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Comparison of comorbidities in the pre-pandemic and COVID-19 pandemic periods: a population-based study in Brazil

Comparação de comorbidades nos períodos pré-pandêmico e pandêmico da COVID-19: estudo brasileiro de base populacional

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ABSTRACT

Objective: To compare the prevalence of comorbidities in patients with severe acute respiratory syndrome (SARS) in the pre-pandemic and pandemic periods. **Methods:** This quantitative, cross-sectional, and analytical study used data from the Brazilian Ministry of Health and included individuals from the five Brazilian macro-regions (Southeast, South, Midwest, North, and Northeast) diagnosed with SARS in the pre-pandemic and pandemic periods. Descriptive and bivariate analyses using the chi-square test were performed with the Statistical Package for the Social Sciences for Windows® (SPSS), version 24.0. In the second stage, bivariate and multiple analyses were conducted using binary logistic regression, with variables retained at a significance level of <0.05. Odds ratios (OR), adjusted odds ratios (aOR), and 95% confidence intervals (95% CI) were calculated. **Results:** Comorbidities were more prevalent during the pandemic period. The aOR for individuals with SARS to have cardiovascular diseases during the pandemic was 4.85 (95% CI 4.72–4.98) compared with the pre-pandemic period. Individuals with SARS were also more likely to have diabetes during the pandemic (aOR 3.68; 95% CI 3.57–3.80), as well as obesity (aOR 2.56; 95% CI 2.43–2.70), compared with the pre-pandemic period. **Conclusion:** The data from this study suggest the need to establish reinforcement measures in primary care services to prevent complications in individuals with SARS.

Keywords: COVID-19; comorbidity; severe acute respiratory syndrome; obesity; diabetes mellitus; prevalence.

RESUMO

Objetivo: comparar a prevalência de comorbidades em pacientes com síndrome respiratória aguda grave (SRAG) nos períodos pré-pandêmico e pandêmico. **Métodos:** estudo quantitativo, transversal e analítico, realizado com dados do Ministério da Saúde do Brasil, envolvendo indivíduos das cinco macrorregiões brasileiras (Sudeste, Sul, Centro-Oeste, Norte e Nordeste) com diagnóstico de SRAG nos períodos pré-pandêmico e pandêmico. Análises descritivas e bivariadas, por meio do teste do qui-quadrado, foram realizadas com o *Statistical Package for the Social Sciences* for Windows® (SPSS), versão 24.0. Na segunda etapa, efetuaram-se análises bivariadas e múltiplas por regressão logística binária, mantendo-se as variáveis com nível de significância < 0,05. Adicionalmente, foram utilizados *odds ratio* (OR), OR ajustado (aOR) e intervalos de confiança de 95% (IC95%). **Resultados:** as comorbidades foram mais prevalentes no período pandêmico. A aOR para indivíduos com SRAG que apresentaram doenças cardiovasculares durante a pandemia foi de 4,85 (IC95%: 4,72–4,98) em relação ao período pré-pandêmico. Indivíduos com SRAG apresentaram maior probabilidade de diabetes durante a pandemia (aOR: 3,68; IC95%: 3,57–3,80), bem como de obesidade (aOR: 2,56; IC95%: 2,43–2,70), em comparação ao período pré-pandêmico. **Conclusão:** os dados deste estudo sugerem necessidade de estabelecer medidas de reforço nos serviços de atenção primária para prevenir complicações em indivíduos com SRAG.

Palavras-chave: COVID-19; comorbidade; síndrome respiratória aguda grave; obesidade; diabetes mellitus; prevalência.

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INTRODUCTION

In the last two decades, the global population has witnessed the emergence of epidemics caused by a family of viruses, the coronaviruses (CoV). These viruses were responsible for severe acute respiratory syndrome (SARS), first documented in China in 2002, and Middle East respiratory syndrome (MERS), reported in Saudi Arabia in 2012.[1-3] In December 2019, a new human coronavirus, SARS-CoV-2, was identified in Wuhan, China, leading to Coronavirus Disease 2019 (COVID-19).[1-3]

The SARS-CoV-2 virus has demonstrated significant virulence and is transmitted through contact with an infected person or contaminated fluids, with varying clinical manifestations among patients.[1-3] Advanced age and the presence of comorbidities such as obesity, cardiovascular diseases (CVD), and diabetes mellitus (DM) have been identified as risk factors for severe COVID-19.[4]

In recent decades, the number of people living with obesity has nearly tripled, reaching more than 650 million individuals worldwide.[5,6] In Brazil, this condition has increased across all age groups and acts as a precursor to other risk factors, such as DM, cardiovascular diseases (CVD), and systemic arterial hypertension (SAH).[4-7] Obesity is a chronic inflammatory condition resulting from the abnormal accumulation of fat, leading to dysfunctional adipose tissue.[4-7] The association between obesity and COVID-19 has demonstrated an increased risk of alterations in glucose metabolism and impairment of the cardiovascular system.[7]

The COVID-19 infection manifests with respiratory symptoms; however, SARS-CoV-2 can affect various organs, including the heart, causing severe cardiovascular sequelae. This occurs when the virus binds to the angiotensin-converting enzyme 2 (ACE2) receptor, which is highly expressed in coronary cells, resulting in an increased risk of complications and patient mortality.[8-9]

Brazil is among the countries with the highest number of individuals infected by SARS-CoV-2 worldwide. Subsequently, SARS-CoV-2 became part of the Sistema de Informação da Vigilância Epidemiológica da Gripe/SIVEP–Gripe (Influenza Epidemiological Surveillance Information System), established in 2009 by the initiative of the Brazilian Ministry of Health, specifically by the Secretaria de Vigilância em Saúde/SVS–MS (Secretariat of Health Surveillance – Ministry of Health).

Other respiratory viruses, including Influenza A (H1N1), Influenza A (H3N2), and Influenza B (B/Yamagata and B/Victoria), have also been incorporated into the system.[10] Therefore, this study aimed to compare the prevalence of comorbidities in patients with SARS in the pre-pandemic and pandemic periods.

METHODS

A quantitative, cross-sectional, and analytical study was conducted using data from the Influenza Epidemiological Surveillance Information System (SIVEP–Gripe) of the Brazilian Ministry of Health, accessible at https://sivepgripe.saude.gov.br/sivepgripe/.

The SIVEP–Gripe includes sociodemographic and clinical data related to the diagnosis of severe acute respiratory syndrome (SARS) caused by various agents (COVID-19, Influenza, Parainfluenza, and Adenovirus). Patients from all five Brazilian macro-regions—Southeast, South, Midwest, North, and Northeast—were included in this analysis.

The diagnosis of severe acute respiratory syndrome (SARS) caused by COVID-19 was confirmed through the real-time reverse transcription polymerase chain reaction (RT-PCR) test to detect viral RNA in samples, as this is the standard test for detecting SARS-CoV-2.

The variables included in this study were: gender (male, female); race (white, non-white); sore throat (no, yes); cardiovascular diseases (no, yes); kidney disease (no, yes); immunosuppression (no, yes); diabetes (no, yes); obesity (no, yes); and need for ventilatory support (no, yes).

The outcome variable for comparing cases was the notification period, categorized as pre-pandemic (2018–2019) and pandemic (2020–2021).

The analysis was conducted using the Statistical Package for the Social Sciences for Windows® (SPSS), version 24.0. Descriptive analysis was performed using absolute (n) and relative frequencies (%), and bivariate analysis was conducted using Pearson's chi-square test (χ^2) to identify potential associations between the etiology of SARS and the other investigated variables.

A significance level (α) of less than or equal to 0.05 ($p \leq 0.05$) was adopted.

The second stage of the statistical analysis involved bivariate and multiple analyses using binary logistic regression. Variables with a significance level < 0.05 remained in the final model.

Additionally, odds ratio (OR) and adjusted odds ratio (aOR) were calculated with their respective 95% confidence intervals (95% CI).

For multiple analyses, the presence of multicollinearity was assessed using tolerance and variance inflation factor (VIF) values, and the quality and fit of the final model were evaluated using the Omnibus and Hosmer–Lemeshow tests.

The analyzed data are secondary and publicly available; thus, approval from a Research Ethics Committee was waived.

RESULTS

A total of 1,087,683 notified cases of SARS were analyzed in this study, with 95,803 cases in the pre-pandemic period and 991,880 in the pandemic period.

In both periods, a higher prevalence of males was observed, at 54.2% and 51.2%, respectively.

Ethnicity showed different distributions between the two periods, with a higher proportion of whites (57.0%) in the pre-pandemic period and a lower proportion (48.8%) in the pandemic period.

Regarding clinical factors, sore throat presented a prevalence close to 20% in both periods.

All comorbidities showed a higher prevalence in the pandemic period (Table 1)

Table 1. Bivariate analysis of sociodemographic and clinical characteristics in the pre-pandemic and pandemic periods.

Variables	Pre-pandemic n (%)	Pandemic n (%)	*p*-valor
Gender			
Female	46,727 (48.8)	454,185 (45.8)	<0.001
Male	49,056 (51.2)	537,386 (54.2)	
Ethnicity			
White	46,278 (57.0)	381,417 (48.8)	<0.001
Non-white	34,941 (43.0)	400,263 (51.2)	
Sore throat			
No	70,084 (81.2)	561,460 (77.4)	<0.001
Yes	16,189 (18.8)	164,385 (22.6)	
Cardiopathy			
No	53,207 (83.9)	194,078 (37.8)	<0.001
Yes	10,217 (16.1)	319,252 (62.2)	
Kidney disease			
No	60,488 (96.3)	364,439 (89,8)	<0,001
Yes	2,296 (3.7)	41,264 (10.2)	
Immunosuppression			
No	58,956 (93.9)	369.442 (92.0)	<0,001
Yes	3,824 (6.1)	32,203 (8.0)	
Diabetes			
No	56,148 (89.0)	253,693 (53.1)	<0,001
Yes	6,974 (11.0)	224,413 (46.9)	
Obesity			
No	60,136 (96.5)	352,836 (87.9)	<0,001
Yes	2,166 (3.5)	48,558 (12.1)	
Ventilatory support			
No	34,870 (38.0)	257,727 (31.3)	<0,001
Yes	56,866 (62.0)	566,526 (68.7)	

The variables included in the multiple analysis showed appropriate tolerance and variance inflation factor (VIF) values, indicating the absence of multicollinearity.

Male patients had a higher proportion of cases in the pandemic period (aOR 1.12; 95% CI 1.10–1.15). Regarding race, the highest proportion was among non-white individuals (aOR 1.40; 95% CI 1.37–1.43), and adjusted values were very similar to the crude OR values. It was observed that the likelihood of having a sore throat during the pandemic was 1.27 times that in the pre-pandemic period.

However, in the multiple models, the aOR for sore throat was 20% lower compared with the pre-pandemic period. The adjusted odds of individuals with SARS having cardiovascular diseases during the pandemic were 4.85 (95% CI 4.72–4.98) times the odds of having the same health condition in the pre-pandemic period (Table 2).

The aOR for patients with SARS having kidney disease (aOR 1.58; 95% CI 1.49–1.66) and being immunosuppressed (aOR 1.58; 95% CI 1.51–1.65) during the pandemic were very similar.

Individuals with SARS had a higher likelihood of being diabetic during the pandemic (aOR 3.68; 95% CI 3.57–3.80) compared with the pre-pandemic period. Among patients with obesity, the pandemic period also proved to be a risk factor for the development of SARS (aOR 2.56; 95% CI 2.43–2.70). It was also observed that, for the clinical variables, there was a reduction in the OR from bivariate to multiple analysis, except for the need for ventilatory support. In the pandemic period, the adjusted odds of individuals with SARS requiring ventilatory support were 1.55 (95% CI 1.51–1.58), contrasting with the crude OR of 1.34 (95% CI 1.33–1.36) (Table 2).

Table 2. Result of binary logistic regression bivariate and multivariate with OR and aOR for the presence of variables in the pandemic period compared to the pre-pandemic period.

Variables	OR (95% IC)	*p*-valor	aOR (95% IC)	*p*-valor
Gender				
Female	1.00	<0.001	1.00	<0.001
Male	1.27 (1.11–1.14)		1.12(1.10–1.15)	
Ethnicity				
White	1.00	<0.001	1.00	<0.001
Non-white	1.39 (1.37–1.41)		1.40 (1.37–1.43)	
Sore throat				
No	1.00	<0.001	1.00	<0.001
Yes	1.27 (1.24–1.29)		0.80 (0.78–0.83)	
Cardiopathy				
No	1.00	<0.001	1.00	<0.001
Yes	8.56 (8.38–8.75)		4.85 (4.72–4.98)	
Kidney disease				
No	1.00	<0,001	1.00	<0,001
Yes	2.98 (2.85–3.11)		1.57 (1.49–1.66)	
Immunosuppression				
No	1.00	<0,001	1.00	<0,001
Yes	1.34 (1.30–1.39)		1.58 (1.51–1.66)	
Diabetes				
No	1.00	<0,001	1.00	<0,001
Yes	7.12 (6.94–7.30)		3.68 (3.57–3.80)	
Obesity				
No	1.00	<0,001	1.00	<0,001
Yes	3.82 (3.65–3.99)		2.56 (2.43–2.70)	
Ventilatory support				
No	1.00	<0,001	1.00	<0,001
Yes	1.34 (1.33–1.36)		1.54 (1.51–1.58)	

DISCUSSION

A total of 1,087,683 cases of SARS were analyzed in this study, representing a higher incidence during the pandemic period compared with the pre-pandemic period. Brazil is among the countries with the highest number of individuals infected by SARS-CoV-2 worldwide.[10]

The results of this analysis showed a higher prevalence of males among SARS patients during the pandemic period compared with the pre-pandemic period.

Male individuals were more likely to be diagnosed with SARS due to COVID-19 and had more severe cases and higher mortality rates, probably because male and female sex hormones influence susceptibility to SARS-CoV-2 infection, as they affect adaptive and innate immune responses. This results in lower susceptibility to viral infections among women, which can be attributed to the protective role of the X chromosome, sex hormones–mainly estrogen–and lifestyle.[11-14]

Comparative studies on racial differences in health and outcomes from COVID-19 in three countries – South Africa, Brazil, and the United States of America (USA) – revealed that women were more affected in the USA and South Africa, but there were more deaths among men.

In Brazil, the vast majority of men were infected by the SARS-CoV-2 virus, which confirms the analyses of this study.[15] In South Africa, the higher number of female cases may be due to exposure to roles related to healthcare and teaching, as well as healthcare-seeking behaviors.[15]

In Brazil, there are limited data on COVID-19 by ethnic/racial group. In this analysis, ethnicity showed a higher proportion of whites in the pre-pandemic period and a lower proportion in the pandemic period.

Individuals diagnosed with SARS due to COVID-19 had a higher likelihood of being non-white compared with white individuals, with adjusted values very similar to the crude odds ratio.

Previous studies in the USA showed that African American/Black and Hispanic populations had higher rates of SARS-CoV-2 infection and mortality than non-Hispanic white populations.[12]

Another analysis[15] reinforces these findings, indicating that individuals of African descent and minority populations are at a higher risk of COVID-19-related infections and hospitalizations than white patients in multiracial societies.

A study focused on the largest Brazilian city, São Paulo, showed that Black men had a higher risk of death. In contrast, white individuals had a greater chance of needing intensive care, and mixed-race individuals were protected against intensive care unit (ICU) hospitalization.[16]

COVID-19 manifests through a wide spectrum of symptoms, without standardization of characteristics. The Ministry of Health considers fever, cough, respiratory discomfort, and fatigue the most common clinical symptoms of COVID-19. In this analysis, sore throat in the pandemic period was less frequent.

A systematic review[17] showed that symptoms such as runny nose, dyspnea, and sore throat were less frequent in cases of COVID-19 compared with influenza, indicating differences in clinical manifestations between the two pneumonias. Therefore, sore throat was considered a mild symptom in the reports of most patients.[18]

The clinical manifestations of anosmia and ageusia were considered important in screening patients with suspected COVID-19 but were not observed in the pre-pandemic period.[19-21]

Among the pre-existing comorbidities assessed, patients with SARS showed a higher prevalence in the pandemic period than in the pre-pandemic period.

The most frequent comorbidities were heart disease, diabetes mellitus, and obesity, followed by kidney disease and immunosuppression.

Comorbidities associated with COVID-19 were considered responsible for increasing the risk of severe lung injury, hospitalization, ICU admission, and mortality, especially among individuals over 60 years of age, a condition confirmed in previous studies.[22-24]

In the presence of comorbidities, it is established that SARS-CoV-2 uses ACE2 receptors, which are strongly expressed on the surface of host cells, to enter the cell, a process associated with increased release of pro-protein convertase, responsible for viral entry.[24]

It has been observed that the kidney can be one of the targets of SARS-CoV-2 infection due to the increased expression of ACE2 in renal tissues.[22-24] This study found a higher aOR for kidney disease during the pandemic period, which may be related to this increased vulnerability.

Patients with SARS during the pandemic period were found to have a significantly higher chance of developing heart disease compared with the pre-pandemic period.[24-26]

Cardiovascular diseases were also found to be the most common pre-existing comorbidities during COVID-19 infection.[24-26] Therefore, cardiovascular diseases have become a significant risk factor for patients with COVID-19, especially when associated with other comorbidities such as hypertension, diabetes, and obesity. This results in increased disease severity and mortality.[24-26]

Obesity is a clinical condition considered a global public health problem, associated with an increased risk of developing clinical complications and having a poor prognosis in individuals with COVID-19, as well as in severe influenza pneumonia.[25,26]

COVID-19 and influenza pneumonia can involve systemic inflammatory processes and airway compromise, in addition to affecting the immune and endocrine systems, posing a high cardiovascular risk.[26] Therefore, obese patients infected with SARS-CoV-2 are at a higher risk of progressing to severe COVID-19, requiring ICU admission, mechanical ventilation, experiencing shock and acute kidney failure, and facing a higher mortality rate.[26]

Individuals with SARS showed a higher chance of being diabetic during the pandemic period compared with the pre-pandemic period.

According to previous studies, in diabetic patients with COVID-19, ACE2 receptors are activated by the high expression of a protease called furin, which facilitates viral entry into the host cell. This process is responsible for disrupting the immune response and is associated with increased pulmonary inflammation and decreased insulin levels.[24,27,28]

A meta-analysis found that diabetes increased the risk of COVID-19 severity by 2.3 times and the risk of mortality by 2.5 times.[27,28]

Diabetes, one of the most frequent comorbidities in people with COVID-19, was associated with high hospitalization rates and a greater risk of impairment of innate and humoral immunity, severe pneumonia, and higher mortality.[28]

In this study, during the pandemic period, the aOR of individuals with SARS requiring ventilatory support was higher than that of those who did not require ventilatory support.

This study presents limitations. Secondary databases may contain errors or missing information, limiting the reliability of the findings. The limited variables available in secondary databases restrict the depth of analysis and may overlook crucial factors.

Additionally, the lack of detailed contextual information makes it challenging to interpret the findings accurately. Nevertheless, we underscore the use of multiple regression analyses performed on an extensive database with a substantial sample size as a noteworthy strength.

CONCLUSION

Brazil experienced a coronavirus pandemic that greatly affected the health of its population. During the pandemic, a higher number of males and non-white individuals were affected by severe acute respiratory syndrome (SARS) compared with the pre-pandemic period.

There was also a higher prevalence of comorbidities such as cardiovascular diseases, diabetes, obesity, kidney disease, and immunosuppression among patients with SARS during the pandemic. These comorbidities increased the likelihood of severe lung injury, hospitalization, ICU admission, and mortality.

The study highlights the need to strengthen primary care services to prevent complications in individuals with SARS and avoid hospitalizations.

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Conflicts of Interest

None declared.

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