



First and second COVID-19 waves in Brazil: A cross-sectional study of patients' characteristics related to hospitalization and in-hospital mortality

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Summary

Background Background The second wave of the COVID-19 pandemic was more aggressive in Brazil compared to other countries around the globe. Considering the Brazilian peculiarities, we analyze the in-hospital mortality concerning socio-epidemiological characteristics of patients and the health system of all states during the first and second waves of COVID-19.

Methods We performed a cross-sectional study of hospitalized patients with positive RT-PCR for SARS-CoV-2 in Brazil. Data was obtained from the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe) and comprised the period from February 25, 2020, to April 30, 2021, separated in two waves on November 5, 2020. We performed a descriptive study of patients analyzing socio-demographic characteristics, symptoms, comorbidities, and risk factors stratified by age. In addition, we analyzed in-hospital and intensive care unit (ICU) mortality in both waves and how it varies in each Brazilian state.

Findings Between February 25, 2020 and April 30, 2021, 678 235 patients were admitted with a positive RT-PCR for SARS-CoV-2, with 325 903 and 352 332 patients for the first and second wave, respectively. The mean age of patients was 59 · 65 (IQR 48 · 0 - 72 · 0). In total, 379 817 (56 · 00%) patients had a risk factor or comorbidity. In-hospital mortality increased from 34 · 81% in the first to 39 · 30% in the second wave. In the second wave, there were more ICU admissions, use of non-invasive and invasive ventilation, and increased mortality for younger age groups. The southern and southeastern regions of Brazil had the highest hospitalization rates per 100 000 inhabitants. However, the in-hospital mortality rate was higher in the northern and northeastern states of the country. Racial differences were observed in clinical outcomes, with White being the most prevalent hospitalized population, but with Blacks/Browns (Pardos) having higher mortality rates. Younger age groups had more considerable differences in mortality as compared to groups with and without comorbidities in both waves.

Interpretation We observed a more considerable burden on the Brazilian hospital system throughout the second wave. Furthermore, the north and northeast of Brazil, which present lower Human Development Indexes, concentrated the most in-hospital mortality rates. The highest mortality rates are also shown among vulnerable social groups. Finally, we believe that the results can help to understand the behavior of the COVID-19 pandemic in Brazil, helping to define public policies, allocate resources, and improve strategies for vaccination of priority groups.

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Research in context

Evidence before this study

We conducted a PubMed search for studies describing the behavior of the first and second waves of COVID-19 in hospitals worldwide. The search terms used were: "COVID-19" OR "SARS-CoV-2" OR "COVID" AND "hospital" OR "critical care" OR "ICU" AND "wave" AND "mortality". For the most part, studies from other countries show that the second wave of the COVID-19 pandemic was less aggressive. However, the socio-epidemiological characteristics and in-hospital mortality during the two waves of the pandemic in Brazil are still shallow, and the previous studies focus on the most general characteristics, especially for the second wave.

Added value of this study

In this analysis, we evaluated 678 235 hospitalizations during the first and second waves in Brazil. We observed a more considerable burden on the hospital system in the second wave and the prevalence of the P.1 (Gamma) variant with an increase in hospitalization and mortality rates. In addition, in-hospital mortality showed a considerable increase from the first to the second wave, especially in patients between 20-60 years. The data also showed social and access differences to the health system, with higher mortality rates in more vulnerable social groups. Finally, the highest mortality rates were observed in the Brazilian states of the north and northeast regions.

Implication of all the available evidence

It was expected that in Brazil, as reported in other countries, the second wave would be less severe due to investment and the experience of the first wave. Nevertheless, our analysis demonstrated that Brazil faced a second wave more severe than the first one. In general, even with some states in the north and northeast having a higher number of hospital beds per 100 000 inhabitants than other states in Brazil, this increase could not reduce lethality compared to the numbers in the southern region. These differences between in-hospital mortality evidence that the opening of new hospital beds was not enough to mitigate the effects of the pandemic in Brazil. As alternatives, it is necessary to adopt effective non-pharmacological measures, better primary care protocols, qualification of health professionals, and a national policy to fight the pandemic. Another point that deserves attention is implementing initiatives to reach the most vulnerable population in society. Also, monitoring through genomic analysis of confirmed SARS-CoV-2 cases needs to be expanded in Brazil for better pandemic management.

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic started in Wuhan Province,

China, spreading globally and impacting the countries in different ways. The world has more than 190 375 116 cases, 4 088 293 deaths, and around 2 billion (13·40% of the population) people fully vaccinated (until July 22, 2021). Brazil had its first case of COVID-19 on February 25, 2020,¹ and since then faced 19 376 574 cases, 542 214 deaths, and 35 168 730 (17·26% of the population) people fully vaccinated (until July 22, 2021).²

The high transmissibility of SARS-CoV-2 caused a rapid increase in the number of infected individuals. These high numbers added to the broad spectrum of symptoms, and the rapid evolution to severe cases has made the COVID-19 pandemic unique in comparison to others already faced.³ The contagion and evolution characteristics of the COVID-19 pandemic generated an overload on healthcare systems worldwide. The responses have been different and dependent on the capacity of each system to restructure and absorb a growing demand for supplies and intensive care unit (ICU) beds.⁴

In this paper, we investigated the sociodemographic characteristics of patients between the two waves of COVID-19. The main characteristics evaluated were symptoms, risk factors, use of hospital resources, notifications, admissions, and mortality in each Brazilian state. To that end, we employ a dataset from the national surveillance system (SIVEP-Gripe) that reports on hospitalized patients in Brazil with severe acute respiratory infections (SARI) due to COVID-19. We also intend to analyze the prevalence of variants reported throughout the pandemic in Brazil. Considering the context, our study aims to assist in decision-making in public health policies and can be used as a starting point in other health scenarios worldwide.

Methods

Study design and data sources

We performed a descriptive study of publicly available epidemiological data relating to hospitalizations of SARI with COVID-19 in Brazil. The analysis was based on SIVEP-Gripe data from February 25, 2020, until April 30, 2021. SIVEP-Gripe is an official anonymized system from the Brazilian Ministry of Health for the notification of hospitalized cases and deaths from SARI in Brazil.⁵ We included all patients registered in SIVEP-Gripe who had been admitted to the hospital, had a positive RT-PCR test result for SARS-CoV-2, and had an outcome of discharge or death related to COVID-19.

We divided the SIVEP-Gripe data into three sets: whole pandemic, first and second waves. The first wave consists of patients admitted by COVID-19 from February 25, 2020, to November 5, 2020. For the second wave, we considered patients admitted by COVID-19 from November 6, 2020, to April 30, 2021. We use as the definition of an epidemic wave an increasing

number of cases with a defined peak followed by a period with a defined valley.⁶ Therefore, we described it as an epidemic wave. In this period, the division of waves was based on the point with the lowest 7-day moving average for cases confirmed by COVID-19 in Brazil.

As complementary information to our study, we surveyed the genomic analyzes collected from patients with SARS-CoV-2 variants. Genomic analyzes were obtained from the Global Initiative on Sharing Avian Influenza Database (GISAID), totaling 12 586 cases.⁷ The cases brought correspond to the genomic analyzes collected during the same period as the SIVEP-Gripe data. In Brazil, the Oswaldo Cruz Foundation (Fiocruz) manages the SARS-CoV-2 Genomic Surveillance, centralizing the results of all analyzes that are sent to GISAID.⁸

Due to the continental proportions and different responses of the Brazilian states, we evaluated the population characteristics and active hospital beds in each state. Therefore, we used population estimates from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística*, IBGE) for the year 2020.⁹ Finally, we analyzed the number of hospital beds and ICU beds for the two periods comprising the end of the first (October 2020) and second waves (April 2021) of COVID-19 in each Brazilian state from the TABNET database.¹⁰ A detailed description of the information for each dataset is provided in [Appendix 1](#) (pp 1–2).

Statistical analysis

Data was presented using descriptive statistics, including frequency, distribution, and characteristics related to hospitalized cases reported to the SIVEP-Gripe. For continuous variables, we calculated the mean, median, standard deviation, and interquartile range. In turn, for categorical variables, we analyzed frequency and percentage. We stratified patients into seven age groups based on the patient's admission date and birth, as follows: 0–19, 20–39, 40–49, 50–59, 60–69, 70–79. These age groups are in line with similar studies in the literature [11,12].

We looked at hospitalized SARI patients characteristics in the two waves of the COVID-19 pandemic. In this sense, we considered the incidence and frequency of the following variables: sociodemographic characteristics, symptoms, comorbidities, and risk factors at the time of hospitalization. Comparisons between the first and second waves of COVID-19 were reported in percentages, percentage differences, and with a confidence interval of 99.5%. In addition, we analyzed incidence and mortality rates for hospitalizations, ICU admission, and the use of noninvasive and invasive ventilation. Finally, we analyzed hospitalization rates, beds, and deaths per population in each state in Brazil.

To assess the behavior of hospitalizations and deaths related to the percentage of prevalence of the main

variants of SARS-CoV-2 during the pandemic in Brazil, we grouped genomic analyzes and hospitalizations by epidemiological week. We considered the genomic analysis from the 8th epidemiological week based on the first official notification of SARS-CoV-2 in Brazil (Feb 25, 2020). As our study considers periods related to the years 2020 and 2021, the epidemiological weeks of 2021 were considered a sequence of the epidemiological weeks of 2020. In this way, we analyzed the frequency of the main variants per epidemiological week of collection and the cumulative incidence of hospitalizations and deaths based on the patient's admission date.

Following ethically agreed principles on open data, this analysis did not require ethical approval in Brazil. Furthermore, we disregarded records with missing data in the analysis. In this situation, we provide the number of patients considered in the respective table or figure. Analyzes were conducted using the Python programming language and the Pandas and NumPy libraries.

Role of the funding source

The funders had no role in any decision about the manuscript.

Results

Between February 25, 2020 and April 30, 2021, 1 785 054 cases were reported in SIVEP-Gripe ([Fig. 1](#)). Among them, 1 785 038 (99.99%) cases were hospitalized, and 762 844 (42.73%) had a positive RT-PCR for SARS-CoV-2. Of the 762 844 cases with positive RT-PCR test, 678 235 (88.90%) cases had an outcome related to COVID-19. Therefore, our final sample was 678 235 cases, divided into two waves: first wave with 325 903 (48.05%) cases and second wave with 352 332 (51.95%) cases.

[Table 1](#) presents the characterization of our data. The mean population age for the whole pandemic was 59 years (IQR 48.0 - 72.0). Cases were distributed among seven age groups, but in general, there was a slight predominance of cases in the age group 60 to 69 years (148 302 (21.87%)). In both waves, the number of males hospitalized by COVID-19 was higher than that of females ([Table 2](#)). Male patients represented 56.13% and 54.99% of the hospitalizations in the first and second waves, respectively. In-hospital mortality rates were slightly higher for males than for females during the whole pandemic (37.60% vs. 36.57% of deaths, respectively).¹³ The difference is higher during the first wave (33.72% of female death vs. 35.66% of male death).

There was a predominance of hospitalized White individuals, representing 55.87% of the total data, followed by the Black/Brown (Pardos) population (42.65%) ([Table 2](#)). Asian and Indigenous people represented 1.49% of the cases in our data. The mortality

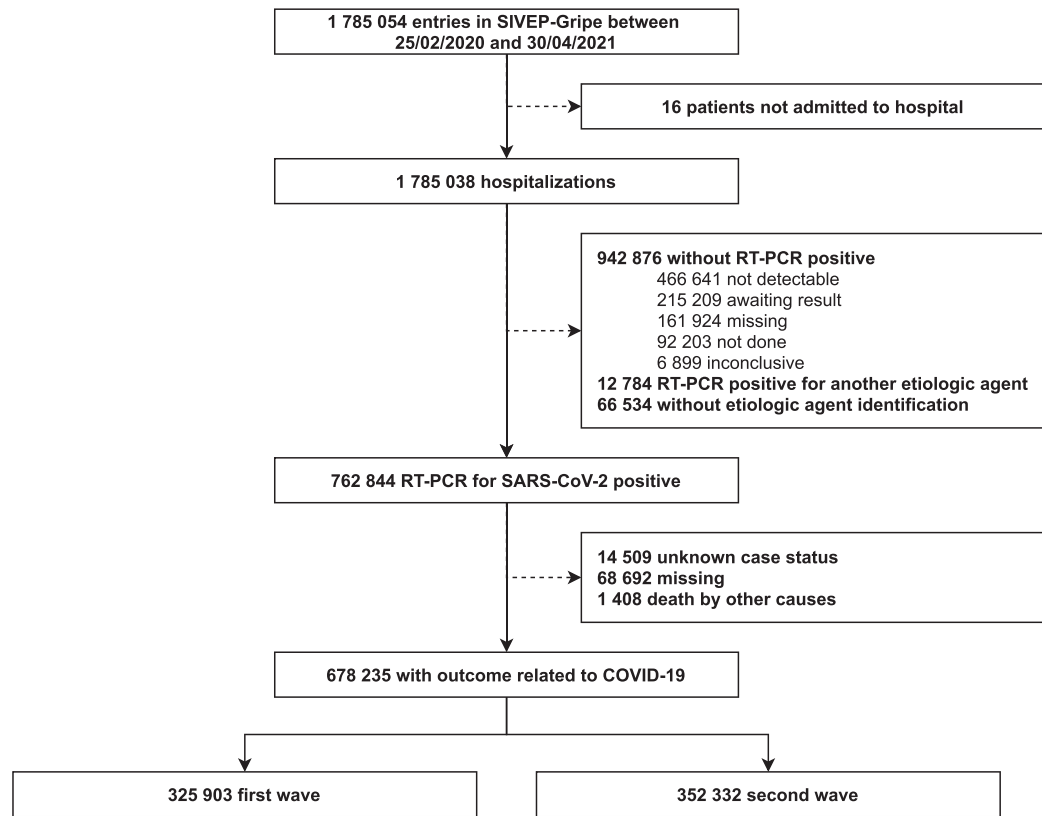


Figure 1. Study profile. Note: The continuous line represents the number of cases that met each of the cutoff criteria. Meanwhile, the dashed line informs the number of patients that were removed from the original dataset. The analysis period considered is from February 25, 2020, to April 30, 2021. We considered all hospitalizations in this period and divided them into two waves. The first wave corresponds to the period from February 25, 2020, to November 5, 2020. The second wave corresponds to the period from November 6, 2020, to April 30, 2021. SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2. RT-PCR = Reverse transcription polymerase chain reaction.

rate was higher among Black/Brown (Pardos) people and decreased inversely to the educational level. Furthermore, the mortality rate is 30% higher among illiterate people compared with those with a college degree. The number of hospitalized patients from rural and peripheral areas represents around 3% of the total data. However, these populations have mortality rates about 6% higher than the urban population.

During the first wave, according to genomic analyzes (Fig. 2), the variants with the highest prevalence in Brazil were B.1.1.28 (20 ~ 30%) and B.1.1.33 (10 ~ 35%). At the end of the first wave, genomic analyzes indicate a prevalence of approximately 20% of the P.2 (Zeta) variant in SARS-CoV-2 cases in Brazil. During the second wave, the P.2 and P.1 (Gamma) variants were the most prevalent. The P.2 variant had the highest prevalence during 50th to 60th epidemiological weeks (~20%). From the 60th epidemiological week onwards, the P.1 variant ranged from 60% to approximately 90% of the variants circulating in Brazil.

The first case of SARS-CoV-2 in Brazil was identified in the 8th epidemiological week (February 25, 2020).¹

From the first case to the peak of the pandemic to the first wave (Fig. 2) was just 12 weeks. During 20th to 30th epidemiological weeks, Brazil had 15 000 hospitalizations and 5 000 deaths from COVID-19 per week. In the 30th to 44th epidemiological weeks, corresponding to the first wave, there is a substantial decline in cases and deaths. The end of this period also characterizes the division between the first and second waves of our study. In the second wave, between 60th to 70th weeks, Brazil reached the maximum peak for the pandemic, with more than 25 000 hospitalizations and 10 000 deaths per epidemiological week.

Of the 678 235 hospitalizations, there were 251 910 deaths (37 · 14%) (Table 3). Among these deaths, 113 444 (45 · 03%) occurred in the first wave and 138 466 (54 · 97%). ICU admissions correspond for 245 304 (36 · 17%) of the SARI cases reported in SIVEP-Gripe during the whole pandemic. In the first wave, 115 018 (46 · 89%) cases were admitted to the ICU, with 64 589 (56 · 16%) deaths. In the second wave, 130 286 (53 · 11%) cases were admitted to the ICU, with 83 781 (64 · 31%) deaths.

	Whole pandemic (n = 678 235)	First wave (n = 325 903)	Second wave (n = 352 332)
Age, in years			
Min - Max	0 - 116	0 - 116	0 - 114
Mean (SD)	59.65 (17.63)	59.69 (18.28)	59.61 (17.01)
Median (IQR)	61 (48.0 - 72.0)	61 (47.0 - 73.0)	61 (48.0 - 72.0)
Age groups, in years			
0 to 19	10 152 (1.50%)	5 983 (1.84%)	4 169 (1.18%)
20 to 39	82 214 (12.12%)	40 842 (12.53%)	41 372 (11.74%)
40 to 49	96 950 (14.29%)	45 996 (14.11%)	50 954 (14.46%)
50 to 59	128 931 (19.01%)	59 966 (18.40%)	68 965 (19.57%)
60 to 69	148 303 (21.87%)	67 562 (20.73%)	80 741 (22.92%)
70 to 79	121 879 (17.97%)	58 145 (17.84%)	63 734 (18.09%)
80 +	89 806 (13.24%)	47 409 (14.55%)	42 397 (12.03%)
Sex (n = 678 159)	678 159 (99.99%)	325 857 (99.99%)	352 302 (99.99%)
Female	301 521 (44.46%)	142 942 (43.87%)	158 579 (45.01%)
Male	376 638 (55.54%)	182 915 (56.13%)	193 723 (54.99%)
Self-reported race/ethnicity ^a (n = 534 956)	534 956 (78.87%)	245 170 (75.23%)	289 786 (82.25%)
White	298 887 (55.87%)	128 382 (52.36%)	170 505 (58.84%)
Black/Brown	228 134 (42.65%)	112 545 (45.90%)	115 589 (39.89%)
Asian	6 934 (1.30%)	3 575 (1.46%)	3 359 (1.16%)
Indigenous	1 001 (0.19%)	668 (0.27%)	333 (0.11%)
Scholarship (n = 239 709)	239 709 (35.34%)	115 260 (35.37%)	124 449 (35.32%)
Illiterate	13 744 (5.73%)	7 260 (6.30%)	6 484 (5.21%)
Elementary School	62 953 (26.26%)	30 355 (26.34%)	32 598 (26.19%)
Middle School	45 712 (19.07%)	21 736 (18.86%)	23 976 (19.27%)
High School	77 903 (32.50%)	37 101 (32.19%)	40 802 (32.79%)
College / University	39 397 (16.44%)	18 808 (16.32%)	20 589 (16.54%)
Risk factors (n = 379 817)	379 817 (56.00%)	184 309 (56.55%)	195 508 (55.49%)
Chronic Cardiovascular Disease	241 695 (63.63%)	116 563 (63.24%)	125 132 (64.00%)
Diabetes mellitus	171 845 (45.24%)	85 713 (46.51%)	86 132 (44.06%)
Obesity	54 066 (14.23%)	19 879 (10.79%)	34 187 (17.49%)
Chronic Kidney Disease	26 516 (6.98%)	14 858 (8.06%)	11 658 (5.96%)
Chronic Neurological Disease	26 059 (6.86%)	14 334 (7.78%)	11 725 (6.00%)
Other Chronic Pneumatopathy	25 121 (6.61%)	13 491 (7.32%)	11 630 (5.95%)
Asthma	18 467 (4.86%)	9 261 (5.02%)	9 206 (4.71%)
Immunodeficiency or Immunodepression	17 525 (4.61%)	9 821 (5.33%)	7 704 (3.94%)
Chronic Liver Disease	5 884 (1.55%)	3 158 (1.71%)	2 726 (1.39%)
Chronic Hematological Disease	5 132 (1.35%)	2 934 (1.59%)	2 198 (1.12%)
Down syndrome	1 823 (0.48%)	863 (0.47%)	960 (0.49%)
Puerperal ^b	1 492 (0.39%)	812 (0.44%)	680 (0.35%)
Without risk factors	298 418 (44.00%)	141 594 (43.45%)	156 824 (44.51%)
Symptoms (n = 658 529)	658 529 (97.09%)	315 995 (96.96%)	342 534 (97.22%)
Dyspnea	487 205 (73.98%)	230 661 (73.00%)	256 544 (74.90%)
Cough	472 161 (71.70%)	234 597 (74.24%)	237 564 (69.35%)
Oxygen saturation < 95%	429 751 (65.26%)	191 834 (60.71%)	237 917 (69.46%)
Fever	404 358 (61.40%)	209 651 (66.35%)	194 707 (56.84%)
Respiratory discomfort	387 116 (58.78%)	184 994 (58.54%)	202 122 (59.01%)
Fatigue	122 379 (18.58%)	28 759 (9.10%)	93 620 (27.33%)
Sore throat	112 758 (17.12%)	55 780 (17.65%)	56 978 (16.63%)
Diarrhea	93 356 (14.18%)	45 063 (14.26%)	48 293 (14.10%)
Vomit	53 293 (8.09%)	26 002 (8.23%)	27 291 (7.97%)
Loss of taste	50 978 (7.74%)	15 040 (4.76%)	35 938 (10.49%)
Loss of smell	50 606 (7.68%)	15 016 (4.75%)	35 590 (10.39%)
Abdominal pain	26 770 (4.07%)	7 239 (2.29%)	19 531 (5.70%)
Without symptoms	19 706 (2.91%)	9 908 (3.04%)	9 798 (2.78%)

Table 1: Patient characteristics stratified by wave.

Notes: SD = Standard deviation. IQR = Interquartile range. ^aRace/ethnicity declared by the patient: *Branca* (White); *Amarela* (Asian); *Preta* (Black)/*Parda* (Brown); and, *Indigena* (Indigenous). ^bWe only consider puerperal or parturient women up to 50 years of age.

	Whole pandemic		First Wave		Second Wave		Second wave vs first wave	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Difference	99 · 5% CI
Sex								
Female	301 521 (44 · 46%)	110 256 (36 · 57%)	142 942 (43 · 87%)	48 205 (33 · 72%)	158 579 (45 · 01%)	62 051 (39 · 13%)	5 · 41%	· 06 - 5 · 75
Male	376 638 (55 · 54%)	141 627 (37 · 60%)	182 915 (56 · 13%)	65 227 (35 · 66%)	193 723 (54 · 99%)	76 400 (39 · 44%)	3 · 78%	· 47 - 4 · 09
Total	678 159	251 883 (37 · 14%)	325 857 (48 · 05%)	113 432 (34 · 81%)	352 302 (51 · 95%)	138 451 (39 · 30%)	3 · 78%	· 26 - 4 · 72
Self-reported race/ethnicity								
White	298 887 (55 · 87%)	110 230 (36 · 88%)	128 382 (52 · 36%)	43 540 (33 · 91%)	170 505 (58 · 84%)	66 690 (39 · 11%)	5 · 20%	· 85 - 5 · 55
Black/Brown	228 134 (42 · 65%)	93 867 (41 · 15%)	112 545 (45 · 90%)	43 982 (39 · 08%)	115 589 (39 · 89%)	49 885 (43 · 16%)	4 · 08%	· 67 - 4 · 48
Asian	6 934 (1 · 30%)	2 585 (37 · 28%)	3 575 (1 · 46%)	1 278 (35 · 75%)	3 359 (1 · 16%)	1 307 (38 · 91%)	3 · 16%	· 88 - 5 · 44
Indigenous	1 001 (0 · 19%)	374 (37 · 36%)	668 (0 · 27%)	253 (37 · 87%)	333 (0 · 11%)	121 (36 · 34%)	-1 · 53%	-7 · 77 - 4 · 86
Total	534 956	207 056 (38 · 71%)	245 170 (45 · 83%)	89 053 (36 · 32%)	289 786 (54 · 17%)	118 003 (40 · 72%)	4 · 40%	· 14 - 4 · 66
Scholarity								
Illiterate	13 744 (5 · 73%)	7 847 (57 · 09%)	7 260 (6 · 30%)	4 118 (56 · 72%)	6 484 (5 · 21%)	3 729 (57 · 51%)	0 · 79%	-0 · 87 - 2 · 45
Elementary School	62 953 (26 · 26%)	31 171 (49 · 51%)	30 355 (26 · 34%)	14 219 (46 · 84%)	32 598 (26 · 19%)	16 952 (52 · 00%)	5 · 16%	· 38 - 5 · 94
Middle School	45 712 (19 · 07%)	19 166 (41 · 93%)	21 736 (18 · 86%)	8 482 (39 · 02%)	23 976 (19 · 27%)	10 684 (44 · 56%)	5 · 54%	· 63 - 6 · 44
High School	77 903 (32 · 50%)	24 219 (31 · 09%)	37 101 (32 · 19%)	10 201 (27 · 50%)	40 802 (32 · 79%)	14 018 (34 · 36%)	6 · 86%	· 21 - 7 · 51
College / University	39 397 (16 · 44%)	10 326 (26 · 21%)	18 808 (16 · 32%)	4 127 (21 · 94%)	20 589 (16 · 54%)	6 199 (30 · 11%)	8 · 17%	· 30 - 9 · 03
Total	239 709	92 729 (38 · 68%)	115 260 (48 · 08%)	41 147 (35 · 70%)	124 449 (51 · 92%)	51 582 (41 · 45%)	5 · 75%	· 36 - 6 · 14
Geographic zone								
Urban	584 140 (96 · 66%)	215 310 (36 · 86%)	281 272 (96 · 81%)	97 349 (34 · 61%)	302 868 (96 · 53%)	117 961 (38 · 95%)	4 · 34%	· 09 - 4 · 58
Rural	18 316 (3 · 03%)	8 024 (43 · 81%)	8 367 (2 · 88%)	3 525 (42 · 13%)	9 949 (3 · 17%)	4 499 (45 · 22%)	3 · 09%	· 65 - 4 · 53
Periphery	1 842 (0 · 30%)	767 (41 · 64%)	888 (0 · 31%)	364 (40 · 99%)	954 (0 · 30%)	403 (42 · 24%)	1 · 25%	-3 · 25 - 5 · 74
Total	604 298	224 101 (37 · 08%)	290 527 (48 · 08%)	101 238 (34 · 85%)	313 771 (51 · 92%)	122 863 (39 · 16%)	4 · 31%	· 07 - 4 · 55

Table 2: Mortality stratified by sociodemographic characteristics and wave.

Note: We only consider data that have an informed outcome. Proportions are calculated based on complete records for sex, self-reported race/ethnicity, education, and geographic area of residence. ^aData on race/ethnicity were collected as self-reported race or skin colour, classified as *Branco* (White), *Preto* (Black), *Pardo* (Brown), *Amarelo* (Asian), or *Indígena* (Indigenous) The percentages of cases are calculated based on the total for each stratification (whole pandemic, first wave, or second wave). Percentages of deaths are calculated based on the total number of cases for each sociodemographic characteristics stratified by whole pandemic, first wave, or second wave.

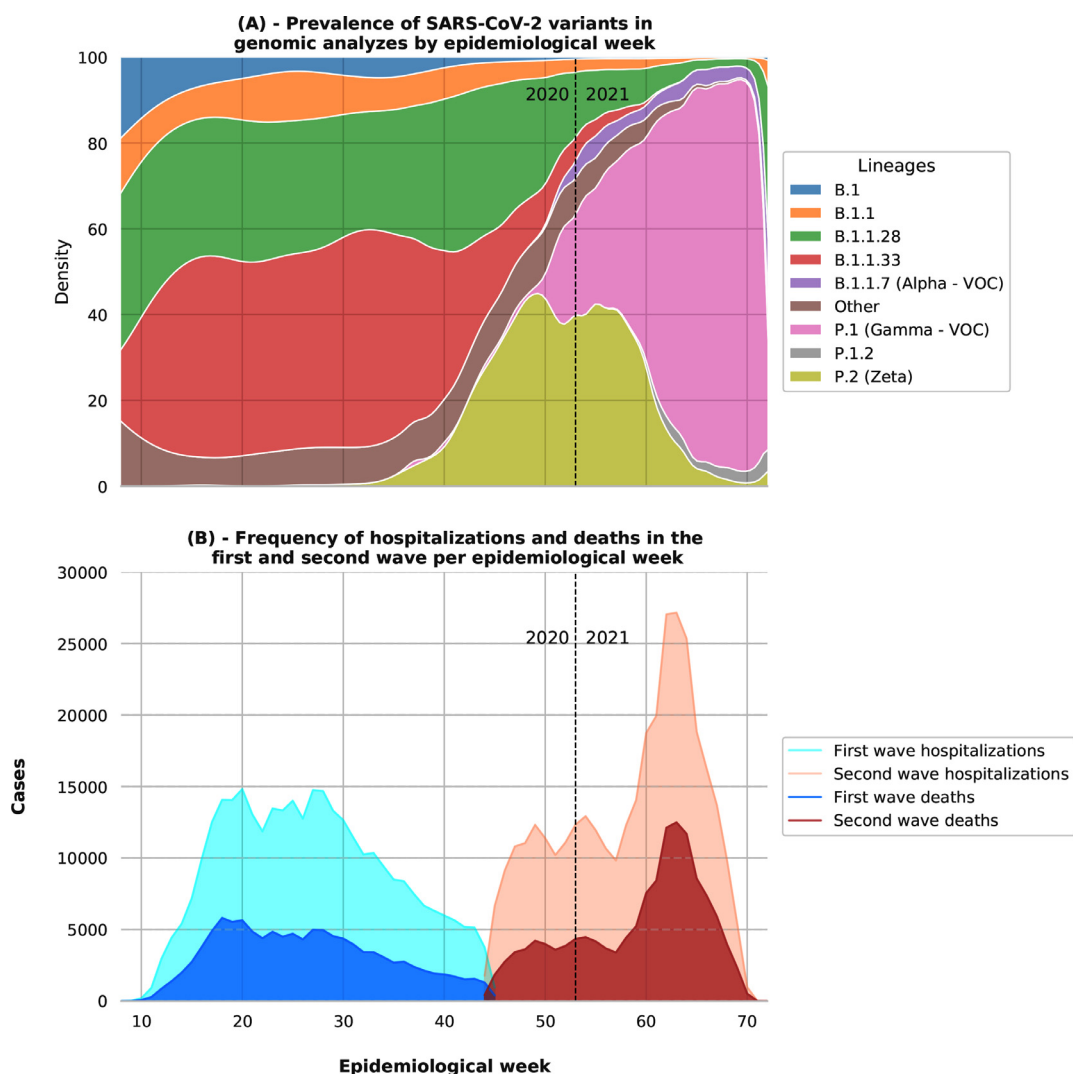


Figure 2. Prevalence of variants and frequency of hospitalizations and deaths from SARS-CoV-2 in Brazil. Note: the genomic analyzes considered were carried out in Brazil and made available in the GISAID database. The analysis period considered is from February 25, 2020, to April 30, 2021. We considered all hospitalizations in this period and divided them into two waves. The first wave corresponds to the period from February 25, 2020 to November 5, 2020. The second wave corresponds to the period from November 6, 2020 to April 30, 2021. With a programmatic objective, the World Health Organization (WHO) classified the variants as Variants of Concern (VOC) or Variants of Interest (VOI), depending on their transmissibility, virulence, clinical presentation, their ability to impact the epidemiological picture of the pandemic, and its power to reduce the effectiveness of public health measures, diagnostic tests, therapeutic measures or vaccines.¹⁴

The overall mortality for cases that used non-invasive ventilation was 27·68% (Table 3). Of the hospitalized patients, 137 638 (20·29%) required invasive mechanical ventilation, with a mortality rate of 77·95% and 83·18% for the first and second waves, respectively. 158 389 (65·82%) of ICU admissions occurred on the same day of hospitalization (Table 4). The overall mortality rate in the ICU during the pandemic was 60·38%. After one day of hospitalization, 24 875 cases were admitted to the ICU. For patients who had a late

admission to the ICU, more than eight days after hospitalization, the mortality rate was 79·17%.

The highest admissions rates in hospital beds and ICUs per 100 000 inhabitants in Brazil during the first and second wave are mainly concentrated in the states of *Distrito Federal* (DF), *São Paulo* (SP), *Paraná* (PR), and *Rio Grande do Sul* (RS) (Figs. 3 and 4). The overall mortality rate in the first and second wave for every 1 000 hospitalizations is higher mainly in the states of the North and Northeast region of the country, with

Age group	Whole pandemic		First wave		Second wave		Second wave vs first wave	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Difference	99·5% CI
Hospitalizations stratified by age group and wave								
0 to 19	10 152 (1·50%)	969 (9·54%)	5 983 (1·84%)	548 (9·16%)	4 169 (1·18%)	421 (10·10%)	0·94%	−0·22 - 2·12
20 to 39	82 214 (12·12%)	11 666 (14·19%)	40 842 (12·53%)	4 530 (11·09%)	41 372 (11·74%)	7 136 (17·25%)	6·16%	·68 - 6·63
40 to 49	96 950 (14·29%)	19 375 (19·98%)	45 996 (14·11%)	7 574 (16·47%)	50 954 (14·46%)	11 801 (23·16%)	6·69%	·19 - 7·19
50 to 59	128 931 (19·01%)	36 310 (28·16%)	59 966 (18·40%)	14 759 (24·61%)	68 965 (19·57%)	21 551 (31·25%)	6·64%	·15 - 7·12
60 to 69	148 303 (21·87%)	61 602 (41·54%)	67 562 (20·73%)	26 166 (38·73%)	80 741 (22·92%)	35 436 (43·89%)	5·16%	·66 - 5·66
70 to 79	121 879 (17·97%)	64 746 (53·12%)	58 145 (17·84%)	29 743 (51·15%)	63 734 (18·09%)	35 003 (54·92%)	3·77%	·21 - 4·33
80 +	89 806 (13·24%)	57 242 (63·74%)	47 409 (14·55%)	30 124 (63·54%)	42 397 (12·03%)	27 118 (63·96%)	0·42%	−0·21 - 1·05
Total	678 235	251 910 (37·14%)	325 903 (48·05%)	113 444 (34·81%)	352 332 (51·95%)	138 466 (39·30%)	4·49%	·26 - 4·72
ICU admissions stratified by age group and wave								
0 to 19	2 825 (1·15%)	626 (22·16%)	1 616 (1·40%)	349 (21·60%)	1 209 (0·93%)	277 (22·91%)	1·31%	−1·77 - 4·44
20 to 39	22 458 (9·16%)	7 640 (34·02%)	10 310 (8·96%)	2 807 (27·23%)	12 148 (9·32%)	4 833 (39·78%)	12·55%	·33 - 13·78
40 to 49	29 454 (12·01%)	12 293 (41·74%)	13 096 (11·39%)	4 522 (34·53%)	16 358 (12·56%)	7 771 (47·51%)	12·98%	·86 - 14·09
50 to 59	44 359 (18·08%)	22 938 (51·71%)	19 865 (17·27%)	8 916 (44·88%)	24 494 (18·80%)	14 022 (57·25%)	12·37%	·43 - 13·29
60 to 69	58 258 (23·75%)	37 891 (65·04%)	25 934 (22·55%)	15 498 (59·76%)	32 324 (24·81%)	22 393 (69·28%)	9·52%	·74 - 10·30
70 to 79	51 553 (21·02%)	38 165 (74·03%)	24 424 (21·23%)	17 186 (70·37%)	27 129 (20·82%)	20 979 (77·33%)	6·96%	·21 - 7·72
80 +	36 397 (14·84%)	28 817 (79·17%)	19 773 (17·19%)	15 311 (77·43%)	16 624 (12·76%)	13 506 (81·24%)	3·81%	·98 - 4·64
Total	245 304	148 370 (60·48%)	115 018 (46·89%)	64 589 (56·16%)	130 286 (53·11%)	83 781 (64·31%)	8·15%	·76 - 8·54
Use of non-invasive respiratory stratified by age group and wave								
0 to 19	3 332 (1·01%)	186 (5·58%)	1 780 (1·23%)	98 (5·51%)	1 552 (0·83%)	88 (5·67%)	0·16%	−1·40 - 1·76
20 to 39	38 124 (11·50%)	3 394 (8·90%)	15 923 (11·05%)	1 157 (7·27%)	22 201 (11·85%)	2 237 (10·08%)	2·81%	·24 - 3·37
40 to 49	48 541 (14·64%)	6 037 (12·44%)	20 404 (14·15%)	2 126 (10·42%)	28 137 (15·02%)	3 911 (13·90%)	3·48%	·90 - 4·06
50 to 59	65 108 (19·64%)	11 696 (17·96%)	27 533 (19·10%)	4 444 (16·14%)	37 575 (20·06%)	7 252 (19·30%)	3·16%	·57 - 3·75
60 to 69	72 200 (21·78%)	20 875 (28·91%)	30 180 (20·94%)	8 170 (27·07%)	42 020 (22·43%)	12 705 (30·24%)	3·17%	·50 - 3·83
70 to 79	58 118 (17·53%)	23 710 (40·80%)	25 707 (17·83%)	10 049 (39·09%)	32 411 (17·30%)	13 661 (42·15%)	3·06%	·26 - 3·86
80 +	46 083 (13·90%)	25 874 (56·15%)	22 626 (15·70%)	12 589 (55·64%)	23 457 (12·52%)	13 285 (56·64%)	1·00%	·09 - 1·90
Total	331 506	91 772 (27·68%)	144 153 (43·48%)	38 633 (26·80%)	187 353 (56·52%)	53 139 (28·36%)	1·56%	·26 - 1·87
Use of invasive respiratory stratified by age group and wave								
0 to 19	1 133 (0·82%)	553 (48·81%)	660 (1·08%)	306 (46·36%)	473 (0·62%)	247 (52·22%)	5·86%	−0·04 - 11·70
20 to 39	10 227 (7·43%)	6 182 (60·45%)	4 244 (6·92%)	2 288 (53·91%)	5 983 (7·84%)	3 894 (65·08%)	11·17%	·24 - 13·09
40 to 49	14 394 (10·46%)	9 715 (67·49%)	5 845 (9·54%)	3 598 (61·56%)	8 549 (11·20%)	6 117 (71·55%)	9·99%	·42 - 11·57
50 to 59	24 226 (17·60%)	18 104 (74·73%)	10 002 (16·32%)	6 957 (69·56%)	14 224 (18·63%)	11 147 (78·37%)	8·81%	·69 - 9·94
60 to 69	35 197 (25·57%)	29 266 (83·15%)	14 988 (24·45%)	11 917 (79·51%)	20 209 (26·47%)	17 349 (85·85%)	6·34%	·53 - 7·14
70 to 79	31 998 (23·25%)	28 460 (88·94%)	14 643 (23·89%)	12 680 (86·59%)	17 355 (22·73%)	15 780 (90·92%)	4·33%	·63 - 5·03
80 +	20 463 (14·87%)	18 999 (92·85%)	10 915 (17·81%)	10 036 (91·95%)	9 548 (12·51%)	8 963 (93·87%)	1·92%	·22 - 2·63
Total	137 638	111 279 (80·85%)	61 297 (44·53%)	47 782 (77·95%)	76 341 (55·47%)	63 497 (83·18%)	5·23%	·80 - 5·65

Table 3: Use of hospital resources stratified by age group and wave.

Note: We only consider data that have an informed outcome. Proportions are calculated based on complete records of ICU admission, use of non-invasive ventilation, and invasive mechanical ventilation. ICU = Intensive Care Unit

Days until admission to the ICU	Whole pandemic			First Wave			Second wave			Second wave vs first wave		
	ICU admission	Deaths		ICU admission	Deaths		ICU admission	Deaths		Difference		99.5% CI
0	158 389 (65.82%)	90 015 (56.83%)		77 759 (68.56%)	41 279 (53.09%)		80 630 (63.39%)	48 736 (60.44%)		7.35%		6.87 - 7.84
1	24 875 (10.34%)	15 086 (60.65%)		11 860 (10.46%)	6 771 (57.09%)		13 015 (10.23%)	8 315 (63.89%)		6.80%		5.58 - 8.01
2	14 836 (6.17%)	9 711 (65.46%)		6 176 (5.45%)	3 782 (61.24%)		8 660 (6.81%)	5 929 (68.46%)		7.22%		5.67 - 8.79
3	10 818 (4.50%)	7 218 (66.72%)		4 417 (3.89%)	2 737 (61.97%)		6 401 (5.03%)	4 481 (70.00%)		8.03%		6.22 - 9.86
4	7 788 (3.24%)	5 271 (67.68%)		3 215 (2.83%)	2 013 (62.61%)		4 573 (3.60%)	3 258 (71.24%)		8.63%		6.51 - 10.76
5	5 620 (2.34%)	3 933 (69.98%)		2 274 (2.00%)	1 461 (64.25%)		3 346 (2.63%)	2 472 (73.88%)		9.63%		7.17 - 12.10
6	4 037 (1.68%)	2 901 (71.86%)		1 644 (1.45%)	1 079 (65.63%)		2 393 (1.88%)	1 822 (76.14%)		10.51%		7.65 - 13.37
7	2 910 (1.21%)	2 165 (74.40%)		1 125 (0.99%)	784 (69.69%)		1 785 (1.40%)	1 381 (77.37%)		7.68%		4.39 - 11.01
8+	11 355 (4.72%)	8 989 (79.16%)		4 955 (4.37%)	3 646 (73.58%)		6 400 (5.03%)	5 343 (83.48%)		9.90%		8.38 - 11.43
Total	240 628	145 289 (60.38%)		113 425 (47.14%)	63 552 (56.03%)		127 203 (52.86%)	81 737 (64.26%)		8.23%		7.84 - 8.62

Table 4: Mortality rate per days from hospitalization to admission to the ICU.

Note: We only consider data that have an informed outcome. Only patients admitted to the ICU were considered. Days until admission to the ICU were calculated based on the date of hospitalization and admission to the ICU.

emphasis on the increase in the mortality rate in almost all states in the second wave (Fig. 3).

Analyzing the mortality rates between the groups with and without risk factors, we can observe a more considerable mortality rate among younger age groups, especially in the 20–39 age group (Appendix 1 (p 30)). In addition, there was an increase in the prevalence of mortality for all comorbidities evaluated in the second wave (Fig. 5). Cardiovascular disease was the most prevalent among the risk factors analyzed in this study. Furthermore, diabetes-related mortality increased from 44.66% to 49.22% from the first to the second wave. The most considerable differences in mortality for risk factors between the first and second wave were for puerperal women, with an increase of 12.72%, and obese patients, with 8.70%.

According to the Table 1, COVID-19 presented symptoms were predominantly respiratory and constitutional, such as fever and fatigue. Oxygen saturation < 95% is more frequent for elderly patients. In general, there was a relative predominance in percentage terms of constitutional, respiratory, neurological, and gastrointestinal symptoms among patients with 60 to 79 years. The increase in gastrointestinal, neurological symptoms and oxygen desaturation in the second wave is evident.

Discussion

We analyzed 678 235 patients hospitalized with SARI due to COVID-19 between February 25, 2020 and April 30, 2021. Data was taken from a nationwide public dataset. The second wave, in our study, corresponds to a shorter period compared to the first wave. However, there were more patients admitted to the hospital during the second wave. In the first wave, the highest number of hospitalizations occurred during the 27th epidemiological week, reaching 14 825 hospitalizations. Meanwhile, in early 2021, during the second wave, Brazil faced a substantial and rapid increase in hospital admissions, reaching a peak of 27 154 admissions during the 63rd epidemiological week, which corresponds to an increase of 83.16% in the number of hospitalizations as compared to the first wave.

A meta-analysis of the 3 111 714 globally reported COVID-19 cases indicates that males have a higher chance of contracting the disease and having death as outcome.¹⁵ Numbers collected between January 1, 2020 until June 1, 2020, demonstrated that male patients have almost three times the odds of requiring ICU admission and higher odds of death compared to females.¹⁵ Our data also demonstrates a greater male demand for ICU beds in both waves. However, when we compare the mortality rates of patients admitted to ICUs, Brazilian women are slightly higher. In the second wave, when we analyze the use of invasive mechanical ventilation, we observed mortality rates reaching 83.17% (Appendix 1 (pp 4–5)). These rates are

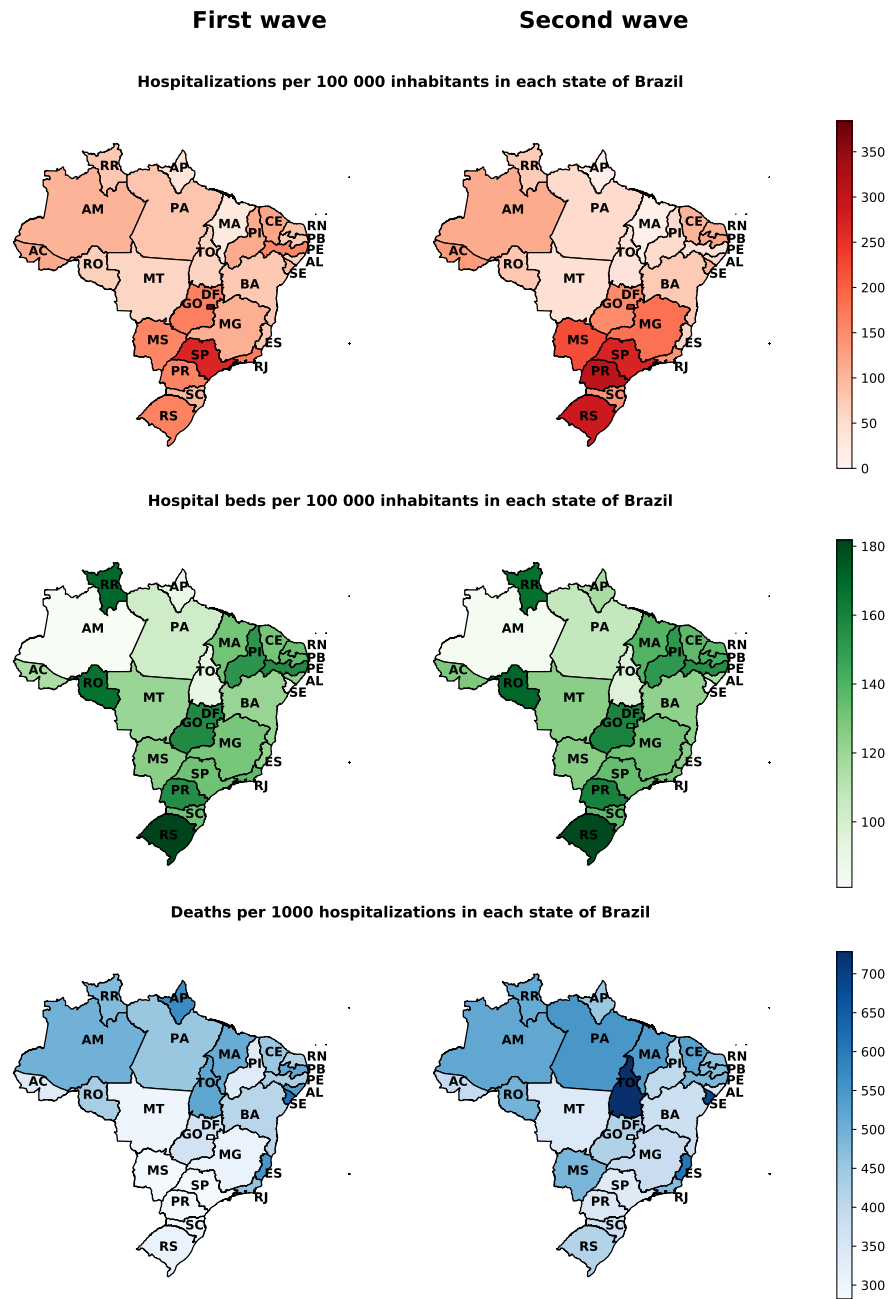


Figure 3. Hospital admission rates, hospital beds per 100 000 inhabitants, and in-hospital mortality per 1 000 admissions due to COVID-19 in the first and second wave, stratified by the Brazilian state. Note: the population considered for each state is an official estimate from Brazilian government agencies. The number of hospital beds considered was based on data for the first wave of October 2020 and the second wave of April 2021. The number of hospital beds per state was obtained from TABNET. Hospitalizations and deaths were assigned to each state according to hospital location.

extremely high in comparison to studies from other countries, which indicate a mortality between 47·90% (patients up to 40 years old) and 77·10% (71–80 years).¹⁶ For patients over 80 years old and who used invasive mechanical ventilation, the mortality rate

(84·40%) is similar to those described in another study.¹⁶

Differently from other races/ethnicities, during the second wave, the mortality among Indigenous people showed lower values (Table 2). This fact may have

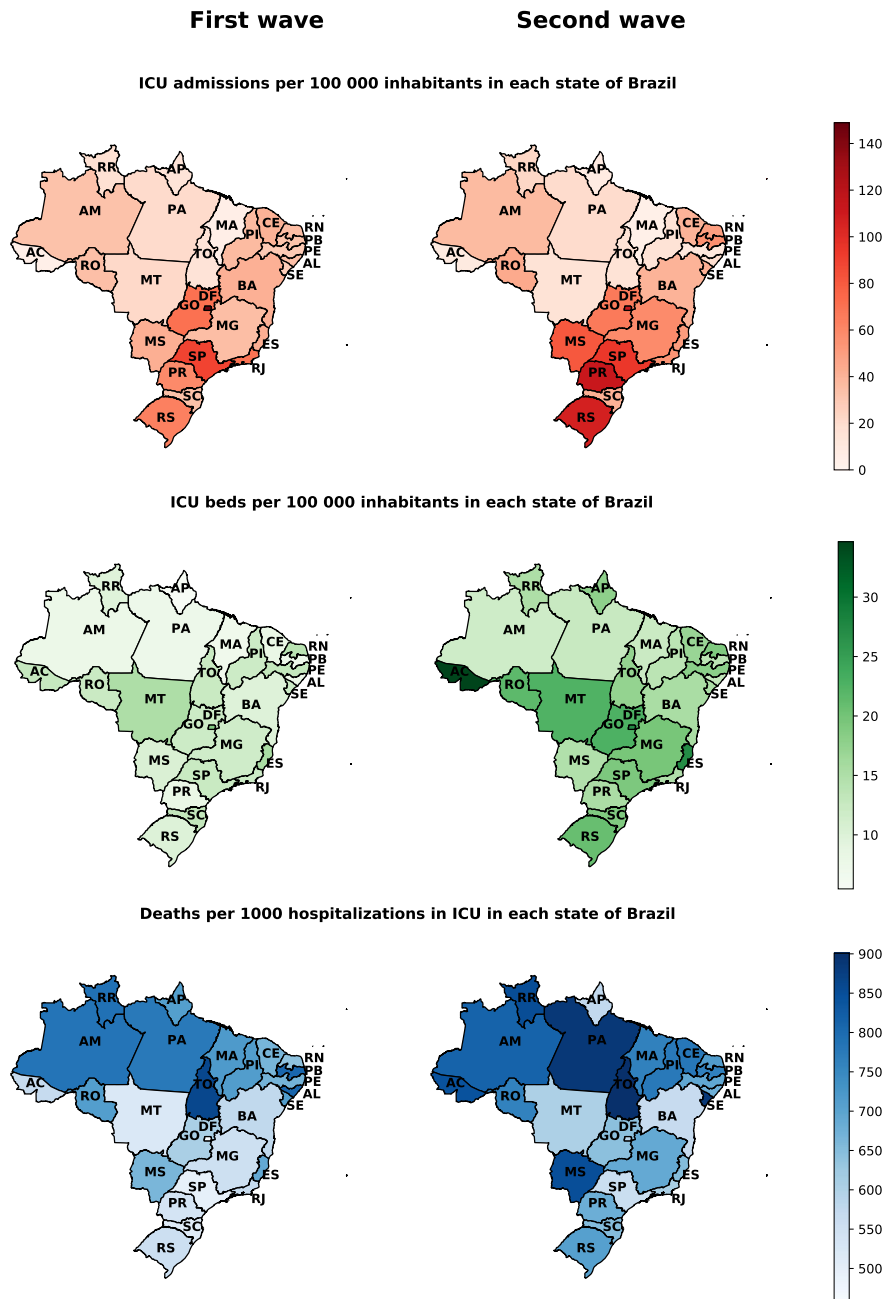


Figure 4. ICU admission rates, ICU beds per 100 000 inhabitants, and in-ICU mortality per 1 000 admissions due to COVID-19 in the first and second wave, stratified by the Brazilian state. Note: the population considered for each state is an official estimate from Brazilian government agencies. The number of ICU beds considered was based on data for the first wave of October 2020 and the second wave of April 2021. The number of ICU beds per state was obtained from TABNET. ICU admissions and deaths were assigned to each state according to hospital location.

occurred because the vaccination of this group began in January 2021. A United Kingdom (UK) study noted a robust association between Non-White race and COVID-19 mortality.¹⁷ Despite the Black/Brown (Pardos) race being the predominant race in the Brazilian population,¹⁸ the data indicates that it represents

42·65% of hospital admissions, while the White population represented 55·87%. These numbers can be related to that, historically, the Brazilian Black/Brown (Pardos) population has disadvantages regarding housing conditions, income distribution, education, and also less access to health systems.¹⁹

Mortality of patients with risk factors
First wave mortality: 34.81% - Second wave mortality: 39.30%

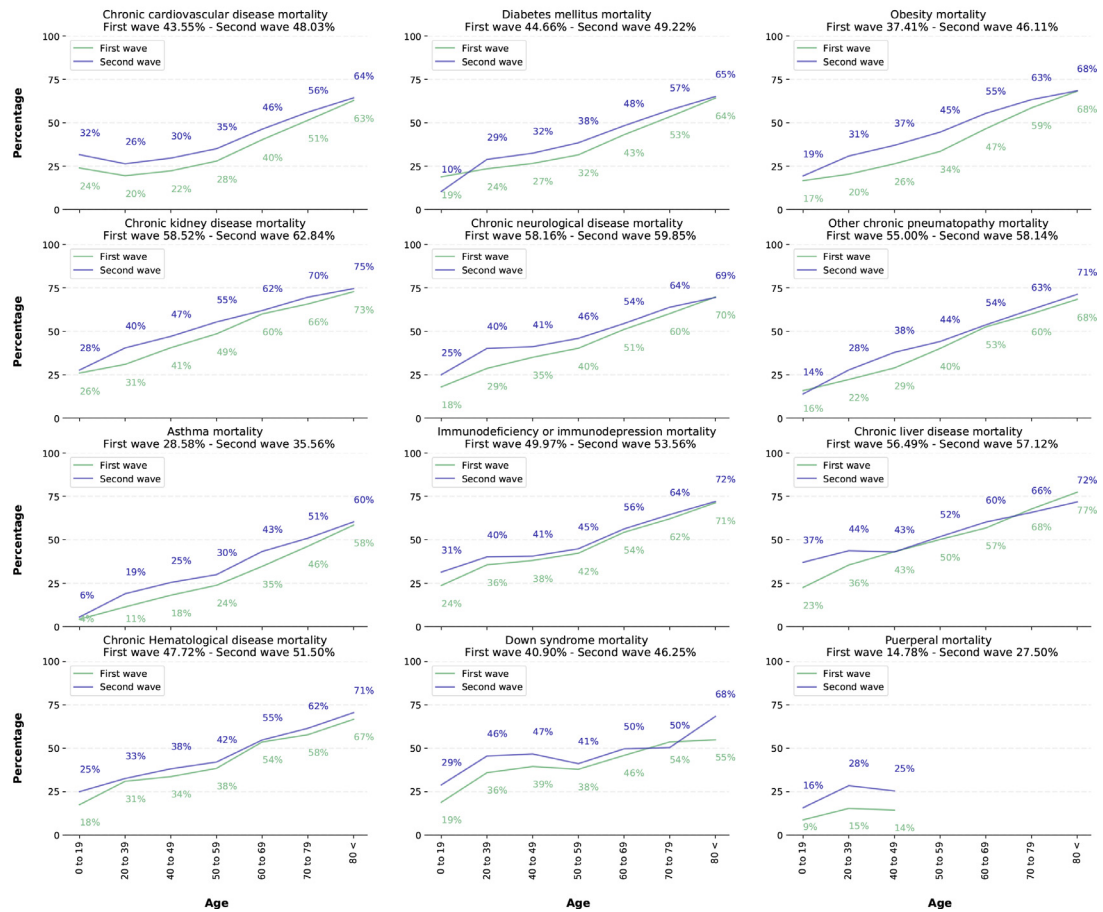


Figure 5. In-hospital mortality rate of patients with comorbidities in the first and second wave of the COVID-19 pandemic in Brazil. Note: We only considered patients with comorbidities informed at the time of admission. Death rates are calculated based on patients with reported outcomes. We only consider puerperal or parturient women up to 50 years of age.

Races/ethnicities and education are strong predictors of mortality, being jointly associated with the region of residence as social determinants for differences in access to health services in Brazil.¹² In our study, 32.5% of all cases of hospitalized COVID-19 patients attended high school. However, the highest mortality rate is seen in the illiterate population (a mortality rate among illiterates of 57.09% in the whole pandemic) followed by the population who attended elementary school (49.51% of deaths), middle school (41.93% of deaths), high school (31.09% of deaths), and college (26.21%). The pattern of mortality considering education remained the same in both waves, with mortality rates increasing inversely proportional to the level of education. Furthermore, the Brazilian death registration system shows an increase in the disparity of deaths in COVID-19 concerning the education level.²⁰

The people from rural areas, despite representing a small portion of the studied data, have higher mortality

rates, during the whole pandemic, than the urban population. This is probably because the regions furthest away from urban centers often do not have adequate health infrastructure and resources. Therefore, the delay and complications during the patient transfer to hospitals with better infrastructure may be related to higher mortality in the rural population. People who live on the peripheries of cities and those from rural areas, mostly with lower educational levels, with more considerable household crowding, and lower-income, also presented higher in-hospital mortality in other Brazilian studies.^{12,20}

Among the main variants detected in Brazil are P.1 and P.2. P.1, considered Variants of Concern (VOC), had its first case in the 40th epidemiological week in October 2020 (Fig. 2). P.2 was identified for the first time in April 2020 in the 16th epidemiological week (Fig. 2). The increase in the prevalence of P.1 and P.2 among sequenced variants coincides with the beginning

of the second wave in Brazil. The association between the variants and the increase in cases and hospitalizations was evidenced in the city of Manaus, Amazonas (AM), where the P.1 variant was first reported.²¹ The P.2 variant, carrying the E484K mutation, being a variant derived from the B.1.1.28 lineage, was the most prevalent variant among the sequenced variants of patients who developed symptoms in the state of Rio de Janeiro.²² These strains have been spreading rapidly, and both P.2 and P.1 were recently found in documented cases of SARS-CoV-2 re-infection.²³ Variants P.1 and P.2 accounted for approximately 75% of the variants sequenced in Brazil around the 55th epidemiological week. From the 60th epidemiological week onwards, the P.1 variant was predominant for the cases sequenced in Brazil.

Thus far, there is not much information about the transmissibility of the P.1 variant. However, it shares several acquired mutations from B.1.1.7 (Alpha), first identified in the UK and considered to be VOC, and which appears to be associated with increased transmissibility of SARS-CoV-2 in several countries.²⁴ B.1.1.7 was also associated with a higher risk of hospitalization compared to other variants.²⁵ In addition, B.1.1.7 showed an increase in severity for adults over 30.²⁶

The prevalence of P.1 corresponds to the increase in hospitalizations for SARI in Brazil (Table 3). Comparing both waves, it was observed similar percentages of hospitalizations for all age groups. However, there were higher percentages of deaths among hospitalized patients at the second wave for several age groups, especially among 20 to 69 years old. The same happened when looking at ICU admissions—for the major age groups, there was a slight increase in percentages of patients admitted in ICU at the second wave, but a higher difference when looking at deaths. The increase in hospitalization and death rates in younger groups during the second period may be partially related to the vaccination campaign in Brazil, which at first prioritized the elderly age groups. Another hypothesis is related to the behavior of P.1 in younger age groups. According to a study conducted in eight European countries, considering P.1 cases was observed between 3.0 and 13.1 times higher odds of hospitalization in the age groups 20–39, 40–59, and 60–79, as well as a 2.9–13.9 times higher odds of ICU admission (40–59, 60–79, and 80+ age groups).²⁷

These evidences suggest that the second wave was more severe and presented higher lethality rates in Brazil than the first one. In the second wave, a higher number of patients demanding ICUs admission, and invasive mechanical ventilation. These results are impressive, especially regarding the worsening outcomes seen for young age groups at the second wave. Previous studies have already described that the second wave around the world had affected a higher percentage of young people than the first one.^{28,29} However, in

contrast to what was seen in Brazil, most countries reported better outcomes for patients at the second wave. One study from Japan, for example, showed that severe respiratory conditions, the need for invasive mechanical ventilation, and mortality rates were higher during the first wave of the disease.²⁸ In Spain, Germany, Italy, and Belgium, similar results were obtained.^{29–31} The discrepancies between Brazil and other countries are probably related to the lower preparation of the healthcare system to deal with the second wave and the inefficiency of the preventive social actions, such as social distancing and vaccination.^{11,21} Another hypothesis for a more severe second wave in Brazil compared to other countries is the emergence and prevalence of P.1, which has higher rates of transmission and hospital admissions.^{27,32}

Discrepancies on COVID-19 hospitalizations and mortality between the two waves were also observed among Brazilian states, possibly due to social, political, and economic differences. When looking at state differences for hospitalizations, we can observe that the southern states, such as *Rio Grande do Sul* (RS), *Santa Catarina* (SC), and *Paraná* (PR) presented higher hospitalization rates per 100 000 inhabitants in the second wave (Fig. 3). Moreover, almost all states presented higher rates per 100 000 inhabitants and deaths per 1 000 in ICU admissions at the second wave. It is important to note, however, that the mortality rate for 1 000 ICU admissions is higher in northern states, which present lower Human Development Indexes and weakened health assistance quality.³³ The Brazilian states considerably increased the number of hospital and ICU beds per 100 000 inhabitants from the first to the second wave. However, we can observe in the Figs. 3 and 4, especially in Northern Brazil, that despite the increase in hospital beds, the mortality rates in the second wave compared to the first wave were considerably superiors. In summary, the results described support the hypothesis that the increase in hospital and ICU beds alone is not enough to prevent deaths from COVID-19. As evidenced by other articles, joint efforts are needed to increase the capacity of beds with an adequate hospital structure with qualified professionals, medical supplies, supplemental oxygen, and the adoption of non-pharmacological measures to contain the advance of outbreaks of COVID-19.^{34–38}

For Brazil, the regional differences observed during the COVID-19 pandemic could also be due to social and health inequities, local strategies regarding social distancing and preventive actions, quality and readiness of health services, availability of supplies and medical resources, different SARS-CoV-2 variant prevalence, treatment strategies, as well as the availability of qualified human resources. These hypotheses are corroborated by a report of the UK Health Foundation,³⁹ indicating that hospital capacity, especially beds, was the main determinant of differences in COVID-19

deaths across the world. The study further demonstrates that countries with higher bed capacity were more likely to lockdown earlier to reduce transmission and, hence, the burden on the health system.³⁹

Another issue concerning COVID-19 prognosis is related to the waiting time for hospital and ICU admission. Table 4 shows that the percentage of deaths increases in all ages when the number of days until hospital and ICU admission increases. Saito et al. (2021) observed a lower mortality rate in Japan in their second wave even when stratifying data for age and severity of symptoms at admission, which they suggested could be due to the shorter time between disease onset and hospital admission at the second wave.²⁸ In this sense, the efficiency of bed management is also an important factor when dealing with the pandemic.⁴⁰ A retrospective observational cohort with patients hospitalized in Lombardy, Italy, observed an increase in mortality with the increase in the interval between the first symptoms and admission to the ICU, from six days onwards.⁴¹

Patients with comorbidities are usually associated with higher mortality among cases of COVID-19.⁴² Our data showed a high prevalence of comorbidities among patients who died and increased mortality between the first and second waves. The most prevalent comorbidity in our data was cardiovascular disease, followed by diabetes, which is similar to the findings of other studies.^{42,43} We observed that individuals with kidney disease had considerably higher mortality, with rates reaching 62–84% in the second wave. Survival analysis performed in Italian cohort studies showed an association between older age and decreased glomerular filtration rate with a higher risk of death.⁴⁴

The difference between COVID-19 mortality in the population with or without risk factors during the whole pandemic is more considerable among the younger age groups (Appendix (p 30)). The difference between mortality percentages is inversely proportional to age and practically does not exist in the age group above 80. Specifically for diabetes, a decrease in the risk of mortality in adults has already been identified in Mexico as the patients' age increases. The study also indicates that there is no association between mortality due to COVID-19 and diabetes in patients over 80 years old.⁴⁵ Another point that can influence mortality for patients with comorbidities is the reduction in the continuous care of chronic diseases.⁴⁶

Telemedicine was one of the ways found during the pandemic for the continuity of care for chronic patients.⁴⁶ However, the population with lower income and scholarly, which also is the one most affected by comorbidities in Brazil,⁴⁷ also has less access to telemedicine. Thus, the association of comorbidities with less access to primary care may have contributed to higher mortality rates observed in lower-income or less-educated groups. Furthermore, a study in the southern region of Brazil during the pandemic showed an

association of multimorbidity with a greater chance of impaired management of chronic diseases. The study also related a reduction in access to medication and the search for face-to-face care among low-income people.⁴⁸

In January 2021, P.1 was the main COVID-19 variant identified in the Amazon region. It is important to highlight that there was an increase in mortality in the same period compared to April and May 2020 in this region, especially among women and between people with 20 to 59 years old.³² In this way, we can hypothesize that the differences found in mortality and the presented symptoms (gastrointestinal, neurological, and respiratory symptoms—including desaturation) from the first to the second wave were related to the variant P.1. In fact, variant P.1 can be 1.7 and 2.4 times more transmissible than Amazon non-P1 lineages. Also, the infections are 1.2 to 1.9 times more likely to result in mortality in the period after the emergence of P.1 than before, even considering that inferred cross-immunity and inadequate medical care access can considerably impact the estimates of this relative risk.³²

The present study has some limitations, as described next. The data analyzed in this article are observational and comprise an arbitrary subset of all SARI cases due to COVID-19 hospitalized in Brazil during February 25, 2020, to April 30, 2021. Furthermore, our study was limited to describing the intragroup behavior of the pandemic using an analysis based on crude rates without age standardization. We believe that crude rates can help determine the specific burden and needs of services for certain populations. Although Brazil centralizes information on SARI cases and outcomes due to COVID-19, the lack of information on patient care limited our ability to provide details of patients' evolution during treatment. There may be some losses in the notification of patients admitted by SARI, as the notification is performed manually by health professionals due to the lack of interoperability of hospital systems with the national notification system. Symptoms and comorbidities refer only to information collected and sent to SIVEP-Gripe by the hospitals. Furthermore, it is not possible to analyze the severity of the disease at the time of admission. Serological/clinical-epidemiological tests can be used to confirm the diagnosis of COVID-19 in Brazil. Therefore, mortality rates may be overestimated, as we only analyzed patients with positive RT-PCR for SARS-CoV-2. Finally, due to the deficiency in the genetic sequencing of confirmed cases of SARS-CoV-2, we cannot only attribute the increase in hospital burden to the new variants.

In conclusion, this study analyzes a Brazilian national dataset of COVID-19 hospitalized cases with SARI. We described the clinical and socio-demographic characteristics of patients hospitalized in Brazil stratified into the first and second waves. Despite efforts to increase the hospital structure during the pandemic, the second wave of COVID-19 in Brazil exhibited a

higher in-hospital mortality rate in almost all ages, races/ethnicities, and social groups. We hope that our study can help to understand better a load of COVID-19 in the hospital system in Brazil and contribute to the definition of public policies. Finally, efforts are needed to improve the surveillance system for SARS-CoV-2 variants in Brazil, along with campaigns to encourage population vaccination.

Contributors

FAZ, BD, JNS, NTB, APA, MLRI, CAC, GOR, and APWCM participated in the design and concept of the study. FAZ, HCB, IGS, and LB acquired data. FAZ and BD did statistical analyses. FAZ, BD, JNS, NTB, APA, MLRI, and APWCM wrote the first version of the manuscript. CAC, and GOR supervised the study. CAC, GOR, RSA, RRR, SJR contributed to reviewing and editing the manuscript. All authors had full access to all data in the study, participated in data interpretation, revised the manuscript, and approved the final version of the manuscript for publication.

Data sharing

All de-identified data, including individual participant data, are publicly available. The data sources are described in the manuscript and in appendix (p 1).

Editor note

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Declaration of Competing Interests

The authors declare no conflicts of interest.

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Supplementary material

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2021.100107

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