



# Severe Acute Respiratory Syndrome in older adults amid the COVID-19 pandemic and associated factors

Tasso Kfuri Araújo Mafra<sup>1</sup>   
Julio Cesar Stobbe<sup>1</sup>   
Renata dos Santos Rabello<sup>1</sup>   
Ivana Loraine Lindemann<sup>1</sup>   
Shana Ginar da Silva<sup>2</sup> 

## Abstract

Severe Acute Respiratory Syndrome (SARS) is one of the most worrying respiratory diseases, characterized by a flu-like condition associated with tachypnea or hypoxemia, with saturation below 95% in ambient air. In the context of the new coronavirus (SARS-CoV-2) pandemic, exponential growth in cases was observed, with the elderly being the most affected population group. This study aimed to describe SARS cases, as well as socio-demographic and health-associated factors in the elderly population of a city in the north of Rio Grande do Sul state, Brazil. This is an epidemiological study carried out by Influenza Epidemiological Surveillance Information System. The information was made available by the Municipal Health Department of the Passo Fundo between January 1st and December 31st, 2020. In the descriptive analysis, the distribution of absolute (n) and relative (%) frequencies of the variables of interest was performed. Crude and adjusted odds ratios were estimated using Logistic Regression. A total of 1,268 SARS notifications were observed in the elderly, 72% of which were caused by covid-19. The lethality was high (40.9%), mainly among men and those with low education, with the presence of at least one risk factor, especially chronic kidney disease. It is expected that the associations highlighted in this study can help to develop health policies aimed at the health of the elderly, especially by strengthening actions in primary health care.

**Keywords:** Severe Acute Respiratory Syndrome. COVID-19. Respiratory diseases. Elderly.

<sup>1</sup> Universidade Federal da Fronteira Sul, Curso de Medicina. Passo Fundo, RS, Brasil

<sup>2</sup> Universidade Federal da Fronteira Sul, Programa de Pós-Graduação em Ciências Biomédicas, Curso de Medicina. Passo Fundo, RS, Brasil.

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Correspondence  
Tasso Kfuri Araújo Mafra  
tassokfuri@gmail.com

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## INTRODUCTION

The demographic and epidemiological transitions associated with shifts in population dynamics driven by an increase in life expectancy require structural changes to cater for the growing older population, a group that has been directly affected by the COVID-19 pandemic, exhibiting the highest morbidity and mortality rates<sup>1</sup>. The pandemic has also impacted the social and psychosocial inequalities existing in this population, worsening the risk of poverty, loss of social support, discrimination and isolation, while exacerbating feelings of anxiety, loneliness and sadness<sup>2</sup>.

Severe Acute Respiratory Syndrome (SARS) is one of the most serious respiratory infections affecting older individuals. It is defined as an influenza-like condition accompanied by tachypnea or hypoxemia, with oxygen saturation (SpO<sub>2</sub>) below 95% in ambient air. Up until 2019, the Influenza A virus had been the most prevalent in Brazil. However, this scenario changed after the confirmation of the first cases of the novel coronavirus in early 2020<sup>3</sup>. SARS notification occurs when individuals present with symptoms of this condition and is compulsory when hospitalization is needed or when the condition leads to death, regardless of hospitalization<sup>4</sup>.

The most critical SARS cases involve individuals who have an associated comorbidity, such as diabetes, heart and lung diseases, are older or exposed to external factors, such as stress, work overload, physical inactivity, smoking, which contribute to a lifestyle that favors development of comorbidities and complications<sup>5</sup>. Evidence suggests that the older people constitute the group at highest risk of developing SARS since, in addition to older age, most have pre-existing comorbidities, given the prevalence of chronic diseases tends to rise with age<sup>6</sup>. These chronic conditions may be associated with an impaired immune system and a higher prevalence of chronic degenerative diseases, factors that contribute to faster progression and higher risk of premature death from COVID-19<sup>7</sup>.

Population aging is currently more marked in high-income countries. However, it is plausible that low and middle-income countries (LMIC) with poorer access to health networks, together with comorbidities, increase the risk of a worse prognosis amid COVID-19. Between 2020 and mid-August 2022, the number of recorded SARS cases exceeded 2,000,000 in Brazil, with over 90% of these individuals infected by the SARS-CoV-2 virus that causes COVID-19. The number of SARS deaths in the same period exceeded 450,000, with almost 95% related to the novel coronavirus<sup>8</sup>. In Rio Grande do Sul, by the end of Epidemiological Week (EW) 35 of 2022, over 130,000 SARS cases related to COVID-19 had been admitted to hospitals, of which more than 65,000 died from the disease. It should be noted that the highest rates of hospitalizations, Intensive Care Unit (ICU) admissions and deaths occurred in individuals aged > 60 years, with even higher rates among older people aged > 80 years<sup>9</sup>.

Passo Fundo, considered the capital city of the mid-lowlands region of the state of Rio Grande do Sul (RS), Brazil, had one of the highest cumulative hospitalization rates in the state, with estimates ranging from 320 to 410 cases per 100,000 population. Mortality was estimated at 60-90 cases per 100,000 population, where the older population was the most affected group<sup>10</sup>. In 2021, despite the implementation of immunization campaigns prioritizing vaccination of individuals aged ≥ 60 years, this older age group continued to be the worst affected by the morbidity and mortality outcomes associated with SARS-CoV-2. Thus, identifying and monitoring SARS amid the COVID-19 pandemic, as well as the demographic, socioeconomic and health characteristics of the most affected population, becomes paramount for the adoption of preventive measures and strategies to promote health in the older population, with the aim of reducing the magnitude of respiratory infections in this group.

Thus, the aim of the present study was to investigate the sociodemographic and health characteristics associated with deaths from Severe Acute Respiratory Syndrome in older people from a city in the north of Rio Grande do Sul state.

## METHODS

This study is part of a larger investigation called “Síndrome Respiratória Aguda Grave (SRAG) em Passo Fundo - RS: prevalência de vírus respiratórios e fatores associados” [“Severe Acute Respiratory Syndrome (SARS) in Passo Fundo – RS: prevalence of respiratory viruses and associated factors”], comprising several investigative arms, one of which is secondary data analysis of notified cases of SARS and influenza syndrome due to the novel coronavirus.

An observational epidemiological study analyzing data from the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe) in Passo Fundo, Rio Grande do Sul state was carried out from April to December 2021. The information was made available by the City Health Department, including cases of SARS confirmed and reported between January 1 and December 31, 2020, a period in which no vaccine was yet available in Brazil. This scenario allowed an analysis of mortality outcome without the influence of immunization. Individuals aged 60 years and over, of both sexes and notified as SARS cases in the period defined for the analysis were included in this study.

The variables of interest comprised sociodemographic aspects, such as gender (male; female), age in full years ( $\leq 79$ ;  $\geq 80$ ), race/skin color (white; other), education in years of formal study ( $\leq 5$ ; 6-12;  $> 12$ ). With regard to health variables, the following were assessed: 1) signs and symptoms (fever, cough, sore throat, dyspnea, respiratory distress, O<sub>2</sub> saturation  $< 95\%$ , diarrhea, vomiting, abdominal pain, fatigue, loss of smell and taste); 2) individuals in sample carrying a risk factor, heart disease, liver disease, asthma, diabetes, neurological disease, lung disease, immunodeficiency, chronic kidney disease and obesity; and 3) trajectory of reported cases, including Intensive Care Unit (ICU) admission, use of ventilatory support (no; yes, invasive; yes, non-invasive), outcome (recovery; death), final case classification (unspecified SARS; COVID-19 SARS), and confirmation criteria (laboratory; epidemiological; clinical and imaging).

The main outcome of interest was death from SARS, assessed using the outcome variable

(death x recovery). The key exposures involved sociodemographic and health characteristics. In case estimates, the 7-day rolling average was assessed for epidemiological weeks, calculated by adding the number of cases and deaths for each of the seven days and dividing the result by 7, giving weekly average.

Statistical analyses comprised the distribution of absolute (n) and relative (%) frequencies of the variables of interest. For outcome and exposures, crude and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) were estimated using logistic regression. In the adjusted analysis, hierarchical modeling was adopted<sup>11</sup>, with a 5-level model constructed by the authors. The first level (more distal) included demographic variables (gender, age and skin color); the second level socioeconomic variables (education); the third level (presence of risk factors); fourth level (pre-existing morbidities such as obesity, asthma, liver disease, neurological disease, immunosuppression and kidney disease); while the fifth level (proximal) encompassed lung diseases, diabetes mellitus and heart diseases. It is noteworthy that the variables were adjusted for those at the same level and for those at a higher level. All variables were included in the adjusted analysis and selected using the backward method, retaining variables with  $p < 0.20$ . In all tests, the significance level adopted was  $p < 0.05$ .

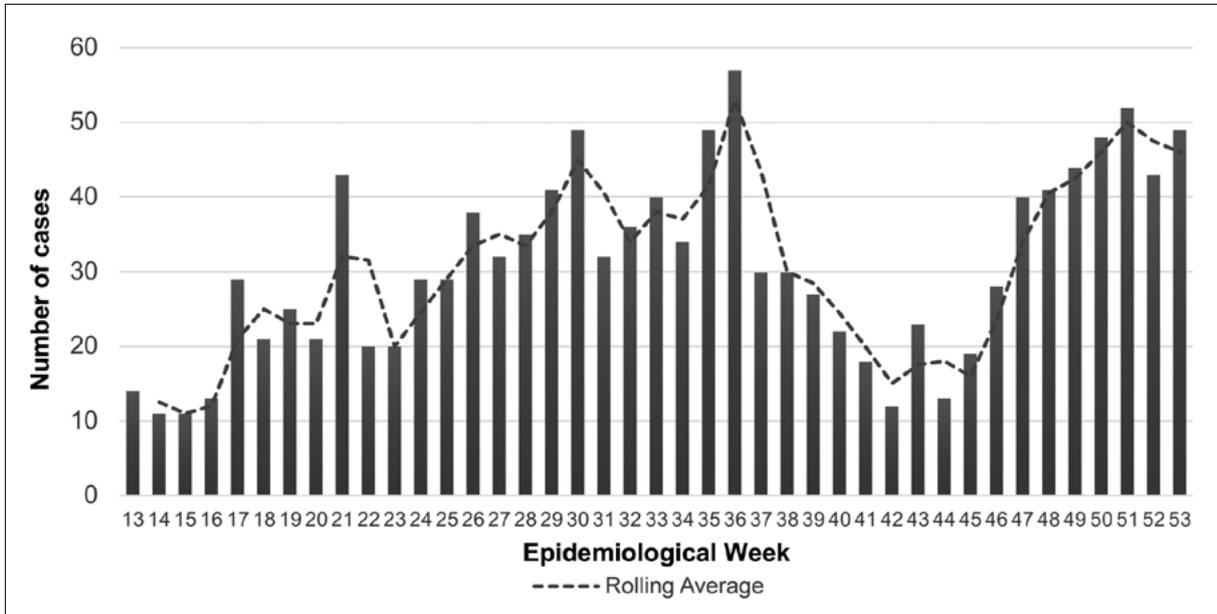
The project was approved under permit number 4 405 773 by the Ethics Committee for Research involving Humans of the Federal University of Fronteira Sul, and all statistical analyses were carried out using the PSPP Software version 1.2.0 and Stata, 12.0, licensed under number 30120505989.

## RESULTS

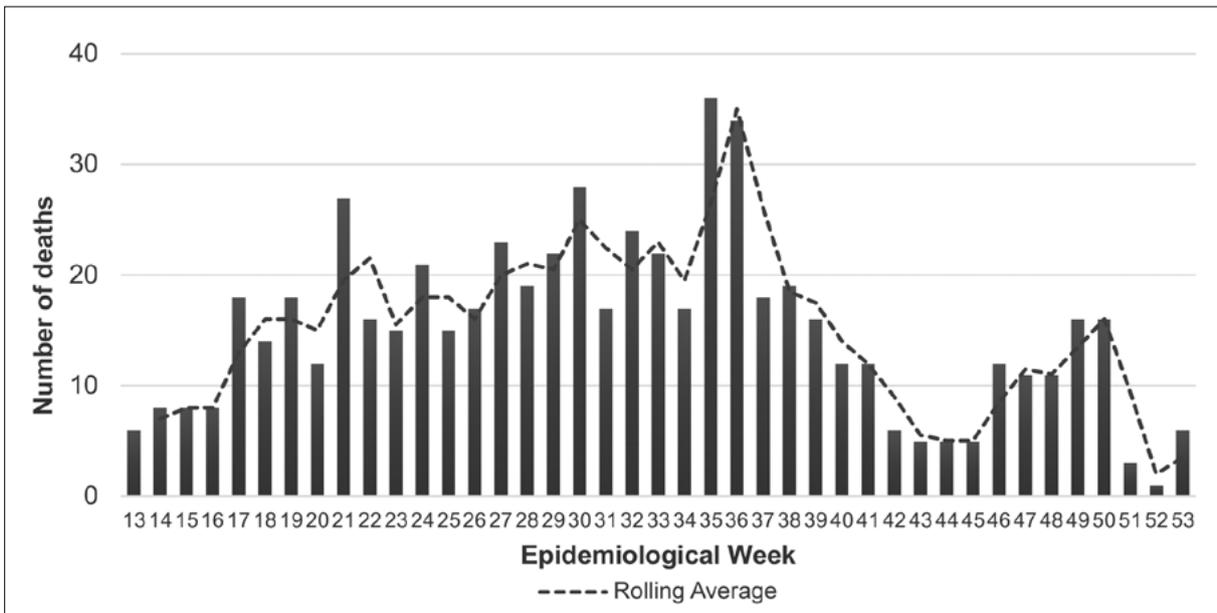
The total number of SARS notifications in older people from Passo Fundo, Rio Grande do Sul state in 2020 was 1,268 cases. The notified SARS cases and deaths, together with the rolling average are shown in Figures 1A and 1B, respectively. The results for cases reveal that notifications first peaked on epidemiological week 21 in May, with a second peak occurring in July during weeks 29 and 30, showing

an upward trend until the end of August during weeks 35 and 36, when the highest peak of the series was reached. Subsequently, case notification rates

decreased, returning to an upward trend in week 47 which continued until week 53 in November and December, when the year ended.



**Figure 1A.** Notified SARS cases in older adults by epidemiological week in Passo Fundo, Rio Grande do Sul state, 2020 (n = 1,268).



**Figure 1B.** Notified SARS deaths in older adults by epidemiological week in Passo Fundo, Rio Grande do Sul state, 2020 (n = 619).

Regarding deaths, there was a sharp rise during epidemiological weeks 35 and 36. This is also the period associated with the highest number of cases notified in Passo Fundo, Rio Grande do Sul state. By contrast, at the end of 2020, despite the substantial increase in the number of cases, the number of registered deaths no longer accompanied the rise in notifications.

The sociodemographic characteristics and aspects related to the trajectory of cases are presented in Table 1. The majority of patients were aged  $\leq 79$  years, over half were male, almost all were white, and most had  $\leq 5$  years of education. Regarding trajectory of cases, a significant number required ICU admission

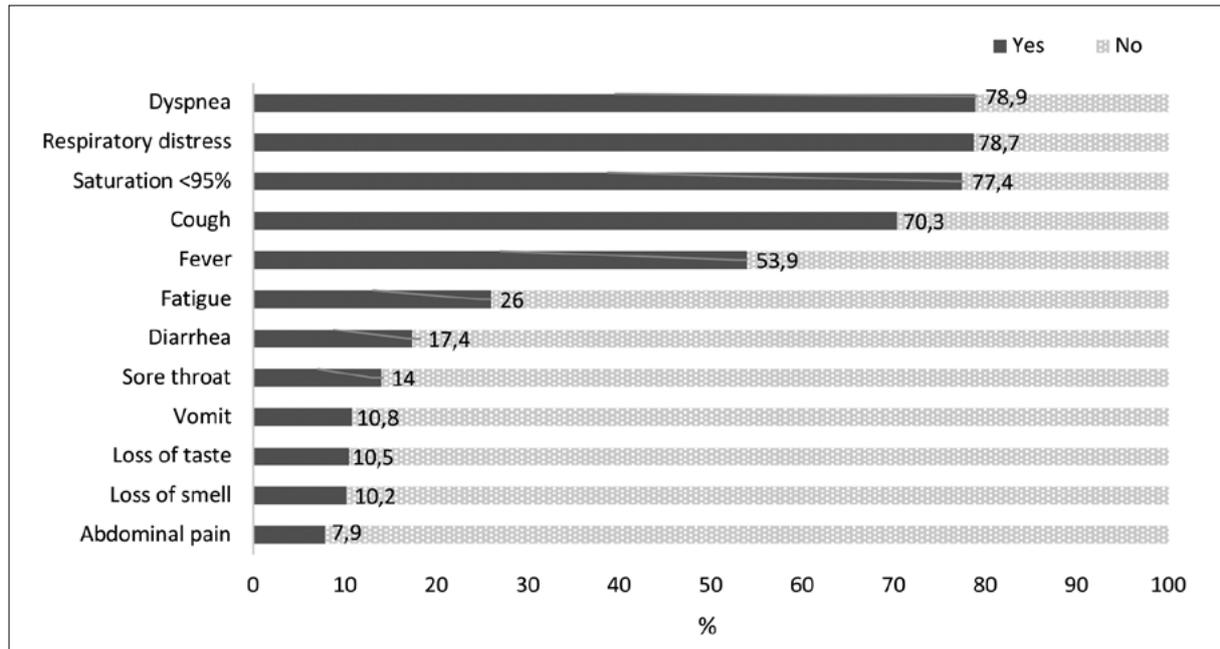
and non-invasive ventilatory support. Lastly, over 2/3 of SARS cases were due to COVID-19, almost all of which were confirmed by laboratory analyses. Most cases progressed to recovery.

Regarding the main symptoms experienced by the patients infected by SARS, the most frequent were dyspnea and respiratory distress (Figure 2). More than 2/3 of the sample also had saturation below 95% and cough, while just over half of the patients reported fever. Fatigue, diarrhea and sore throat were also reported, while the least common symptoms included vomiting, loss of taste, loss of smell and abdominal pain.

**Table 1.** Sociodemographic and health characteristics of older adults infected by Severe Acute Respiratory Syndrome (SARS) notified in Passo Fundo, Rio Grande do Sul, 2020 (n=1,268).

Variable	n (%)
Age (full years)	
≤ 79	936 (73.8)
≥ 80	332 (26.2)
Gender	
Male	672 (53.0)
Female	596 (47.0)
Skin color	
White	1,182 (93.2)
Other (black/yellow/brown/indigenous)	86 (6.8)
Education (years of formal study)	
≤ 5	559 (47.5)
6-12	480 (40.8)
> 12	137 (11.7)
ICU admission	
No	773 (61.5)
Yes	483 (38.5)
Ventilatory support	
No	262 (21.0)
Yes, invasive	304 (24.3)
Yes, non-invasive	683 (54.7)
Outcome*	
Recovery	619 (59.1)
Death	428 (40.9)
Case classification	
Unspecified SARS	350 (28.0)
COVID-19 SARS	913 (72.0)
Confirmation criteria	
Laboratory	1,212 (96.5)
Epidemiological	2 (0.2)
Clinical and Imaging	42 (3.3)

\*Variable with highest number of missing data items: Outcome = 225



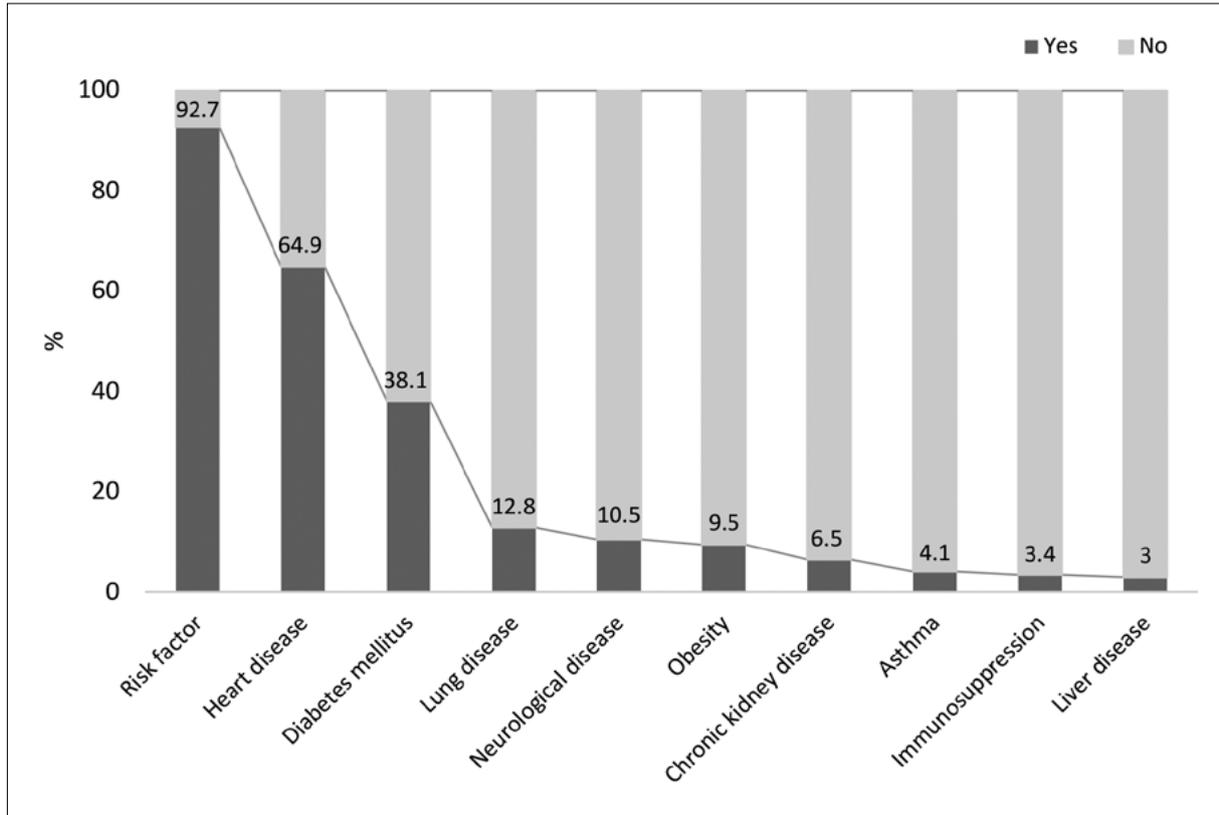
**Figure 2.** Main symptoms reported by older adults infected by Severe Acute Respiratory Syndrome notified in Passo Fundo, Rio Grande do Sul state, 2020.

Regarding the risk factors related to the health status of older individuals infected by SARS, almost all had a comorbidity, with heart disease and diabetes mellitus being the most prevalent. To a lesser extent, lung disease, neurological disease, obesity and chronic kidney disease were also reported. Asthma, immunosuppressive diseases and liver disease were reported by less than 5% of the population analyzed (Figure 3).

The multivariate analysis, after adjusting for possible confounding factors, revealed the gender variable was associated with outcome, with greater chance of death among men (OR=1.40; 95%CI 1.08-1.81) and patients aged  $\geq 80$  years (OR=1.92; 95%CI 1.45-2.55). The likelihood of death was

higher in individuals with  $\leq 5$  years of education (OR=1.83; 95%CI 1.37-2.46) than those who had more education. Having at least one risk factor was significantly associated with outcome (OR=3.63; 95%CI 1.75-7.53) (Table 2).

Regarding comorbidities, only chronic kidney disease remained associated with outcome after adjustment (OR=2.28; 95%CI 1.39-4.05), while individuals with heart disease maintained an inverse association (OR=0.69; 95%CI 0.51-0.92). The results of crude analysis showed that neurological disease was associated with death among the older adults infected by SARS (OR=1.70; 95%CI 1.15-2.52), although this association was not confirmed on the multivariate analysis.



**Figure 3.** Main risk factors in older adults infected by Severe Acute Respiratory Syndrome (SARS) notified in Passo Fundo, Rio Grande do Sul state, 2020.

**Table 2.** Crude and adjusted analysis of SARS deaths in older adults according to sociodemographic and health characteristics. Passo Fundo, Rio Grande do Sul state, 2020.

	Crude			Adjusted <sup>a</sup>		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Gender			0,063			<b>0,010</b>
Female	1.00	-		1.00	-	
Male	1.26	0.99 – 1.62		1.40	1.08-1.81	
Age (full years)			<0.001			<b>&lt;0.001</b>
≤ 79	1.00	-		1.00	-	
≥ 80	1.84	1.40-2.43		1.92	1.45-2.55	
Skin color			0.184			0.144
White	1.00	-		1.00	-	
Other (black/yellow/brown/indigenous)	1.40	0.85 – 2.31		1.46	0.88-2.42	
Education (years)			<b>0.018</b>			<b>0.041</b>
≤ 5	1.71	1.08-2.73		1.83	1.37-2.46	
6-12	1.42	0.88-2.30		1.42	0.88-2.29	
>12	1.00	-		1.00	-	
Presence of risk factor			<b>&lt;0.001</b>			<b>0.001</b>
No	1.00	-		1.00	-	
Yes	4.04	2.03 – 8.01		3.63	1.75-7.53	

to be continued

Continuation of Table 2

	Crude			Adjusted <sup>a</sup>		
	OR	95% CI	<i>p</i>	OR	95% CI	<i>p</i>
Heart disease			<b>0.043</b>			<b>0.013</b>
No	1.00	-		1.00	-	
Yes	0.75	0.57 – 0.99		0.69	0.51-0.92	
Liver disease			0.051			0.087
No	1.00	-		1.00	-	
Yes	2.09	1.00 – 4.39		1.95	0.91-4.21	
Asthma			0.776			0.749
No	1.00	-		1.00	-	
Yes	0.91	0.45 – 1.80		0.88	0.40-1.94	
Diabetes mellitus			0.204			0.095
No	1.00	-		1.00	-	
Yes	1.18	0.91 – 1.53		1.28	0.96-1.69	
Neurological disease			<b>0.008</b>			0.125
No	1.00	-		1.00	-	
Yes	1.70	1.15 – 2.52		1.39	0.91-2.13	
Pneumopathy			0.788			0.959
No	1.00	-		1.00	-	
Yes	1.05	0.73 – 1.50		0.99	0.67-1.46	
Immunosuppression			0.331			0.234
No	1.00	-		1.00	-	
Yes	1.38	0.72 – 2.64		1.54	0.76-3.12	
Chronic kidney disease			<b>0.002</b>			<b>0.001</b>
No	1.00	-		1.00	-	
Yes	2.27	1.36 – 3.78		2.28	1.39-4.05	
Obesity			0.996			0.707
No	1.00	-		1.00	-	
Yes	1.00	0.66 – 1.50		1.09	0.70-1.70	

<sup>a</sup> adjusted for sex, age, education, presence of risk factors, liver disease, neurological disease, chronic kidney disease, diabetes, and heart disease.

## DISCUSSION

The present study identified a greater number of cases of SARS in older people aged  $\geq 79$  years, although the worst prognosis was observed among individuals aged  $> 80$  years. The highest prevalence of cases was found in men with  $\leq 5$  years of education. The occurrence of comorbidities and aggravating factors for respiratory infections in this age group was also reported by similar studies in Brazil<sup>12,13</sup> and other countries<sup>6</sup>, showing that mainly cardiovascular diseases and diabetes mellitus constituted predictive factors for a worse prognosis, particularly related to COVID-19.

Similar results were observed in a previous study of 27,932 participants aged  $> 65$  years assessing the risk factors for COVID-19 in Brazil. The study found that, of the analyzed cases, 42.9% were men, 55.9% were white and 67.0% had not completed primary education<sup>12</sup>. In another study, conducted in China, in which 52% of the sample comprised individuals aged  $> 60$  years, 67% of patients were men and 71% required invasive or non-invasive ventilatory support, the main support measure used for these patients<sup>6</sup>.

Another study carried out in Brazil involving a sample of 67,180 confirmed cases of COVID-19 reported that 57.5% of cases occurred in men and

ICU stay was needed in 30.3% of the hospitalizations analyzed<sup>13</sup>. In this study, being an older male with low education was associated with an unfavorable outcome in relation to death from SARS. A meta-analysis found that male patients aged > 65 years may exhibit higher risk of becoming a critical or fatal case which, together with comorbidities, can significantly affect prognosis<sup>14</sup>.

Typically, men are less likely to access health services to monitor chronic diseases, while low education is a factor known to affect access to health and the adoption of healthy behaviors<sup>[15]</sup>. Additionally, low education is also associated with lower income, which may also affect this outcome<sup>16</sup>.

Evidence from different parts of the world suggests that age is the most significant factor contributing to risk of severe infection by COVID-19, along with its complications and adverse consequences, with immunosenescence or immune remodeling constituting the main reason why the older population is more vulnerable and susceptible to infections, with impaired immune responses<sup>17</sup>.

Regarding signs and symptoms, a higher prevalence of dyspnea, respiratory distress, saturation below 95% and cough was observed in the present study. These results are similar to those found in another study, which reported fever, cough, fatigue, chest pain and dyspnea as the most common symptoms, emerging within 5 days after the incubation period, a shorter timeframe in patients over 70 years compared to the general population<sup>7</sup>.

In another study, 85.2% of individuals presented with cough, while 79.6% reported fever and 76.6% dyspnea, symptoms characterizing SARS<sup>13</sup>. In a similar study carried out in the state of Ceará, Brazil, 86% of cases presented dyspnea, 85.2% had fever, 84.7% cough, and 77.1% experienced respiratory distress<sup>18</sup>. In a Chinese study, among the main symptoms highlighted, 98.0% of cases presented with fever, 77.0% with cough, and 63.5% with dyspnea<sup>[6]</sup>. The present findings are consistent with these results, and the characteristics corroborate the diagnosis of Severe Acute Respiratory Syndrome.

Regarding risk factors, comorbidities often coexist in older patients, and in such cases, individuals with these metabolic factors are more likely to be at risk for diseases and more unfavorable outcomes, exacerbating the severity of symptoms and consequences of COVID-19<sup>14,19</sup>. Multimorbidity is an important factor to be considered in older individuals, representing one of the main predictors of disability associated with inflammation. However, this involves a host of psychosocial processes that can contribute to healthy aging, provided this is associated with control of comorbidities and successful adaptation to health conditions<sup>20</sup>.

Aging is associated with deregulation of immunity in individuals, characterized by an increase in pro-inflammatory factors, promoting a greater probability of developing chronic morbidities which are risk factors for chronic kidney disease, diabetes mellitus, cancer, among others. These inflammatory mechanisms include genetic factors, changes in the body's microbiota, obesity, senescence, cell dysregulation and chronic infections<sup>21</sup>.

In a nationwide Brazilian study, hypertension was the main comorbidity found among the older population, having a prevalence of 43.8%, while more than 58.0% had a chronic non-communicable disease (NCD) considered a risk factor for COVID-19, worsening the severity of SARS cases, with men having more associated comorbidities than women<sup>2</sup>.

In another Brazilian study, involving individuals aged >50 years, half of the population, or approximately 52.0%, had some form of multimorbidity placing them at risk for severe COVID-19, with this group comprising 59.4% women and 43.5% men. The most prevalent morbidities were heart disease (56.0%), obesity (39%), arthritis (21.0%) and depression (18.5%)<sup>22</sup>. According to a Chinese retrospective study, the comorbidities most associated with older patients with COVID-19 were hypertension (30%), diabetes (19%) and coronary heart disease (8%)<sup>23</sup>. In another study, the main comorbidities found were heart diseases (66.5%) and diabetes mellitus (58.3%)<sup>18</sup>.

The estimated lethality of COVID-19 for individuals with heart disease is 10.5%, diabetes

mellitus 7.3%, chronic respiratory disease 6.3%, hypertension 6%, and with cancer is 5.6%<sup>24</sup>. In addition to higher risks for older patients and those with comorbidities, Chronic Obstructive Pulmonary Disease (COPD) and cardiovascular diseases are important predictors for complications in respiratory infections, in addition to clinical signs and biological markers, indicating inflammation or organ damage, aggravating COVID-19 cases or leading to death<sup>25</sup>.

In this study, the presence of heart disease had an inverse relationship with the occurrence of death in individuals with SARS, a finding that contrasts with the results of other studies. Although prevalent in individuals infected by COVID-19, it is unclear whether cardiovascular disease is an independent risk factor or is mediated by other factors, such as age and presence of other comorbidities<sup>26</sup>. Another study found that death in patients with heart disease was around 10.5%, given the virus can damage myocardial cells as a result of systemic inflammatory responses<sup>27</sup>.

Strengths of the present study include the analysis of the sociodemographic characteristics of the older patients infected by SARS in Passo Fundo, a city recognized as a regional health hub, as well as the prevalence of signs and symptoms, comorbidities and factors associated with a worse prognosis in this population. To the best of our knowledge, this is one of the first studies addressing the issue in the older population from southern Brazil and can serve to help plan and discuss health care policies for the older population.

Given this study entailed an analysis of secondary data, limitations include the possibility of underreporting and poor quality of mandatory reporting forms, with potential incomplete data regarding clinical information, errors in transcription, double-entry or validation, inherent to studies of this kind. Additionally, the data pertains to SARS notifications, therefore, only cases in which

hospitalization was required or that led to death from SARS were included in the investigation. Thus, the study only reports severe cases with influenza symptoms, and does not encompass asymptomatic or mild cases.

## CONCLUSION

In the cases notified in Passo Fundo, Rio Grande do Sul, lethality was higher in individuals aged > 80 years, with sociodemographic characteristics being determinants for the trajectory of SARS, where men and low-educated individuals were the most affected by the death outcome. The lethality observed was high, with the presence of risk factors (particularly chronic kidney disease), along with sociodemographic conditions, determining this outcome.

Regarding the symptoms experienced by the older patients, these were consistent with those recommended by the Ministry of Health for the classification of SARS cases, and the comorbidities associated with the cases reflected the most prevalent conditions in the older population in general, and in individuals infected by COVID-19, the main factor causing SARS in 2020.

It should be noted that the campaign for COVID-19 vaccination in 2021, including older adults as a priority group, changed the course of SARS in this specific population by lowering the number of hospitalizations. However, it is important to mention that older people remain the group most affected by the more severe forms of the disease, leading the morbidity and mortality statistics in 2021 and 2022.

The associations found in this study can help in the planning, management and assessment of health policies and actions by elucidating the priority groups for targeting strategic actions that promote greater self-care and easier access to health services, especially for the older male population.

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## REFERENCES

1. ORGANIZAÇÃO PAN-AMERICANA DA SAÚDE. COVID-19 e as Pessoas Idosas. Paho.org, 2020. Disponível em: <https://www.paho.org/pt/envelhecimento-saudavel/covid-19-e-pessoas-idosas>
2. ROMERO, D. E. et al. Idosos no contexto da pandemia da COVID-19 no Brasil: efeitos nas condições de saúde, renda e trabalho. *Cad. Saúde Pública* 37 (3) 31 Mar 2021. Available: <https://doi.org/10.1590/0102-311X00216620>.
3. DE ARAUJO, K. L. R. et al. Factors associated with severe acute respiratory syndrome in a Brazilian central region. *Ciência e Saúde Coletiva*. [s. l.], v. 25, p. 4121-4130, 2020. Available at: <https://doi.org/10.1590/1413-812320202510.2.26802020>
4. BRASIL; MINISTÉRIO DA SAÚDE. Diretrizes para Diagnóstico e Tratamento da COVID-19. Ministério da Saúde. Brasil. [S.l.], p.81. 2020.
5. SOCIETY, EUROPEAN RESPIRATORY. The Global Impact of Respiratory Disease – Forum of International Respiratory. European Respiratory Society. Sheffield, p. 43. 2017. (ISBN: 9781849840880).
6. YANG, X. et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine*, [s. l.], v. 8, n. 5, p. 475–481, 2020. Available at: [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5)
7. ROTHAN, H. A.; BYRAREDDY, S. N. The epidemiology and pathogenesis of coronavirus (Covid-19) outbreak. *Journal of Autoimmunity*, [s. l.], v. 109, n. January, p. 1–4, 2020.
8. BRASIL; MINISTÉRIO DA SAÚDE, FIOCRUZ. INFOGRIPE Boletim Semanal - 35/2022. [s. l.]. 2022.
9. COERS. BOLETIM EPIDEMIOLÓGICO – COVID-2019 – Semana Epidemiológica 33 de 2022. CENTRO DE OPERAÇÕES DE EMERGÊNCIA DO RIO GRANDE DO SUL/COERS. Porto Alegre, p.1. 2022.
10. COERS. BOLETIM EPIDEMIOLÓGICO – COVID-2019 – Semana Epidemiológica 51 de 2020. CENTRO DE OPERAÇÕES DE EMERGÊNCIA DO RIO GRANDE DO SUL/COERS. Porto Alegre, p.1. 2020.
11. VICTORA, C. et al. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. *Int J Epidemiol*. 1997 Feb;26(1):224-7.
12. REZENDE, L. F. M. et al. Adults at high-risk of severe coronavirus disease-2019 (Covid-19) in Brazil. *Revista de Saude Publica*, [s. l.], v. 54, p. 1–9, 2020. Available at: <https://doi.org/10.11606/S1518-8787.2020054002596>
13. SOUZA, W. M. et al. Epidemiological and clinical characteristics of the COVID-19 epidemic in Brazil. *Nature Human Behaviour*. v.4, p.856-865, 2020. Available at: <https://doi.org/10.1038/s41562-020-0928-4>.
14. ZHENG, Z. et al. Risk factors of critical e mortal COVID-19 cases: A systematic literature review and meta-analysis. *J Infect*, 2020 Aug; 81(2): e16–e25. Available at: <https://doi.org/10.1016/j.jinf.2020.04.021>
15. OLIVEIRA, J. et al. Influência da renda e do nível educacional sobre a condição de saúde percebida e autorreferida de pessoas idosas. *J Health Biol Sci*. 2019 Out-Dez; 7(4):395-398.
16. SALVATO, M. A., FERREIRA, P. C. G, DUARTE, A. J. M. O impacto da escolaridade sobre a distribuição de renda. *Est. econ., São Paulo*, v. 40, n. 4, p. 753-791, 2010. Available at: <https://doi.org/10.1590/S0101-41612010000400001>
17. CHEN, Y. et al. Aging in COVID-19: Vulnerability, immunity and intervention. *Ageing Res Rev*. 2021 Jan; 65: 101205. Available at: doi: 10.1016/j.arr.2020.101205.
18. LEMOS, D. R. et al. Health system collapse 45 days after the detection of COVID-19 in Ceará, Northeast Brazil: a preliminary analysis. *Journal of the Brazilian Society of Tropical Medicine* Vol.:53:(e20200354): 2020. Available: <https://doi.org/10.1590/0037-8682-0354-2020>.
19. MOAZZAMI, B. et al. Metabolic risk factors and risk of Covid-19: A systematic review and meta-analysis. *PloS One*. 2020; 15(12): e0243600. Available at: <https://doi.org/10.1371/journal.pone.0243600>
20. FRIEDMAN, E; SHOREY, C. Inflammation in multimorbidity and disability: An integrative review. *Health Psychol*. 2019 Sep;38(9):791-801. Available: <https://doi.org/10.1037/hea0000749>.
21. FERRUCCI, L; FABBRI, E. Inflammaging: chronic inflammation in ageing, cardiovascular disease, and frailty. *Nat Rev Cardiol*. 2018 Sep; 15(9): 505–522. Available: <https://doi.org/10.1038/s41569-018-0064-2>.
22. NUNES, B. P. et al. Multimorbidade e população em risco para COVID-19 grave no Estudo Longitudinal da Saúde dos Idosos Brasileiros. *Cad. Saúde Pública* 36 (12) 20 Nov 2020. Available: <https://doi.org/10.1590/0102-311X00129620>.

23. ZHOU, F. et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*, [s. l.], v. 395, n. 10229, p. 1054–1062, 2020. Available at: [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)
24. WU, Z; MCGOOGAN, J. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*, v. 323, n. 13, p. 1239-1242, 2020. Available at: <https://doi.org/10.1001/jama.2020.2648>.
25. IZCOVICH, A. et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. *PLoS One*. 2020; 15(11): e0241955. Available at: [doi:10.1371/journal.pone.0241955](https://doi.org/10.1371/journal.pone.0241955)
26. ASKIN, I.; TANRIVERDI, O; ASKIN, H. O efeito da doença de Coronavírus 2019 nas Doenças Cardiovasculares. *Arq. Bras. Cardiologia*. 114 (5); 2020. Available at: <https://doi.org/10.36660/abc.20200273>
27. NASCIMENTO, P. V., CARDOSO, M. S. L. Principais desfechos fatais em indivíduos cardiopatas acometidos por COVID-19. *Enferm. Foco*. 2020, 11 (Esp.2) 46-51.