

Regional heterogeneity of in-hospital mortality of COVID-19 in Brazil

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ABSTRACT

Background: The ongoing Coronavirus disease of 2019 (COVID-19) pandemic has hit Brazil hard in period of different dominant variants. Different COVID-19 variants have swept through the region, resulting that the total number of cases in Brazil is the third highest in the world. This study is aimed at investigating the regional heterogeneity of in-hospital mortality of COVID-19 in Brazil and the effects of vaccination and social inequality.

Methods: We fitted a multivariate mixed-effects Cox model to a national database of inpatient data in Brazil who were admitted for COVID-19 from February 27, 2020 to March 15, 2022. The in-hospital mortality risks of vaccinated and unvaccinated patients were compared, with adjustment for age, state, ethnicity, education and comorbidities. And the effects of variables to in-hospital mortality were also compared. Stratified analysis was conducted across different age groups and vaccine types.

Results: By fitting the multivariate mixed-effects Cox model, we concluded that age was the most important risk factor for death. With regards to educational level, illiterate patients (hazard ratio: 1.63, 95% CI: 1.56–1.70) had a higher risk than those with a university or college degree. Some common comorbidities were more dangerous for hospitalized patients, such as liver disease (HR: 1.46, 95% CI: 1.34–1.59) and immunosuppression (HR: 1.32, 95% CI: 1.26–1.40). In addition, the states involving Sergipe (HR: 1.75, 95% CI: 1.46–2.11), Roraima (HR: 1.65, 95% CI: 1.43–1.92), Maranhão (HR: 1.57, 95% CI: 1.38–1.79), Acre (HR: 1.44, 95% CI: 1.12–1.86), and Rondônia (HR: 1.26, 95% CI: 1.10–1.44) in the north and the northeast region tended to have higher hazard ratios than other area. In terms of vaccine protection, vaccination did not significantly reduce mortality among hospitalized patients. Sinovac and AstraZeneca offered different protection in different regions, and no vaccine provided high protection in all regions.

Conclusion: The study revealed the regional heterogeneity of in-hospital mortality of Covid-19 in Brazil and the effects of vaccination and social inequality. We found that ethnic concentrations were consistent with higher proportion of death cases relative to population size. White Brazilians had more frequent international travel opportunities. As race revealed the intersection of social connections, we speculated that uneven interactions with residential communities partially contribute to the spread of the epidemic. Additionally, the vaccine showed different protection in different regions. In the northern and northeastern regions, AstraZeneca was much more protective than Sinovac, while Sinovac

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was more protective for hospitalized patients with varying numbers of comorbidities in the Central-west, Southeast and South regions.

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1. Introduction

According to The World Health Organization (WHO), there were over 445 million cases have been reported, including about 6 million deaths. In Brazil, although Brazil's population accounts for only 2.73% of the world, 8.07% of reported cases and 11.53% of reported deaths originated from this country ([https://www.who.int/emergencies/diseases/novel-coronavirus-2019.2021, 2021](https://www.who.int/emergencies/diseases/novel-coronavirus-2019.2021,2021)).

Variations in COVID-19 mortality among different ethnic groups reveal inequalities in social structure. Previous studies carried out in the context of developed countries were mainly concentrated on the United States, the United Kingdom and some other European countries. Consistent results indicated that some ethnic minority groups were more vulnerable to SARS-CoV-2 infection such as African American and Black British ([Niedzwiedz et al., 2020](#)). As a continental country composed of many ethnic groups, Brazil had deeply rooted in social inequalities. The Brazilian population was racially divided into five categories involving branco (white), pardo (brown or mixed), preto (black), amarelo (yellow), and caboclo (indigenous) according to the Brazilian Institute of Geography and Statistics. Compared with white ethnicity, Black and Brown Brazilian regarded as underprivileged commonly received lower level of education and income and gain limited access to the healthcare system ([Hone et al., 2017](#)). The epidemic bore witness to such heterogeneous differences. Struggling in the welfare system, vulnerable groups were not guaranteed income support in emergency situations and faced few channels to obtain timely information ([Ahmed et al., 2020](#)). Moreover, the uncertainty of economic conditions may also damage the mental health of disadvantaged groups and exacerbate their pressure, which would reduce the strength of the immune system and therefore increased the susceptibility to a series of viruses ([Patel et al., 2020](#)).

There were three types of COVID-19 vaccines distributed in Brazil, including Coronavac (Sinovac), AZD1222 (AstraZeneca) and BNT162b (Pfizer/BioNTech). By May 15, 2021, in the first dose, Coronavac, AZD1222 and BNT162b vaccines were responsible to vaccinate 9.61%, 6.69% and 0.35% of the Brazilian population. In the second dose, Coronavac, AZD1222 and BNT162b vaccines were responsible for 7.52%, 0.53% and <0.01% of the Brazilian population, respectively ([Boschiero et al., 2021](#)).

While some existing literatures have discussed the unbalanced impact of COVID-19 on social status and ethnicity in developing countries ([Li et al., 2021](#)), this study further examined specific epidemiological characteristics for patients with different ethnicities and education levels in various regions and explored the effect of prevalent comorbidities on in-hospital mortality rates. Moreover, we focused on the efficacy of vaccines in Severe Acute Respiratory Infections (SARI) fatality ratio in patients with different number of comorbidities and different ages, and compared the effectiveness of Sinovac and AstraZeneca vaccines.

2. Methods

2.1. Data collection

The individual patient data used by this study were retrieved from the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe) and spanned the time interval from February 27, 2020 to March 15, 2022. Demographic data by regions were retrieved from the publicly available source according to the Census.

All hospitalized patients with a positive reverse transcription-polymerase chain reaction (RT-PCR) test result for SARS-CoV-2 and a defined outcome of discharge or death during this period were included. Each patient data carried 154 labels involving demographic information and clinical features while the access to some values was restricted by the government. Among these characteristics, age, gender, state, ethnicity, vaccination, comorbidities, education level and date admitted into hospital were selected for our analyses.

Comorbidities were not reported in about 51.4% of cases in the database. We interpreted unavailable values as the absence of such comorbidities. A total of eleven comorbidities were considered in this study, involving cardiovascular disease, hematologic disease, liver disease, neurological disease, kidney disease, down syndrome, asthma, diabetes, immunodeficiency, pulmonary and obesity.

For the periods in which different variants dominated, we set several time intervals corresponding to the three variants that have emerged since the original strain. First, we set the dominant period of the Ancestor strain to March 13, 2020 from November 23, 2020. We then set the Gamma (P.1) variant to dominate from November 23, 2020 to August 16, 2021. The Delta (B.1.617.2) variant dominant period is set for August 16, 2021 to December 6, 2021, and the period after December 16, 2021 is set for Omicron (B.1.1.529) variant dominant period.

2.2. Statistical analysis

In this study, the in-hospital mortality rate as the proportion of deaths after hospitalization was selected to be the interest outcome variable. Pearson's Chi-squared test was firstly performed for categorical variables, and one-way analysis of variance (ANOVA) was examined for continuous variables. Together with the p-value of null hypothesis significance testing, we presented the data showing demographic features and comorbidities and ethnic composition of patients in five macro regions. We used programming language R with package 'dplyr', 'stringr', 'coxme', and 'metafor' in this study.

To quantify the impacts of ethnicity, comorbidities and education at the individual level, we utilized mixed-effects Cox proportional hazards regression analysis (under package "coxme") under the background of geographical differences. Similar to an analysis of mortality in COVID-19 intensive care unit in the United Kingdom (Qian et al., 2020) and an analysis of early-stage mortality in Brazil (Liu et al., 2020), patient-level clinical characteristics involving age, gender, race, education, vaccination and comorbidities were treated as fixed effects while region was regarded as random effects. In terms of categorical variables, White Brazilian, unvaccinated patients, university degree or above and the age group under 40 were set as the reference category for ethnicity, vaccination, education and age respectively. We plotted hazard ratio with 95% confidence interval afterwards in the forest plot.

We subsequently compared the in-hospital mortality rate by age between patients with different features. The features for number of comorbidities, ethnic groups (Sharma et al., 2020) and education level (Halpin et al., 2020) were explored correspondingly. Education level recorded the last grade the patient attended. Then in order to study the efficacy of the vaccine, whether patients had been vaccinated before hospitalization was differentiated. In studies of efficacy of vaccine, we firstly compared the SARI fatality ratio of vaccinated patients and unvaccinated patients with the different number of comorbidities. The SARI fatality ratio was plotted by the number of comorbidities per patient. Next, the SARI fatality ratio was compared between vaccinated and unvaccinated patients of different ages and the SARI fatality ratio was plotted by age. Additionally, for hospitalized patients of different ages and with the different number of comorbidities, by visualizing their fatality ratio, we compared the effectiveness of two most common vaccines (Sinovac and AstraZeneca).

3. Results

3.1. Demographic features of data

We firstly presented the demographic features of our data among patients with death and discharge outcomes. In Table 1, cases were distributed across five age groups, but overall, the proportion of deaths increased with age. Prevalence of deaths was marginally higher in male (34.6%) than in female (34.4%), in Black and Indigenous Brazilians (39.2% and 38.6% respectively) than in other ethnic groups, and in unvaccinated patients (34.7%) than in vaccinated patients (33.4%). There was a slight predominance of hospitalized death proportion in the northeast region, accounting for 42.2% of cases in this area, followed by the north population (37.2%). Compared with illiterate patients (48.4%), mortality rate was around 25% lower in those with a university degree (23.4%). Almost all comorbidities were shown to affect mortality among hospitalized patients. Then Table S1 showed the ethnic composition in each region. In most areas, the percentage of hospitalizations and deaths in the region for ethnic groups was consistent. In the north, northeast and central-west region, Whites had far fewer proportion of hospitalizations and deaths than their population distributions, while Pardos had higher rates of hospitalizations and deaths compared with their population size. However, this relative ratio exhibited opposite characteristics in the southeast and south region.

3.2. Fitted multivariate mixed-effects cox model

For the fitted multivariate mixed-effects Cox model, Fig. 1 showed the fixed effects estimates, and Fig. 2 showed the random effects. Compared with patients younger than 40 years old, patients over 70 years old had a significantly higher rate of hospital mortality (HR: 2.93, 95% CI: 2.82–3.06). Especially, age was observed to be the most critical risk factor for death. With regards to education level, illiterate patients (HR: 1.63, 95% CI: 1.56–1.70) had higher risk than patients with university degree or above. This was followed by some relatively dangerous comorbidities represented by liver disease (HR: 1.46, 95% CI: 1.34–1.59) and immunosuppression (HR: 1.32, 95% CI: 1.26–1.40). In comparison with White Brazilians, Black Brazilians suffered from higher risk of death (HR: 1.07, 95% CI: 1.03–1.12). In addition, significant variations were found between hazard ratios in different Brazilian states. The five states involving Sergipe (HR: 1.75, 95% CI: 1.46–2.11), Roraima (HR: 1.65, 95% CI: 1.43–1.92), Maranhão (HR: 1.57, 95% CI: 1.38–1.79), Acre (HR: 1.44, 95% CI: 1.12–1.86), and Rondônia (HR: 1.26, 95% CI: 1.10–1.44) with the highest hazard ratios were all from the north and the northeast region. The area in these two regions tended to have higher hazard ratios than other states.

3.3. In-hospital mortality rate

We firstly visualized the fatality ratio by age in period of different dominant variants in 27 Brazilian states to provide an overview of respiratory hospitalized mortality in Brazil. From Fig. S1, we were able to check the fatality ratio by age in each period of different dominant variant in 27 Brazilian states. In almost all states, the peak of fatality ratio was concentrated on patients who aged 60 to 70. Additionally, in most states, the fatality ratio of first period of different dominant strains was

Table 1
Explanatory variables of cases.

	Death	Discharge	P-value
Age			< 0.001
< 40 years	6550 (13.0%)	43781 (87.0%)	
40–49 years	9624 (21.7%)	34669 (78.3%)	
50–59 years	16552 (29.9%)	38783 (70.1%)	
60–69 years	20641 (41.1%)	29633 (58.9%)	
> 70 years	42457 (54.8%)	35022 (45.2%)	
Gender			0.106
Female	42227 (34.4%)	80576 (65.6%)	
Male	53597 (34.6%)	101312 (65.4%)	
Region			< 0.001
North	6316 (37.2%)	10659 (62.8%)	
Northeast	13775 (42.2%)	18901 (57.8%)	
Central-west	9698 (33.6%)	19171 (66.4%)	
Southeast	42724 (35.1%)	78911 (64.9%)	
South	23311 (30.1%)	54246 (69.9%)	
Ethnic Group			< 0.001
White	55161 (33.2%)	110806 (66.8%)	
Black	4725 (39.2%)	7337 (60.8%)	
Yellow	883 (33.9%)	1722 (66.1%)	
Pardo	34827 (36.1%)	61660 (63.9%)	
Indigenous	228 (38.6%)	363 (61.4%)	
Education Level			< 0.001
Illiterate	4613 (48.4%)	4924 (51.6%)	
Elementary School	16614 (43.8%)	21293 (56.2%)	
Middle School	8722 (34.5%)	16527 (65.5%)	
High School	10878 (26.8%)	29678 (73.2%)	
University	4052 (23.4%)	13291 (76.6%)	
Vaccine			< 0.001
Vaccinated	11645 (33.4%)	23271 (66.6%)	
Unvaccinated	84179 (34.7%)	158617 (65.3%)	
Comorbidities			< 0.001
Cardiovascular Disease	37783 (45.5%)	45241 (54.5%)	
Hematology	668 (48.2%)	719 (51.8%)	
Down syndrome	361 (42.9%)	480 (57.1%)	
Liver Disease	1044 (56.8%)	794 (43.2%)	
Asthma	1990 (31.8%)	4276 (68.2%)	
Diabetes	27592 (46.7%)	31484 (53.3%)	
Neurological Disease	4966 (54.4%)	4158 (45.6%)	
Pulmonary	4433 (55.0%)	3634 (45.0%)	
Immunodepression	2834 (54.5%)	2366 (45.5%)	
Renal	4858 (60.1%)	3220 (39.9%)	
Obesity	11203 (42.8%)	14964 (57.2%)	

significantly higher than that of other covid strains. It meant the mortality rate of respiratory inpatients during the Wild strain dominance period was much higher than that of respiratory inpatients during the other variants dominance periods. For third and fourth period of different dominant variants which dominated by Delta (B.1.617.2) and Omicron (B.1.1.529) variants, the fatality ratio seemed to remain relatively low across all age groups.

Then we studied the in-hospital fatality rate by age between patients with different comorbidities, education level and ethnical groups. In Fig. 3, it exhibited the variation of in-hospital mortality rate in patients with different number of comorbidities. Generally, the risk of death for hospitalized patients increased with the number of comorbidities. The biggest risk gap between one and none comorbidity (around 20%) was larger than that between multiple comorbidities (less than 10%). A more considerable mortality rate was observed in teenagers with three kinds of comorbidities. Fig. S2 showed how mortality rates change with age of different ethnicities in Brazil. In middle age (30–60 years old), no significant disparities were examined across races. Older (more than 70 years old) Indigenous, Yellow and Black Brazilian as well as indigenous population of infants had a higher risk of death. In indigenous youth (15–24 years old), the risk was relatively lower. In Fig. S3, we demonstrated the comparison of in-hospital mortality rate for patients with different levels of education. For cases under the age of 80, higher education indicated relatively lower risk. The difference in mortality between illiterate and patients with a certain level of education was greater than that between patients with different schooling lengths. Notably, both gaps reached the peak at around age 18 and gradually decreased thereafter. Nevertheless, little differences were detected for patients around 80 years old.

3.4. Efficacy of vaccines

In the study of vaccination efficacy, Fig. 4 showed the variation in SARI fatality ratios between vaccinated and unvaccinated patients by the number of comorbidities and regional differences. Based on similar income levels and health conditions, the

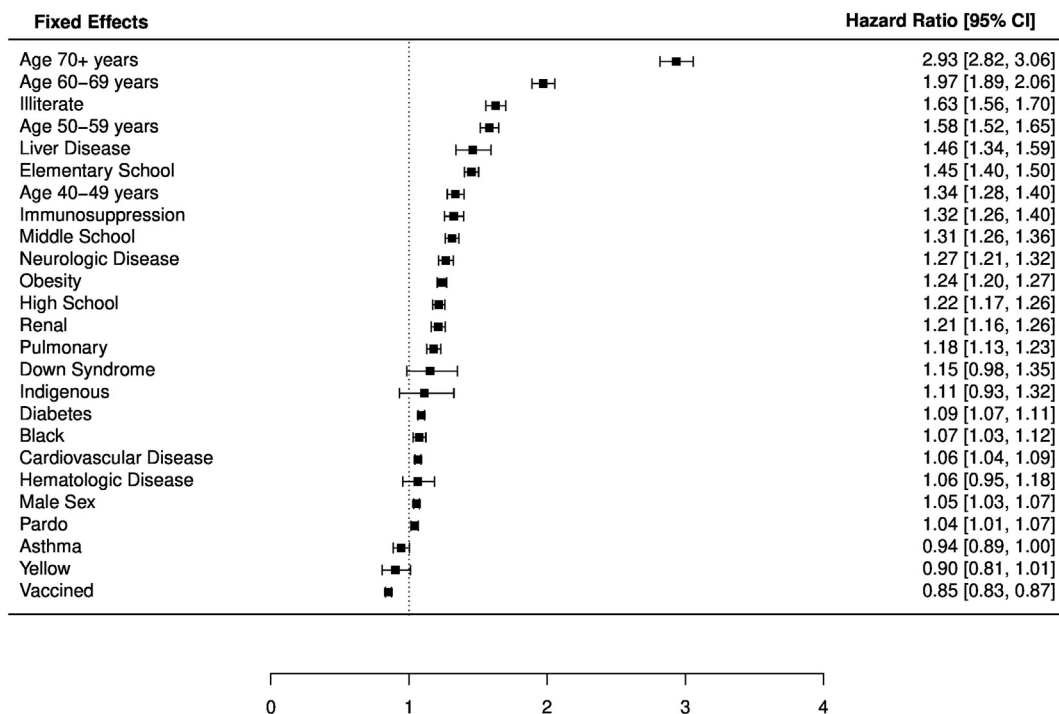


Fig. 1. Risk of death by clinical features (fixed effects).

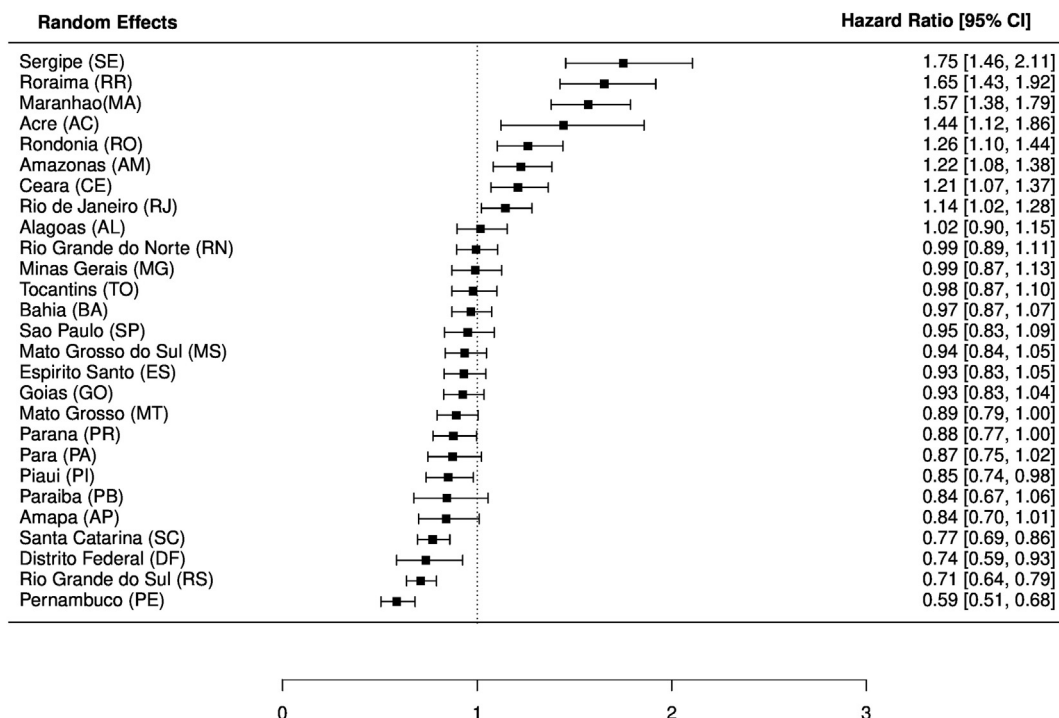


Fig. 2. Risk of death by states (random effects).

regions were divided into five areas with the greatest differences were presented. In general, vaccination did not significantly help these patients with comorbidities. Among vaccinated and unvaccinated cases, the fatality rates were higher for Wild stain and Gamma (P.1) variant than for Delta (B.1.617.2) and Omicron (B.1.1.529) variant. For the period dominated by all of four strains, the fatality ratios increased with the number of comorbidities, reached the peak at around 5 comorbidities and

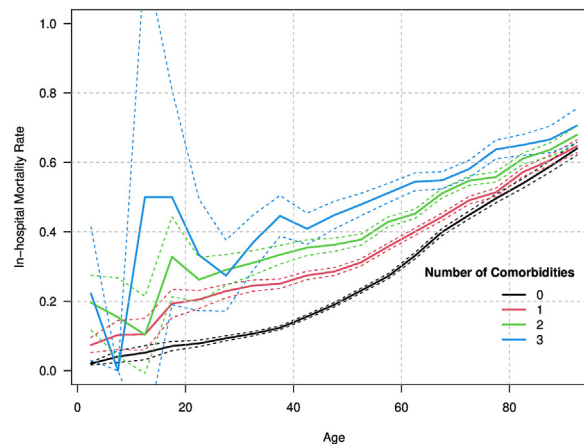


Fig. 3. In-hospital Mortality Rate by Age between Patients with Different Comorbidities. The black line shows patients with no comorbidities. The red line, the green line and the blue line represent patients with one, two, and three kinds of comorbidities, respectively.

decreased thereafter. For the comparison in SARI fatality ratios between vaccinated and unvaccinated patients by age and regional differences, from Fig. S4, there was no significant change in SARI fatality ratio for all age groups after vaccination compared with non-vaccination.

In order to investigate the effectiveness of two types of vaccines involving Sinovac and AstraZeneca, for hospitalized patients with the different number of comorbidities, we compared their fatality ratio in two maximally contrasting regions. In Fig. 5, for the period dominated by Gamma (P.1) variant, in general, AstraZeneca was more effective than Sinovac in preventing the deaths of hospitalized patients, but in Central-west, Southeast and South region, Sinovac demonstrated high protection in patients with more than four comorbidities. In Delta (B.1.617.2) variant dominated period, both of two vaccines showed similar protection for the hospitalized patients with no more than four comorbidities, and for patients with four or more comorbidities, Sinovac showed a greater protective effect than AstraZeneca. For the period dominated by Omicron (B.1.1.529) variant, in North and Northeast region, AstraZeneca demonstrated much greater protection than Sinovac, but in Central-west, Southeast and South region, Sinovac was more protective for patients with the different number of comorbidities. And for hospitalized patients of different ages, Fig. S5 showed the effectiveness of two vaccines for patients of different ages. Sinovac was more effective in reducing SARI fatality ratio of patients under 60 during transmission of the Gamma (P.1) variant, and AstraZeneca showed greater protection for patients older than 60. For Delta (B.1.617.2) variant, in Central-west, Southeast and South region, AstraZeneca was more effective in reducing children and elderly patients' SARI

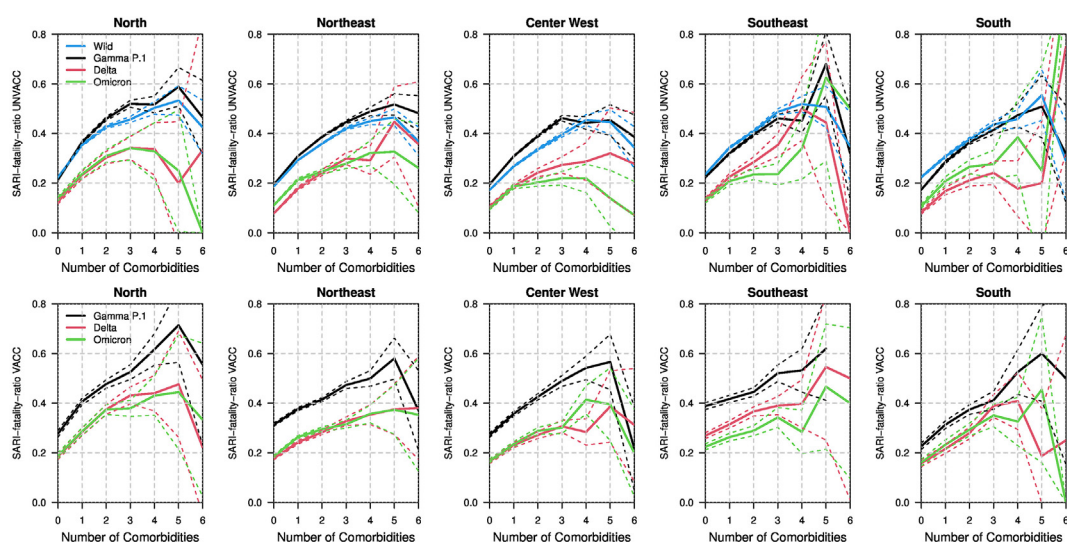


Fig. 4. SARI-fatality ratio in vaccinated and unvaccinated patients by the number of comorbidities and regional differences. Each color represents a period dominated by a variant. The black line represents the Gamma (P.1) variant dominated period, the red line shows the Delta (B.1.617.2) variant dominated period, and the green line indicates the Omicron (B.1.1.529) dominated period.

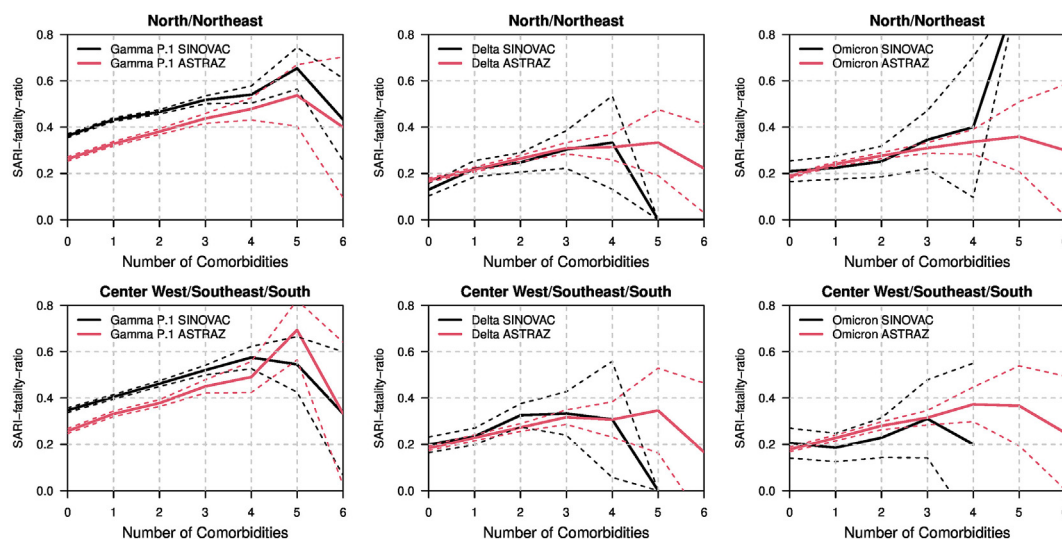


Fig. 5. SINOVA vs. ASTRAZ by the number of comorbidities. Comparing the effectiveness of two vaccines for patients with the different number of comorbidities. The red line represents the AstraZeneca and black line represents Sinovac. And the SARI-fatality-ratios were plotted with 95% confidence interval displayed by the dashed lines.

fatality ratio, and in North and Northeast region, Sinovac offered better protection than AstraZeneca across all age ranges. Similarly, the greater protection of Sinovac in the North and Northeast region was also reflected during the Omicron (B.1.1.529) strain epidemic, but in Center West, Southeast and South region, patients aged between 40 and 60 who received AstraZeneca vaccine were better protected.

4. Discussion and conclusion

Consistent with findings worldwide, our study found that death cases were more prevalent in the elderly (Liu et al., 2020), men (Sharma et al., 2020) and patients with several comorbidities (Halpin et al., 2020). Furthermore, according to (Brizzi et al., 2022), Brizzi et al. used the same data and focused on spatio-temporal fluctuations in COVID-19 mortality rates in Brazilian hospitals. They chose capitals of 14 Brazil states with gamma virus epidemic periods as time range, and they found the Brazilian COVID-19 in-hospital mortality of geographical and time fluctuations was mainly related to geographic inequalities and shortage of health care ability by using Bayesian model, and estimated that if no geographic inequalities and pandemic medical pressure in hospitals in 14 cities, about half of COVID-19 deaths were preventable. The difference is that we looked at trends in the geographic distribution of in-hospital mortality among ethnic groups in Brazil and used models to explore inequality among ethnic groups.

By examining the racial composition and mortality rates in each region (Table S1), we detected racial variations in different area. Compared with regional population size, the percentage of hospitalizations and deaths for Pardo Brazilian was higher in the north, northeast and central-west region, while that for White Brazilian was higher in the southeast and south region. It is worth noting that Pardo population were concentrated in the north and northeast region, while white groups are mostly present in the south and southeast region. This seemed to show that ethnic concentrations are consistent with higher proportion of death cases relative to population size. White Brazilians had more frequent international travel opportunities. As race revealed the intersection of social connections (Neely & Samura, 2011), we speculated that uneven interactions with residential communities partially contributed to the spread of the epidemic. In the study of racial inequality, Peres et al. used different methods (Peres et al., 2021). They used the same data set in this study, and using logistic regression models to assess the association between self-reported race and in-hospital mortality after adjusting for clinical characteristics and comorbidities. The median age was 61 years, 57% were male, 35% self-reported as black/brown, and 35.4% self-reported as white. The overall in-hospital mortality rate was 37%. Black/brown patients had a higher in-hospital mortality rate than white patients (42% vs. 37%) and were admitted to intensive care units (ICU) less frequently (32% vs. 36%). Among hospitalized COVID-19 adults in Brazil, black/brown patients had higher in-hospital mortality rates, used fewer hospital resources, and were more likely to get sick than white patients. Racial disparities in health outcomes and access to health care illustrated the need to implement strategies to reduce inequities.

Among the cox regression model (Fig. 1), age was a dominant risk factor for death. Additionally, liver disease was the most significant risk factor for in-hospital mortality. For patients with cirrhosis and SARS-CoV-2 infection, notable high rates of mortality and hepatic decompensation were observed. This may be due to the potential role of immune dysfunction related to cirrhosis (Marjot et al., 2021). This finding can assist us in discussing methods of SARS-CoV-2 vaccination in Brazilian patients

with liver cirrhosis or post-liver transplants. In addition, obesity was found to be another dangerous comorbid feature. Many mechanisms cooperatively explained this effect (Popkin et al., 2020). A major concern was raised that the vaccine will be less effective in obese people. From the relationship between mortality rate and the number of comorbidities (Fig. 3), we may discover that the risk of death greatly increased when there is at least one comorbidity.

Compared with White people, Black people suffered from higher risk of death. This racial inequality had deep social roots and reflected the plight of minorities. Many underprivileged groups such as Black and Pardo Brazilians acted as health and nursing workers and lived in an environment susceptible to infection, thus disproportionately being exposed to the risk factors. In the short term, policymakers need to act quickly to prevent the spread of the virus in vulnerable areas. Baqui et al. used similar methods with us (Baqui et al., 2020). The difference is that they used SIVEP-Gripe dataset to conduct the cross-section research of ethnic and regional difference in hospital mortality rates for COVID-19 in Brazil. As a cross-section research, the time span of the data was limited to a few months, and the authors assessed regional differences in admissions to hospitals for COVID-19 by state and in two socio-economic sub-regions (five in our study). In addition, the authors plotted the number of comorbidities among survivors and non-survivors and the distribution of comorbidities by race.

In our study, survival analysis also showed that the area in the north and northeast regions tended to have higher hazard ratios than other states (Fig. 2). The north-eastern region was the poorest region in Brazil, traditionally combining export-oriented plantation farming with subsistence farming. Of particular note are the very poor areas of the North and North-East regions. The difference in economic level was obvious in peasant households. Rural poverty rate was especially high in the western Amazon. This economic situation made them more likely to face some social factors involving poor access to water and limited access to the Internet, which may prevent them from receiving information on preventive measures against the virus (de Le ó n- Mart í nez et al., 2020). Additionally, climate had a critical impact on COVID-19. For the tropical regions, such favourable climatic conditions could facilitate the spread of the outbreak. This unusual rainy season that affected humidity was likely to be responsible for the high mortality rate. For areas involving Amazonas (AM), Maranhão (MA) and Ceará (CE) located in the north and northeast region, similar situations may occur. In contrast, hours of solar radiation helped control the spread of COVID-19 in relatively drier and sunnier conditions (Martins et al., 2020).

Education was shown to be a strong risk factor for mortality as well. The finding from Fig. S3 indicated the positive correlation between higher education and relatively lower risk. For people with less education, they were more likely to face unemployment problems and in the context of COVID-19, job loss could be very troubling for individuals. Workers with a high school education or less account for a much larger share in the total unemployed than in the working-age population (Daly et al., 2020). The crisis had exacerbated this inequality in the labor market. It was also essential to note the unequal access to education. Education level was also mentioned as a risk factor in a scientific report (Baqui et al., 2021). Unlike the multivariate mixed-effects Cox model, the authors used machine learning prediction algorithms to explain the complex interdependencies that may exist between indicators. The predictive task was formulated as a binary classification problem of hospital mortality, with 0 representing death and 1 representing recovery. The analysis was performed using XGB, and logistic regression, K-nearest neighbour, neural network, random forest, and support vector machine algorithms were also evaluated. They found that socioeconomic, geographic and structural factors were more important than individual comorbidities in Brazil. The important factors were: housing conditions and their development indicators, distance to hospitals (especially in rural and less developed areas), education level and hospital financing model and pressure.

In the study of vaccine effectiveness, Cerqueira-Silva et al. (2022) showed the effect of age on the effectiveness and duration of vaccine protection against Vaxzevria and CoronaVac (Cerqueira-Silva et al., 2022). They extracted information not only from SIVEP-Gripe but e-SUS-Notifica to estimate vaccine effectiveness (VE) using a negative binomial regression model adjusted for sociodemographic characteristics. Besides the effects of VE on mortality (which is similar to our work) which was 92.3%, the authors also explored the VE on hospitalization and ICU admission which were 91.4% and 91.1% for Vaxzevria. And for CoronaVac, the VE on these three factors were 71.2%, 72.2% and 73.7%. The VE of all outcomes decreased gradually with age. In our work, we found that for hospitalized patients with the different number of comorbidities, the vaccines did not show the significantly protection, and the SARI fatality ratio increased with the number of comorbidities, reached the peak at around 5 comorbidities. By comparing the effectiveness of Sinovac and AstraZeneca vaccines, for patients with the different number of comorbidities, in general, AstraZeneca was more effective than Sinovac in preventing the deaths of hospitalized patients in the period dominated by Gamma (P.1) variant. In Delta (B.1.617.2) variant dominated period, Sinovac had a much higher protective effect than AstraZeneca for patients with 4 or more comorbidities, and for Omicron (B.1.1.529) variant, in North and Northeast region, AstraZeneca demonstrated much greater protection than Sinovac, but in Central-west, Southeast and South region, Sinovac was more protective in hospitalized patients with different number of comorbidities.

5. Limitation

Our analysis only based on hospitalized patients and data on out-of-hospital mortality rates were not considered. Limitations in case determination and bias due to missing information may not be excluded. There may also be cases where hospitalization was delayed due to lack of information. Inequalities in access to health care would be further amplified. Additionally, reinfection was not considered in our study and there were only some patient samples have been sequenced, so there may be a misclassification bias for variants.

Ethics approval and consent to participate

This study only reanalysed publicly available data which were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Not applicable.

Availability of data and materials

All the data are public available from the data suppliers.

The individual patient data from (SIVEP-Gripe) is available at <https://opendatasus.saude.gov.br/dataset/srag-2021-e-2022#>

Demographic data is available at <https://www.ibge.gov.br/en/statistics/social/population/26017-social-inequalities-due-to-color-or-race-in-brazil.html?=&t=resultados>.

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Authors' contributions

All authors conceived the study, carried out the analysis, wrote the draft, revised the manuscript critically, and approved it for publishing.

Declaration of competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

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References

- Ahmed, F., et al. (2020). Why inequality could spread COVID-19. *The Lancet Public Health*, 5(5), e240.
- Baquii, P., et al. (2020). Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: A cross-sectional observational study. *The Lancet Global Health*, 8(8), e1018–e1026.
- Baquii, P., et al. (2021). Comparing COVID-19 risk factors in Brazil using machine learning: The importance of socioeconomic, demographic and structural factors. *Scientific Reports*, 11(1), 1–10.
- Boschiero, M. N., Palamim, C. V. C., & Marson, F. A. L. (2021). The hindrances to perform the COVID-19 vaccination in Brazil. *Human Vaccines & Immunotherapeutics*, 17(11), 3989–4004.
- Brizzi, A., et al. (2022). Spatial and temporal fluctuations in COVID-19 fatality rates in Brazilian hospitals. *Nature Medicine*, 1–10.
- Cerqueira-Silva, T., et al. (2022). Influence of age on the effectiveness and duration of protection of Vaxzevria and CoronaVac vaccines: A population-based study. *The Lancet Regional Health-Americas*, 6, Article 100154.
- Daly, M. C., Buckman, S. R., & Seitelman, L. M. (2020). The unequal impact of COVID-19: Why education matters. *FRBSF Economic Letter*, 17, 1–5.
- Halpin, D. M., et al. (2020). Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? *The Lancet Respiratory Medicine*, 8(5), 436–438.
- Hone, T., et al. (2017). Association between expansion of primary healthcare and racial inequalities in mortality amenable to primary care in Brazil: A national longitudinal analysis. *PLoS Medicine*, 14(5), Article e1002306.
- de León-Martínez, L. D., et al. (2020). Critical review of social, environmental and health risk factors in the Mexican indigenous population and their capacity to respond to the COVID-19. *Science of The Total Environment*, 733, Article 139357.
- Li, S. L., et al. (2021). *Social and racial inequalities as contributing factors to COVID-19 vulnerability in São Paulo, Brazil*.
- Liu, K., et al. (2020). Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. *Journal of Infection*, 80(6), e14–e18.
- Marjot, T., et al. (2021). COVID-19 and liver disease: Mechanistic and clinical perspectives. *Nature Reviews Gastroenterology & Hepatology*, 18(5), 348–364.
- Martins, L. D., et al. (2020). How socio-economic and atmospheric variables impact COVID-19 and influenza outbreaks in tropical and subtropical regions of Brazil. *Environmental Research*, 191, Article 110184.
- Neely, B., & Samura, M. (2011). Social geographies of race: Connecting race and space. *Ethnic and Racial Studies*, 34(11), 1933–1952.
- Niedzwiedz, C. L., et al. (2020). Ethnic and socioeconomic differences in SARS-CoV-2 infection: Prospective cohort study using UK Biobank. *BMC Medicine*, 18(1), 1–14.

- Patel, J., et al. (2020). Poverty, inequality and COVID-19: The forgotten vulnerable. *Public Health*, 183, 110.
- Peres, I. T., et al. (2021). Sociodemographic factors associated with COVID-19 in-hospital mortality in Brazil. *Public Health*, 192, 15–20.
- Popkin, B. M., et al. (2020). Individuals with obesity and COVID-19: A global perspective on the epidemiology and biological relationships. *Obesity Reviews*, 21(11), Article e13128.
- Qian, Z., et al. (2020). Between-centre differences for COVID-19 ICU mortality from early data in England. *Intensive Care Medicine*, 46(9), 1779–1780.
- Sharma, G., Volgman, A. S., & Michos, E. D. (2020). Sex differences in mortality from COVID-19 pandemic: Are men vulnerable and women protected? *Case Reports*, 2(9), 1407–1410.
- <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. 2021; Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.