 patients based on the different economical, historical-cultural and healthcare coverage aspects of the regions in a developing country contributes to the development of programs, policies, and health actions to face epidemics. Thus, this study aims to evaluate the association of sociodemographic, clinical and hospitalization variables with mortality among hospitalized patients with SARS.

METHODS

Study design and data collection

This is a cross-sectional study conducted at the Municipal Health Secretariat (Secretaria Municipal de Saúde) in Ituiutaba, Minas Gerais State, between April 4th and October 2nd, 2021. All the SARS notification forms, diagnostic tests for COVID-19, and death certificates were reviewed.

Data collection at the Municipal Health Secretariat was conducted manually by reviewing every SARS occurrence in every hospital of the city, the *Unidade de Pronto*

Atendimento/UPA (Health Center Emergency Room) of Ituiutaba, the Hospital *São José da Sociedade de São Vicente de Paulo*, the Hospital *Nossa Senhora da Abadia* and the Hospital *São Joaquim*, totalizing four hospitals. The investigators were trained to conduct a proper data collection from the forms, death certificates and exams. The record and the number of COVID-19 vaccination doses were confirmed by consulting the Data System (Sistema de Informação) of the National Vaccination Program (Programa Nacional de Imunizações).

Participants and inclusion criteria

This study included a non-probabilistic sample of hospitalized individuals diagnosed with SARS caused by SARS-CoV-2 from both public and private healthcare services of Ituiutaba-MG. The exclusion criteria were applied to notifications with critical absence of identification, clinical and case outcome data and/or without diagnostic examination.

Investigated variables

The covariables assessed were: (1) sociodemographic characteristics (age, sex, race, and years of education); (2) clinical (vaccination scheme, symptoms of SARS, and pre-existing chronic diseases); and (3) hospitalization (total days of hospital stay, days of treatment in the intensive care unit (ICU), need of ICU, and invasive support ventilation). The rapid test diagnosis, serologic and molecular tests were used as evidence of a positive result for SARS-CoV-2 infection and to confirm the cases of SARS registered in the notification sheets. Additionally, the death certificates were used to confirm COVID-19 deaths and for *causa mortis* collection.

Statistical methods

Descriptive statistics of the variables were obtained, and the prevalence of each covariable was calculated. The normality of the data was assessed by Shapiro-Wilk test, and data was presented in the median and interquartile range for data with non-normal distribution. To identify the factors associated with mortality, the group with outcome “discharged” was compared to “death”. Categorical covariables were associated with the outcome variable (hospital discharge or non-survived) and were analyzed by the chi-square test of Pearson. For continuous variables with non-normal distribution, the differences were identified with the Mann-Whitney *U* test. Poisson regression analysis was used by adopting the prevalence ratio (PR) with robust variance and the respective 95% confidence interval (CI). The analysis was performed in two stages, the first with a bivariate-unadjusted model and the second with a multivariate-adjusted model. After the bivariate analysis, the covariables were assessed based on the presence of multicollinearity for metric and categorical variables, adopting the Spearman correlation and the value of contingency coefficient, respectively. Multicollinearity was

assumed when the coefficients were above 0.6. The variables that presented $p<0.05$ in the bivariate model were included in the adjusted model, remaining those with $p<0.03$. Data analysis was performed with JAMOVI (V2.4.8).

Ethics

The research was conducted in accordance with the ethical standards required from Resolutions 466/2012, 510/2016 and 580/2018, from the Brazilian Ministry of Health. The study protocol was submitted to the unified Brazilian platform for registration of research involving human beings (*Plataforma Brasil*) and approved by the Ethics Committee of the Federal University of Uberlândia in June 2022 (CAAE 56051721.2.0000.5152; CEP/UFU n. 5.448.555/2022).

RESULTS

The initial sample comprised 673 notifications of SARS. After the exclusion of forms which did not present identification, clinical, and case outcome data, the analytic sample comprised 592 individuals (age 59.4±16.9; women 46.6%). The participants excluded presented similar observed frequencies for sex and mean age (age 61.5±14.6; women 44.4%).

From April to October, the health services of Ituiutaba-MG received 32,036 notifications, of which 8,770 patients (27.4%) were positive for COVID-19. According to the initial screening of the SARS notifications, approximately 7.7% (n=673) of the positive cases for COVID-19 sought medical care. Using the eligibility criteria of this study, the sample was composed of 592 individuals (6.8%). Most of the diagnosis were done through antigen tests (n=379; 64%) followed by reverse transcription polymerase chain reaction (RT-PCR) (n=144; 24.3%).

Two hundred and eleven (35.6%) patients with SARS who received hospital care (64.4%; n=381) died from COVID-19. From these individuals, older patients (>60 years) with fewer years of education (≤ 5 years of education or illiterate), those vaccinated with two doses and those with preexisting noncommunicable diseases (NCDs), such as cardiovascular disease (CVD) and/or diabetes mellitus (DM), as well as those with pneumopathy, who received care in an intensive care unit (ICU) and required invasive ventilation were significantly associated with death. According to the data, the symptoms of SARS included respiratory distress, dyspnea, and loss of smell and taste (Table 1).

The frequency of patients who died and were admitted to the ICU was higher among those aged 40-59 (n=50; 24.5%) and 60-79 (n=60; 29.4%), followed by patients aged 80 or above (n=32; 15.7%), compared to the younger age group of 20-39 (n=5; 2.4%).

The comorbidities most frequently registered were CVD (50.6%), 31.3% (n=164) corresponding to systemic arterial hypertension, and DM (23.3%), whilst 16% had both CVD and DM. Low oxygen saturation (87.6%) and dyspnea (82.9%) were the symptoms most frequently reported, followed by respiratory distress (67.1%), cough (64.5%), fatigue (40.1%), and fever (38.5%) (Table 1).

Table 1. Characteristics of the population treated in the health service, Ituiutaba, MG, 2021

Variables	**Hospital discharge** n (%)	**Non-survived** n (%)	**Total** n (%)	***p*-value**
Sociodemographic				
Age (years)	52 (22)[c]	67 (24)[c]		<0.01 †
< 20	7 (1.8)	0 (0)	7 (1.2)	<0.01*
20-39	75 (19.7)	6 (2.8)	81 (13.7)	
40-59	177 (46.5)	65 (30.8)	242 (40.9)	
60-79	92 (24.1)	82 (38.9)	174 (29.4)	
≥80	30 (7.9)	58 (27.5)	88 (14.9)	
Sex				
Male	204 (53.5)	112 (53.1)	316 (53.4)	0.914
Female	177 (46.5)	99 (46.9)	276 (46.6)	
Race[a]				
White	194 (54.2)	127 (60.2)	321 (56.4)	0.189
Non-white	164 (45.8)	84 (39.8)	248 (43.6)	
Schooling level[a]				
Illiterate	10 (4.3)	21 (10.8)	31 (7.3)	<0.01*
≤5 years of study	66 (28.6)	91 (46.9)	157 (36.9)	
>6 and ≤12 years of study	126 (54.5)	71 (36.6)	197 (46.4)	
>12 year of study	29 (12.6)	11 (5.7)	40 (9.4)	
Clinical characteristics				
Vaccination scheme[a]				
Complete (2 doses)	64 (16.8)	84 (40)	148 (25)	<0.01*
Incomplete	67 (17.6)	48 (22.9)	115 (19.5)	
Unvaccinated	250 (65.6)	78 (37.1)	328 (55.5)	
Symptoms[a]				
Respiratory distress	240 (63.2)	155 (74.2)	395 (67.1)	0.007*
Diarrhea	62 (16.3)	30 (14.4)	92 (15.6)	0.530
Dyspnea	306 (80.5)	182 (87.1)	488 (82.9)	0.043*
Abdominal pain	31 (8.2)	11 (5.3)	42 (7.1)	0.191
Sore throat	63 (16.6)	28 (13.4)	91 (15.4)	0.307
Fatigue	143 (37.6)	93 (44.5)	236 (40.1)	0.104
Fever	151 (39.7)	76 (36.4)	227 (38.5)	0.421
Loss of smell	43 (11.3)	8 (3.8)	51 (8.7)	0.002*
Loss of taste	63 (16.6)	14 (6.7)	77 (13.1)	0.001*
Saturation (less that <95%)	326 (85.8)	190 (90.9)	516 (87.6)	0.071
Cough	252 (66.3)	128 (61.2)	380 (64.5)	0.218
Vomiting	33 (8.7)	19 (9.1)	52 (8.8)	0.868
Morbidity[a]				
NCDs	196 (60.3)	159 (79.9)	355 (67.7)	<0.01*
CVD	145 (44.6)	120 (60.3)	265 (50.6)	<0.01*
DM	60 (18.5)	62 (31.2)	122 (23.3)	<0.01*
Pneumopathy	7 (2.2)	11 (5.5)	18 (3.4)	0.04*
Obesity	35 (10.8)	29 (14.6)	64 (12.2)	0.197
CVD and DM	40 (12.3)	44 (22.1)	84 (16)	<0.01*
Hospital care[a]				

Infirmary	333 (89.8)	57 (27.9)	390 (67.8)	<0.01*
ICU[b]	38 (10.2)	147 (72.1)	185 (32.2)	
Hospitalization in ICU (days)	0 (0)[c]	4 (11)[c]		<0.01†
Ventilation support[a]				
Non-invasive	308 (91.9)	141 (69.8)	449 (83.6)	<0.01*
Invasive	8 (2.4)	60 (29.7)	68 (12.7)	<0.01*
Total time of hospitalization (days)	5 (8)[c]	10 (12)[c]		<0.01†

*Pearson´s $\chi 2$ test; †Mann-whitney´s Test. Abbreviations: IC95%: confidence interval; NCDs: noncommunicable diseases; DM: diabetes *mellitus;* CVD: Cardiovascular disease; ICU: intensive care unit.
[a]Relative and percentage frequency includes the number of observations without "not reported/missing values" for self-reported data.
[b]The variables under ICU represent patients who received treatment in the hospital and were also admitted to the ICU. [c]Data is presented as median, interquartile range (IQR).

Only the correlation coefficients of the variables DCV and DM, infirmary and non-invasive ventilation exceeded the contingency coefficient (≥0.6). Therefore, they were not considered in the Poisson regression models because they could reduce predictive power. The association of independent variables in the bivariate analysis showed that the factors significantly associated with the outcome death were age, educational level lower than twelve years, vaccination scheme, self-reported symptoms of respiratory distress, dyspnea, loss of smell or taste, self-reported morbidity of CVD, DM, pneumopathy, hospitalization in ICU and use of invasive respiratory support, and total hospitalization time and time spent in the ICU (Table 2).

Older age, pre-existing NCDs, loss of taste and the need for intensive care during hospitalization were the main variables associated with mortality in the adjusted model for patients with SARS-CoV-2 (Table 2). The probability of death increases by 3% for each year of life (PR adjusted²= 1.03; 95%CI 1.015-1.035). The symptom loss of taste (PR adjusted²= 0.54 95%CI 0.36-0.78) and self-reported CVD (PR adjusted²= 0.73 95%CI 0.56-0.96) were less frequent in patients who died. However, the registration of some self-reported NCDs was more frequent in patients who died (PR adjusted²= 1.55; 95%CI 1.1-2.18) than those who were discharged from the hospital. ICU hospitalization was around 3.5 times more common in individuals who succumbed to COVID-19 (PR adjusted²= 3.49, 95%CI 2.7-4.54) compared to those who were discharged from the hospital. The absence of information for independent variables was as follows: 23 for race, 167 for education level, 1 for vaccination, 3 for symptoms, 68 for morbidity, 17 for hospitalization, and 53 for ventilation support.

Table 2. Poisson regression for clinical, sociodemographic, and hospitalization variables and mortality by COVID-19

Variables	**Crude PR (95%CI)**	***p*-value**	**PR adjusted[1]* (95%CI)**	***p*-value**
Sociodemographic				
Age (years)	1.03 (1.023-1.036)	**<0.01**	1.03 (1.015-1.035)	**<0.01***

Race				
White	1.00		-	-
Non-white	0.86 (0.69-1.06)	0.165	-	-
Schooling level				
Illiterate	1.00		1.00	
≤ 5 years of education	0.86 (0.61-1.23)	0.385	0.78 (0.56-1.11)	0.151
>6 and ≤ 12 years of education	0.53 (0.38-0.77)	**<0.01**	0.81 (0.57-1.18)	0.258
> 12 years of education	0.41 (0.23-0.69)	**<0.01**	0.67 (0.39-1.12)	0.137
Clinical variables				
Vaccination scheme				
Unvaccinated	1.00		1.00	
Incomplete	1.76 (1.31-2.34)	**<0.01**	1.01 (0.77-1.31)	0.958
Complete (2 doses)	2.39 (1.86-3.06)	**<0.01**	0.84 (0.60-1.16)	0.283
Symptoms				
Dyspnea				
No	1.00		1.00	
Yes	1.4 (1.02-1.96)	**0.037**	1.26 (0.92-1.74)	0.163
Respiratory distress				
No	1.00		1.00	
Yes	1.41 (1.1-1.82)	**<0.01**	1.01 (0.8-1.28)	0.941
Saturation (less that <95%)				
No	1.00		-	-
Yes	1.42 (0.99-2.11)	0.074	-	-
Fatigue				
No	1.00		-	
Yes	1.2 (0.96-1.49)	0.105	-	-
Loss of smell				
No	1.00		1.00	
Yes	0.42 (0.22-0.71)	**<0.01**	0.78 (0.46-1.27)	0.349
Loss of taste				
No	1.00		1.00	
Yes	0.48 (0.3-0.72)	**<0.01**	0.54 (0.36-0.78)	**<0.01***
Morbidity				
NCDs				
No	1.00		1.00	
Yes	1.89 (1.45-2.51)	**<0.01**	1.55 (1.1-2.18)	**0.012***
CVD				
No	1.00		1.00	
Yes	1.48 (1.19-1.86)	**<0.01**	0.73 (0.56-0.96)	**0.024***
DM				
No	1.00		1.00	
Yes	1.49 (1.17-1.88)	**<0.01**	1.03 (0.82-1.29)	0.818
Pneumopathy				
No	1.00		1.00	
Yes	1.64 (0.98-2.58)	**0.043**	0.99 (0.59-1.58)	0.979
Obesity				
No	1.00		-	-
Yes	1.23 (0.89-1.66)	0.199	-	-
Hospital care				
ICU[a]				
No	1.00		1.00	
Yes	5.44 (4.27-6.99)	**<0.01**	3.49 (2.7-4.54)	**<0.01***
Hospitalization in ICU (days)	1.03 (1.03-1.04)	**<0.01**	1.01 (0.99-1.02)	0.744
Invasive ventilation support				
No	1.00		1.00	
Yes	2.91 (2.29-3.69)	**<0.01**	1.18 (0.94-1.49)	0.158
Total time of hospitalization (days)	1.02 (1.02-1.03)	**<0.01**	1.0 (0.98-1.01)	0.416

Abbreviations: IC95%: confidence interval; PR: prevalence ratio; NCDs: noncommunicable diseases; DM: diabetes mellitus; CVD: Cardiovascular disease; ICU: intensive care unit.

*[1]Model I – all values adjusted for all variables included in the models.

[a]The variables under ICU represent patients who received treatment in the hospital and were also admitted to the ICU.

The *causa mortis* most frequently registered on death certificates were cardiorespiratory arrest (n=46; 21.8%), severe acute respiratory syndrome/SARS (n=37; 17.6%), acute respiratory failure (n=63; 29.8%), septic shock (n=19; 9%), sepsis (n=12, 5.2%) and multiple organ failure (n=8; 3.8%). Furthermore, there were reports of chronic/acute kidney insufficiency (n=24; 11.4%), bacterial pneumonia (n=2; 0.9%), COVID-19 pneumonia (n=50; 23.7%) or both (n=2; 0.9%), and unspecified (n=52; 26.6%), such as underlying conditions (Table S1).

DISCUSSION

The main findings of this study show that age, self-reported chronic disease, loss of taste, CVD, and requirement of ICU were associated with non-survival patients. The second wave of COVID-19 cases, probably the longest and most lethal, occurred between November 2020 and April 2021. In this study, it was not possible to collect genomic data to further differentiate variants. However, the infections registered are attributed to P.1 and P.2 Gamma variants,[12,14] which had a significant effect on mortality[14] and hospitalization rates during the second wave.[12]

The outcome death was more frequent among the patients with two doses of the vaccine than among those who were not vaccinated or had an incomplete vaccination schedule. Another study identified a higher lethality rate among individuals who received two doses[13] of the vaccine, similar to the findings of our study. The improvement of the vaccine coverage varied across the country, and only 50% of the population of the southeastern region had been vaccinated by the 38th epidemiological week of 2021.[14] In addition to vaccine coverage, other factors helped to explain the profile of severe cases and mortality, including older age and the influence of senescence,[10,11] low education,[12] the presence of DCV,[12,13] DM, pneumopathy and longer periods of hospitalization.[8] However, a previous study found that the death probability of individuals who received a post-Omicron booster vaccine dose was lower (-9.3%).[13]

The vaccine against COVID-19 is still the main measure against SARS-CoV-2 infection, hospitalization, and death, and also reduces adverse events associated with the disease.[15] A recent consortium[15] showed that vaccination deficit was associated with a high risk of serious outcomes due to SARS-CoV-2 infection in the age group 16-74 years of age, being 1.26 for the deficit for one dose, 1.88 for two doses, and 1.5 for three doses. The risk is even higher for those over 75 years of age.

The prevalence of chronic diseases increases with aging. Studies show that the risk of mortality increases with comorbidities, including cardiovascular and diabetes diseases.[12,16] The results show a lower prevalence of CVD for the group with outcome death, although the prevalence of some NCD was 55% more frequent for the same group. Investigation into medical records and self-referred variables may contain memory bias, and the report's quality depends on the accuracy of the notification by the health professional. A report[17] indicated that hypertension (32%), diabetes *mellitus* (18%), and CVD (20%) are some of the main morbidities among COVID-19 cases in Latin America. Moreover, this study revealed that the severity of COVID-19 is proportionally higher for those who have multiple comorbidities.[17]

Hypertension is strongly associated with the burden of CVD and early mortality,[18] and its prevalence has been lower in high-income countries than in low and middle-income countries.[19] Evidence shows that the mortality risk associated with COVID-19 is higher with DM, hypertension, and CVD.[20,21] In Latin American countries, the proportion of deaths in patients with COVID-19 is higher among those with chronic kidney and hepatic disease. However, there is no variation[17] under other conditions such as DM and CVD (55%).

Despite the quality of the notifications, as well as the absence of data regarding the SARS-CoV-2 variants, the results are consistent in indicating that older age and the presence of comorbidities help explain mortality. Moreover, this data once again reinforces how important it is to administer booster doses to prevent severe cases and death.

Hypoxemia, acute respiratory distress syndrome (ARDS), metabolic acidosis, coagulopathy, and septic shock can lead to vital organ dysfunction.[7] Reports of cardiac insufficiency, septic shock, and respiratory insufficiency are among the several complications reported in non-survival COVID-19 patients. An analysis involving 19,014 COVID-19 patients and 4,655 non-survivors revealed that pre-existing health conditions were associated with complications, showing that age, comorbidities, and DM were factors associated with respiratory insufficiency. Age, comorbidities, and cardiovascular and cerebrovascular diseases were associated with cardiac insufficiency. Septic shock is associated with factors such as DM, comorbidities, age, hypertension, and cardiovascular diseases.[18]

The profile of the individuals evaluated aligns with the recognized pattern of severe infections, as evidenced in their clinical history, revealing the presence of comorbidities such as hypertension, cardiopathy, and obesity. The data also indicates that respiratory complications and septicemia are reported causes of death; scenarios in which respiratory insufficiency is often managed with mechanical ventilation.[7,20] In this regard, deaths attributed to COVID-19 often have contributory implications that stem from pre-existing health conditions.

Both hospital admission[16] and the length of stay[12] are important factors that influence patient prognosis. The survival rate of women aged 65 or older with a stay that exceeds 11 days was reduced by 50%.[10] The results indicate that the mean hospitalization duration for non-survival individuals was 10 days. Additionally, the diagnosis plays a crucial role in determining the need for hospital care. A study revealed that 14% of 6,068 hospitalized patients developed symptoms after admission with most patients being hospitalized following the onset of symptoms.[22] In Brazil, individuals predominantly sought hospital care after symptoms appeared, suggesting an infection.

The results revealed that most diagnosis were made using antigen tests. A study conducted in Brazilian capitals and in Brasília reported inadequacies between the onset of the symptoms and the diagnostic testing using antigen tests, and that only 32% of the tests were conducted within an appropriate timeframe (mean: 5.9-13.9 days). In other words, more than 50% of the tests were performed outside the recommended time frame.[23,24] Therefore, the predominance of this diagnostic approach as the first line may be limited[25] due to factors that include an increased exposure time to infection without access to healthcare.

Data from a cohort conducted by Danaché et al. (2022)[16] with 827 patients showed that the longest interval (>6 days) between the symptom onset and hospital admission occurred among adult individuals (median: 69; IQR 54-78 years), as well as a higher frequency of admission in the ICU, indicating that age, individual risk perception, and morbidity profile influenced healthcare-seeking behavior.

Moreover, data from COVID-19 cases reported by *SIVEP-gripe* revealed 245,304 (17%) ICU hospitalizations during both the first and the second wave, with the majority of the admissions to the ICU (n=130,286) in the latter. Additionally, 83,781 deaths were reported.[12] Compared to the first wave, ICU hospitalization among younger individuals and the need for ventilatory support were more frequent during the second wave. A study estimated an odds ratio of 2.9-13.9 times for ICU admission among individuals aged 40-59 years, 60-79 years and 80 years or older with the P.1 variant.[25]

Furthermore, cases of hospitalization due to SARS, probably more severe and symptomatic, were gathered by excluding the assessment of positive COVID-19 cases that did not require hospitalization. Nonetheless, the data shows a trend that is consistent with findings reported by other studies.[12,13,18,21] Overall, it encompasses sociodemographic characteristics, clinical aspects, and risk factors for COVID-19 mortality that reflect the reality of medium-sized cities in Brazil and other developing countries.

This study has a limitation regarding the intragroup behavior of hospitalized patients during the pandemic period, attributed to the analysis of raw data due to the quality of the COVID-19 case notifications and the absence of functional hospital systems aligned with the national notification system. Clinical information was frequently incomplete, resulting in the exclusion of certain variables from this study, which potentially introduced bias due to the sample's reduced representativeness. The adjusted analysis aimed to mitigate this effect, however, it may not have elucidated differences between the groups evaluated. Hence, this limitation constrained the ability to fully elucidate certain aspects of the patients' clinical progression. Collaborations between different research groups that conduct studies in locus is a relevant strategy to overcome the inherent limitations regarding the quality of the data since larger samples have the potential to reveal subtle differences hidden in small studies. Data collected by electronic surveillance systems are also affected by limited data integrity and database feeding strategies, therefore, standardized data collection carried out by trained researchers, consulting documents that validate the information present in the notifications, brings the panorama raised by the studies closer to regional realities.

This study evaluated a series of notifications and death certificates from hospitalized patients with SARS on-site. The evaluation of clinical and sociodemographic data revealed that severe patients who died were older, had fewer years of education, had comorbidities, required ICU, and mechanical ventilation. With an adjusted model, this study noticed that mortality among hospitalized patients increases with age and among those also hospitalized in the ICU with chronic diseases. We hope that this study will strengthen the evidence regarding the profile of hospitalized patients with COVID-19, contributing to the creation of new public policies that deal satisfactorily with the logistical challenges of infectious diseases with pandemic potential. Finally, we reinforce the importance of health professional's effort toward the correct notifications, aiming to qualify the actions of the epidemiological surveillance.

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Victor Antonio Ferreira Freire contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review and statistics. **Gustavo Siconello dos Santos** contributed to the bibliographic research, abstract writing, introduction, methodology, discussion, interpretation and description of results, preparation of tables, conclusions, review and statistics. **Morun Bernardino Neto** contributed to the interpretation and description of results, review and

statistics. **Luciana Karen Calábria** contributed to the project administration, bibliographic research, methodology, discussion, interpretation and description of results, conclusions and review. **Alexandre Azenha Alves de Rezende** contributed to the project administration, bibliographic research, methodology, discussion, interpretation and description of results, conclusions and review.

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