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## Retrospective epidemiology of the SARS-CoV-2 (and COVID-19) epidemic among 27 Brazilian cities



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### ABSTRACT

**Background:** Most of the countries facing the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic are still trying to understand the dynamics of the behavior of the virus and dissemination of the new agent.

**Objectives:** A retrospective descriptive epidemiological study of the 26 state capitals of Brazil and its capital, Brasília, was performed to investigate the behavior of the infection and disease caused by SARS-CoV-2.

**Study design:** The data presented were obtained from the State Health Departments and the Brazilian Ministry of Health. Seven epidemiological markers (including the incidence, mortality and case fatality rates and the growth of the epidemic measured by the ratios observed on days 30, 60 and 90) were compared for the initial 90 days of the epidemic for each city.

**Results:** The epidemic spread to the country within 25 days, and deaths occurred as early as nine days from initiation. The incidence and mortality rates ranged from 70 to almost 1,599/100,000 and less than 1 to 1,171/1,000,000, respectively, at the end of the 90-day period of observation. The CFR was less than two up to 12.31%. The magnitude of each marker clustered the cities in different groups. The epidemic was managed differently in each city, with differences in qualified medical services and medical preparedness to face the emergency situation.

**Conclusions:** Although modeling the epidemic has been a constant task, epidemiological data should be pursued to define actual information, such as the prevalence and incidence rates, to understand the unpredictable nature of this emerging infection, including the present policy of vaccination campaigns.

### 1. Introduction

The emergence of a human coronavirus in China rapidly became an explosive epidemic that spread to other countries, leading the World Health Organization to define it as a pandemic in a short time [1]. The impact of the new human virus led to panic and fear, as observed recently with human immunodeficiency virus 1 (HIV-1) [2] and the large information gaps regarding the natural history of a previously unknown virus.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a human *Coronaviridae* causing severe disease (named COVID-19) similar to that observed previously with SARS-CoV and MERS-CoV [3]. Because of the recent entry of SARS-CoV-2 into the human population, information is not readily available to generate consensual effective treatment or prophylactic measures. In Brazil, the number of confirmed cases of infection has surpassed 16,833,682 (by 04 June 2021), with a death toll of more than 470,690 people. Asymptomatic infected people or those with

mild disease that did not require medical attention were not properly accounted for to quantify the values derived from coronavirus infection [4]. Unveiling the clinical and epidemiological aspects of the disease are crucial factors to understand the behavior of SARS-CoV-2 and COVID-19 [5,6].

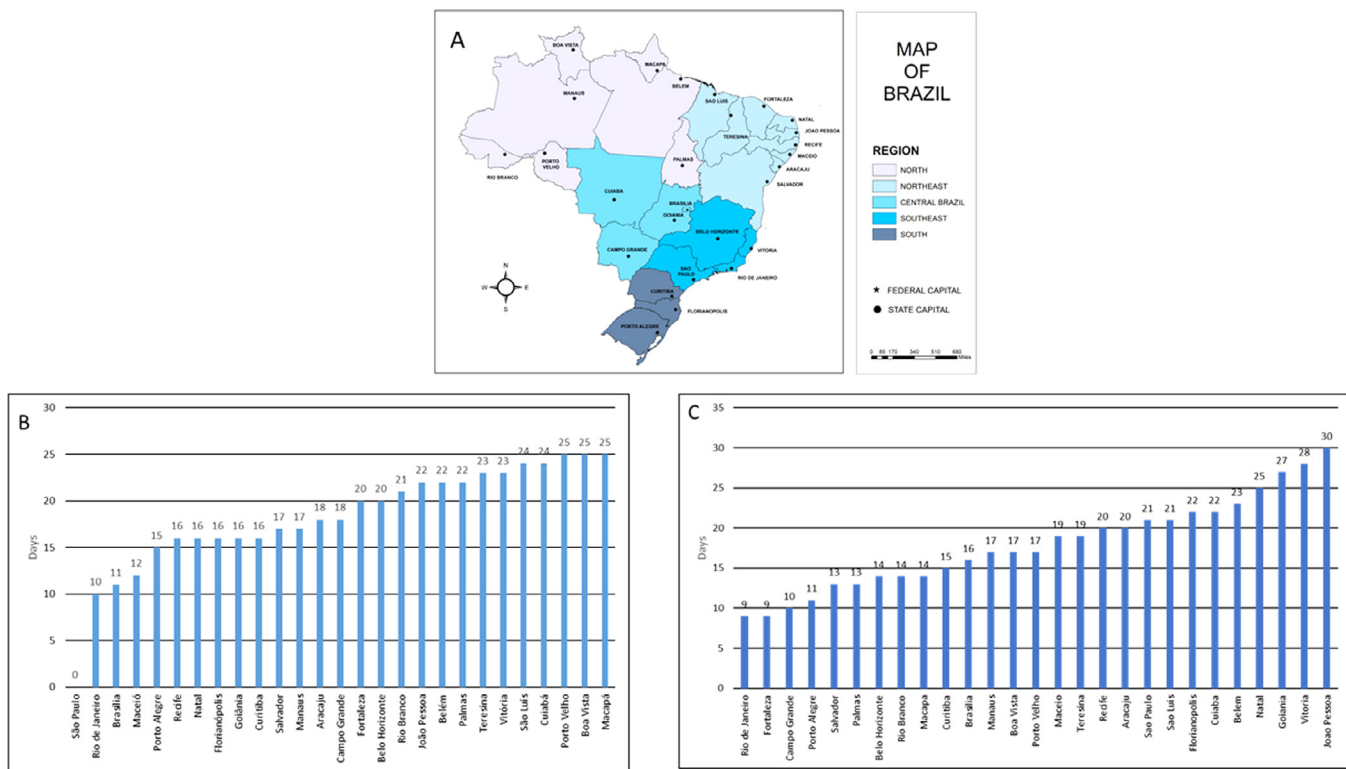
The present study presents the different patterns of infection and disease caused by SARS-CoV-2 in 26 state capitals and the capital of Brazil, providing an important means of comparison of the initial 90 days of the epidemic for each city, covering all geographical regions of the country.

### 2. Materials and methods

#### 2.1. Study design and procedures

The study was a retrospective descriptive report using the information presented in the project “CoVida Network – Science, Information

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**Fig. 1.** (A) Map of Brazil with the 26 state capitals and federal capital, Brasília, according to their geographical and regional location. (B) Interval of time, in days, to detect the first case of infection by SARS-CoV-2 in each city. (C) Interval of time, in days, for each city to register the first death by COVID-19.

and Solidarity”, a collaborative initiative of the Centro de Integração de Dados e Conhecimentos da Saúde (CIDACS/FIOCRUZ-Bahia) and the Universidade Federal da Bahia (UFBA), created to monitor the evolution of the epidemic of SARS-CoV-2 in Brazil. CoVida network data are published in the panel (<https://painel.covid19br.org/>) using the information provided by the State Health Departments and Brazilian Ministry of Health. The initial 90 days of the epidemic in Brazil, for the sake of uniformity, followed the same case definition for the infection by SARS-CoV-2 and the disease COVID-19, in the country as a whole, as established by the Brazilian Ministry of Health [7].

The longitudinal evolution of the epidemic was studied in 26 state capital cities and Brasília in the first 90 days of the epidemic. The initial observation was on 25 February 2020 in Sao Paulo, and the last day was 19 June 2020 when Boa Vista fulfilled the criteria of 90 days of the epidemic.

Seven epidemiological markers were used: (i) time interval in days from the starting point in Sao Paulo in each city; (ii) time interval in days from the first case in each city to the first confirmed death by COVID-19; (iii) absolute number of cases; (iv) incidence rate (IR)/100,000 inhabitants; (v) mortality rate (MR)/1000,000 inhabitants; (vi) case fatality rate (CFR)/100 infected persons; (vii) growth ratio of the incidence and mortality from day 30 to day 90 (D90) of the epidemic. The IR and MR used population estimates according to the Brazilian Institute of Geography and Statistics [8].

The figures and tables were grouped according to either their similarities during the examination period or within a range of the final values observed. The information was recorded in a data bank using Excel 2016 software.

### 2.2. Statistical analysis

Correlation tests were performed among the IR, MR, and CFR on D90 using the following: (i) population density; (ii) human development index; (iii) gross domestic product; (iv) time elapsed between the first case

of infection/disease in the country and first case in each city; (v) time elapsed between the first case in each city and first reported death by COVID-19. Pearson’s correlation coefficient (r) was used and calculated using Minitab 19 Statistical Software with a significance level of 5%.

### 3. Results

On February 25, 2020, the first confirmed infected SARS-CoV-2 person entered the city of Sao Paulo, Brazil. Fig. 1 shows the location of the 27 cities, according to their geographical region (Fig. 1A), time in days to detect the first case of infection in each city following the first case detected in Sao Paulo (Fig. 1B), and time in days to register the first death by COVID-19 in each city (Fig. 1C). Rio de Janeiro was the second city to report the occurrence of COVID-19 ten days after Sao Paulo; the last was a group of cities formed by Boa Vista, Macapá and Porto Velho (within the Amazon region of Brazil), 25 days after the initial detection.

The epidemic started with cities in the States of the Southeast, followed by the Midwest, Northeast, South and North regions. The time required for this transmission was approximately 2 to 3 incubation periods of the disease. Within 12 days, only Sao Paulo, Rio de Janeiro (Southeast region), Brasília (Central Brazil) and Maceio (Northeast) were involved in the epidemic. The subsequent 13 days showed a rapid spread of the virus to the other 23 cities. The median time of the spread was 19 days (first quartile: 16 days and 10 cities included in the epidemic; third quartile: 22.7 days and 20 cities). In Fortaleza and Rio de Janeiro, the first deaths occurred in as short as nine days, but it took 30 days in Joao Pessoa. The median time was 17 days (first quartile: 14 days and 9 cities reporting first death; third quartile: 21.5 days and 20 cities).

The epidemic occurred at different levels within the initial 90 days in each city. Fig. 2 shows the number of cases of disease according to the four groups. São Paulo, Rio de Janeiro and Fortaleza (Fig. 2A) controlled the epidemic until approximately D50, and then a rapid increase occurred to reach from 31,000 to 45,000 cases by D90. Fig. 2B, 2C and 2D show clusters of cities with similar curves, with a delay of the rising

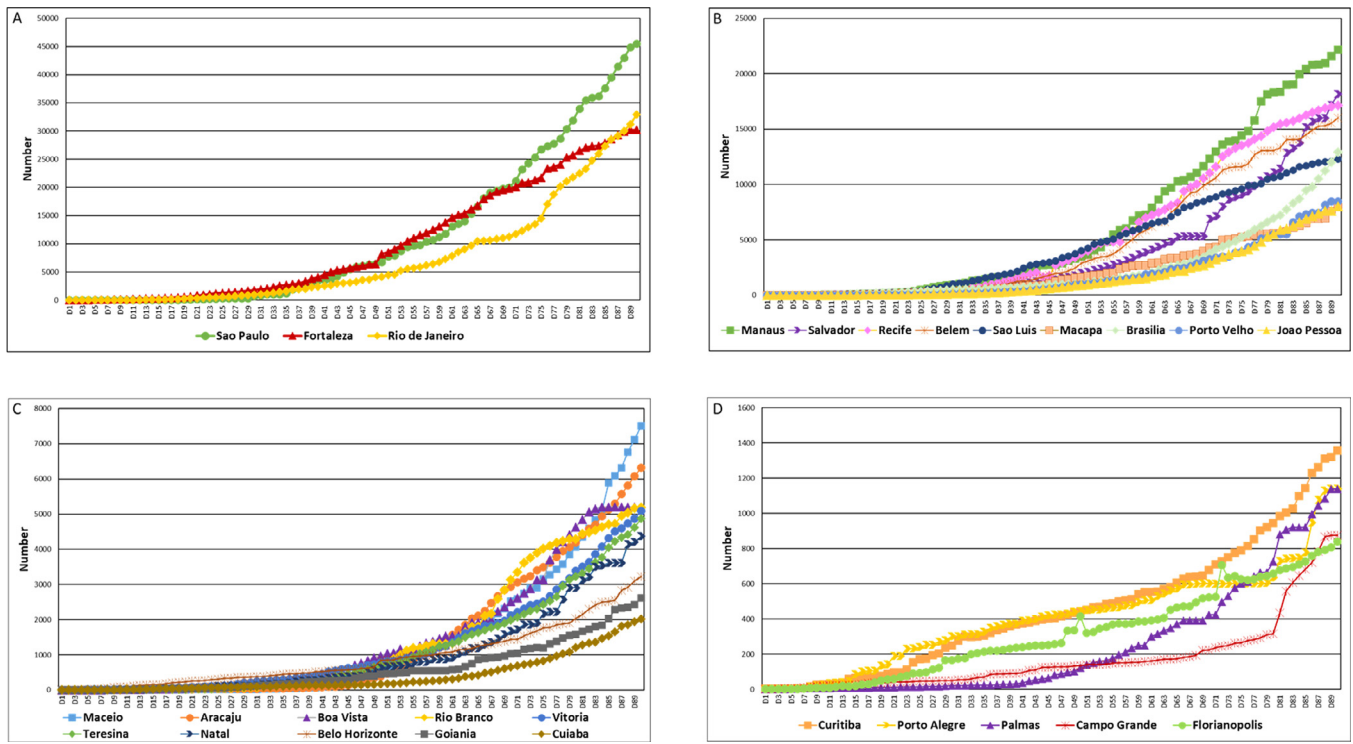


Fig. 2. Number of cases of infection (Fig. 2A, 2B, 2C and 2D) by SARS-CoV-2, according to D1 to D90, in each group of cities in Brazil.

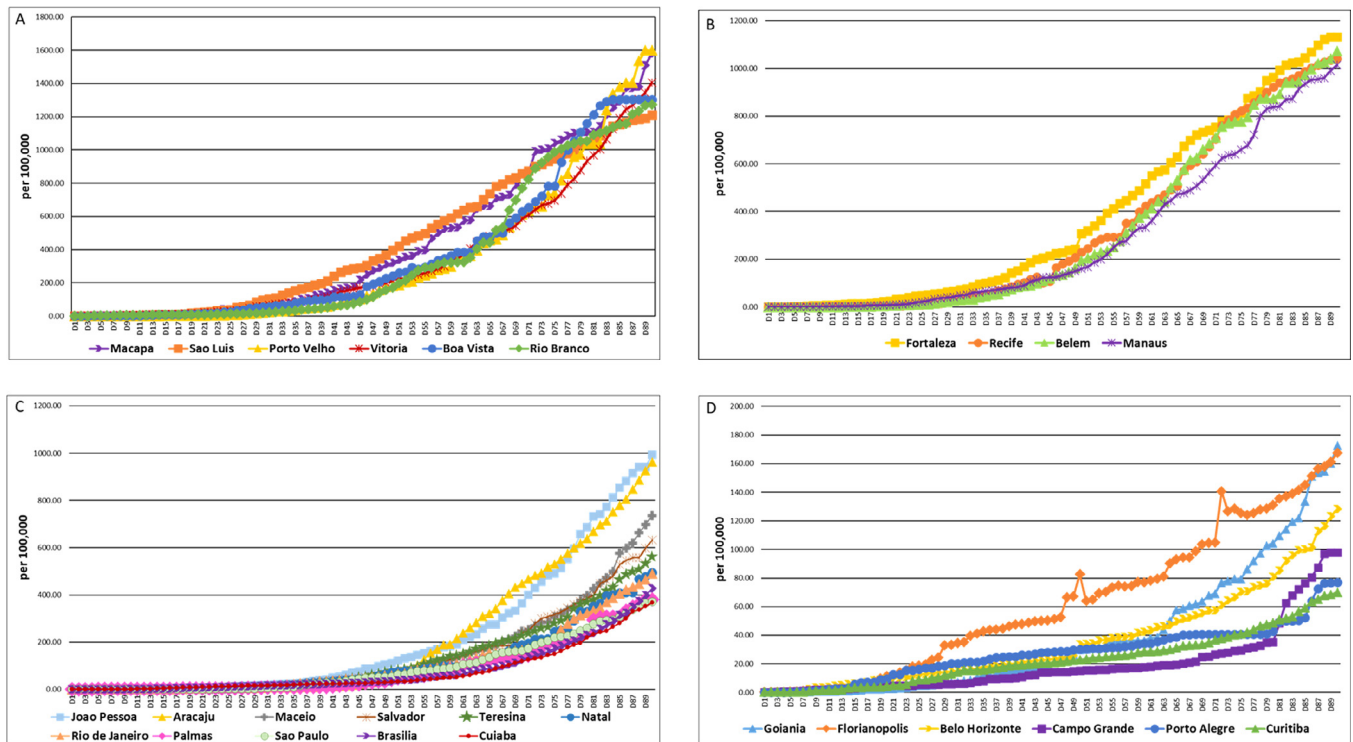


Fig. 3. Incidence rate (per 100,000 inhabitants; Fig. 3A, 3B, 3C and 3D) by SARS-CoV-2, according to D1 to D90, in each group of cities in Brazil.

point (approximately D60 in Fig. 2B), but each with a lower number of cases (8000 – 22,000 in Fig. 2B; 2000 – 8000 in Fig. 2C; 800 – 1350 in Fig. 2D). The group of cities in Fig. 2D, although in a rising trend, showed at least 30 times fewer cases by D90 than in the group in Fig. 2A.

At the end of the observation period, the IR (Fig. 3) varied from approximately 70/100,000 (Curitiba) to almost 1599/100,000 (Porto

Velho). The group in Fig. 3A shows a sharp increase starting on D45, raising the IR from 1209 to 1599/100,000. Fig. 3B shows an increase on D53. Fig. 3C shows a rise on D60. In the last group (Fig. 3D), a rise in the IR occurred ranging from D25 to D60, but the cities showed lower values (70 to 172/100,000). The highest values shown by Goiania (167/100,000) and Florianopolis (172/100,000)

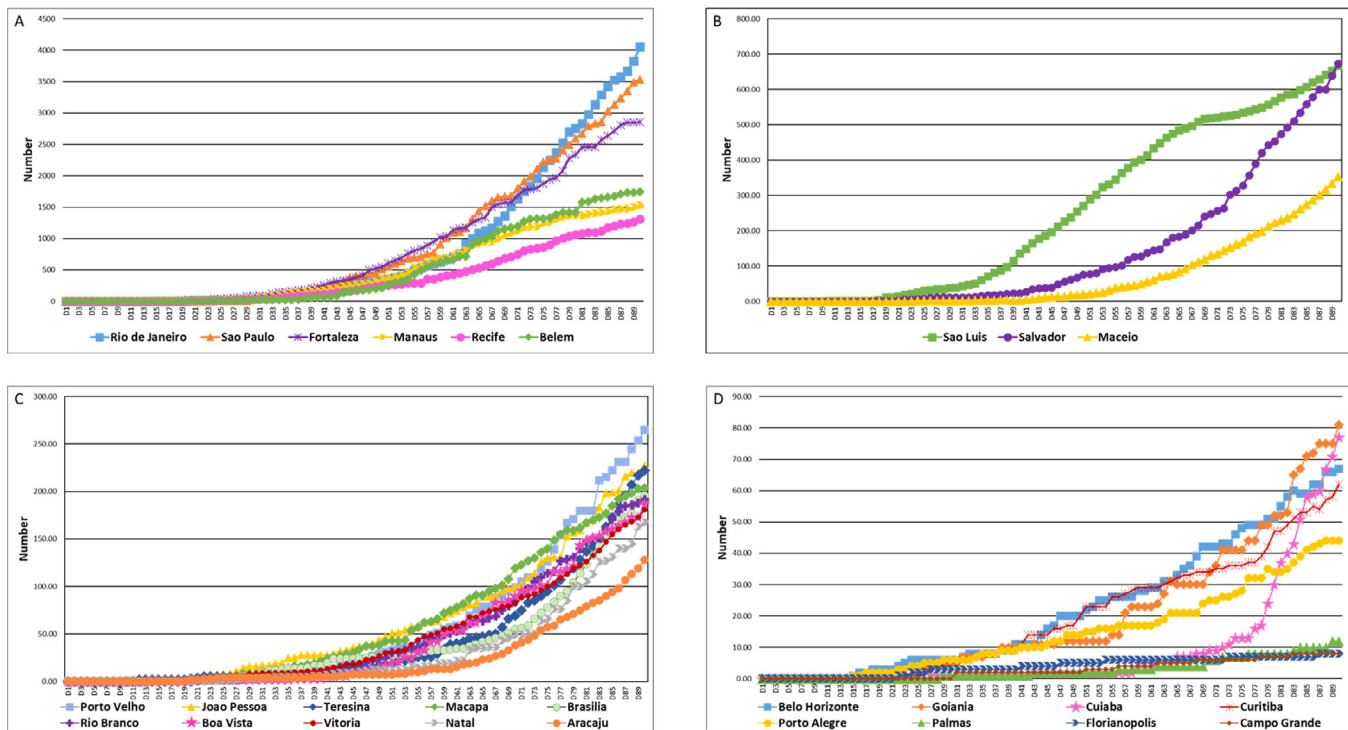


Fig. 4. Number of deaths (Fig. 4A, 4B, 4C and 4D) by COVID-19, according to D1 to D90, in each group of cities in Brazil.

were half of the lowest IR from Cuiaba (366/100,000), as depicted in Fig. 3C.

The first cluster of cities reporting deaths by COVID-19 (Fig. 4A) showed the highest numbers of daily deaths on D90 and a sharp rise by D55. The highest number was in Rio de Janeiro (4055 deaths), representing more than 500 times the number registered in Campo Grande (eight deaths; Fig. 4D).

MR ranged from fewer than 1/1000,000 inhabitants (Campo Grande) up to 1171/1000,000 in Belem and showed rising values in the groups depicted in Fig. 5A (603 – 1071/1000,000) and Fig. 5B (range of 288 – 500/1000,000) from D50 onwards. The third group (Fig. 5C; range: 190 – 256/1000,000) showed a rise at least 10 days later, and the last group (Fig. 5D; range: 0.89 – 65/1000,000) did not show a clear pattern because the rates were usually low.

At the beginning of the epidemic, a large variation was observed in the CFR that was maintained by D90, as shown in Fig. 6A (ranging from 7.76% to 12.31%) and Fig. 6B (ranging from 3.71% to 7.45%). In other cities, the CFR decreased gradually, as shown in Fig. 6C (ranging from 2.02 to 3.59) and Fig. 6D, decreasing to less than 2% on D90. The crude overall case fatality rate was 6.7%.

Table 1 describes the IR of SARS-CoV-2 on D30, D60 and D90 and compares the growth ratios of the epidemic from D30 to D60 and from D30 to D90. Porto Velho was the city with the highest incidence rate (1599.30/100,000), and Curitiba had the lowest (70.20/100,000). However, the growth ratio of the incidence was greater in Maceio, where the epidemic numbers rose more than 341 times (vs. 76.99 in Porto Velho) on D90 compared to those on D30. The slowest advance occurred in Porto Alegre, with a ratio of 3.77 (vs. 5.41 in Curitiba). Among the ten cities with the highest growth ratios of the epidemic, nine were located in the North, Northeast, Central Brazil and Southeast regions of the country. The ten cities with the smallest ratios were from southern, southeastern and central Brazil.

The MR from COVID-19 on D30, D60 and D90, and the comparison of the growth ratios in mortality from D30 to D60 and from D30 to D90 are described in Table 2. Belem showed the highest MR (1171.67/1000,000) and greatest growth ratio in mortality (218.63) compared with D30

Table 1  
Incidence rates of SARS-CoV-2 on D30, D60 and D90 in the state capitals of Brazil and comparison of growth ratios from D30 to D90 (arranged in decreasing order of ratio 90/30).

	D30	D60	D90	Ratio 60/30	Ratio 90/30
Maceio	2.16	133.27	737.33	61.73	341.50
Aracaju	5.33	215.06	962.23	40.37	180.63
Porto Velho	20.77	355.97	1599.30	17.14	76.99
Rio Branco	18.66	323.33	1274.43	17.33	68.30
Sao Paulo	5.89	96.31	371.59	16.34	63.06
Joao Pessoa	17.55	190.35	993.92	10.85	56.63
Palmas	7.02	83.24	380.44	11.86	54.19
Teresina	10.87	145.69	563.92	13.40	51.88
Salvador	12.36	135.46	631.92	10.96	51.13
Recife	25.10	424.37	1041.06	16.91	41.48
Belem	26.06	391.43	1074.06	15.02	41.22
Natal	13.23	98.74	493.94	7.46	37.32
Rio de Janeiro	14.62	108.40	490.42	7.42	33.55
Brasilia	15.52	60.92	428.59	3.93	27.61
Vitoria	57.72	344.94	1406.25	5.98	24.36
Macapa	65.17	534.84	1581.87	8.21	24.27
Goiania	7.19	36.28	172.55	5.05	24.00
Manaus	42.70	332.79	1015.18	7.79	23.78
Boa Vista	55.61	384.01	1304.32	6.91	23.45
Cuiaba	16.51	53.17	366.72	3.22	22.21
Campo Grande	5.69	17.75	97.77	3.12	17.18
Fortaleza	67.21	516.12	1131.74	7.68	16.84
Sao Luis	97.55	615.67	1209.65	6.31	12.40
Belo Horizonte	14.85	42.51	128.34	2.86	8.64
Curitiba	12.98	28.61	70.20	2.20	5.41
Florianopolis	33.34	77.05	167.67	2.31	5.03
Porto Alegre	20.42	34.17	76.90	1.67	3.77

to D90 of the epidemic. The lowest MR was that of Campo Grande (0.89/1000,000), and the lowest growth ratio was two (the ratio was calculated only between D60 and D90 because no deaths by COVID-19 were registered earlier than D30). Cities from the north, northeast and southeast regions presented the highest MR and increases in the mortality growth ratios of the epidemic.

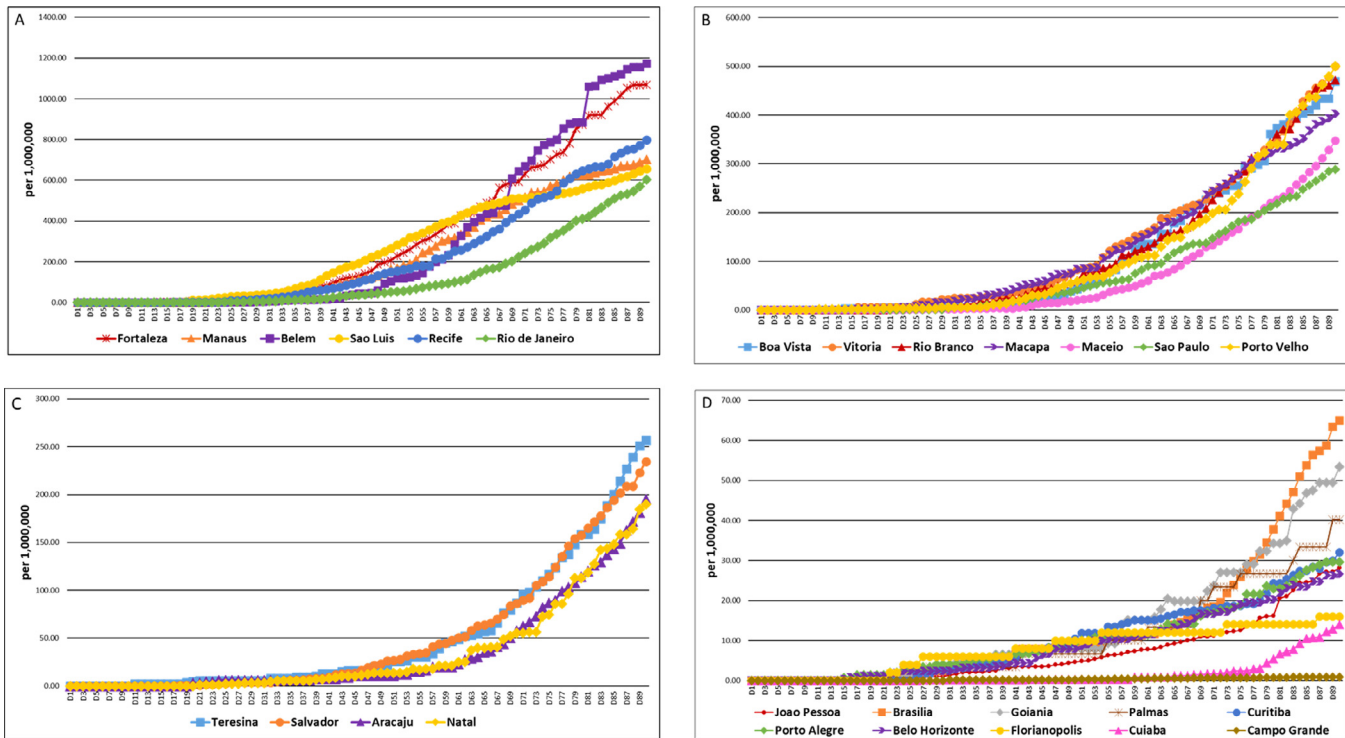


Fig. 5. Mortality rate (per 1000,000 inhabitants; Fig. 5A, 5B, 5C AND 5D) by COVID-19, according to D1 to D90, in each group of cities in Brazil.

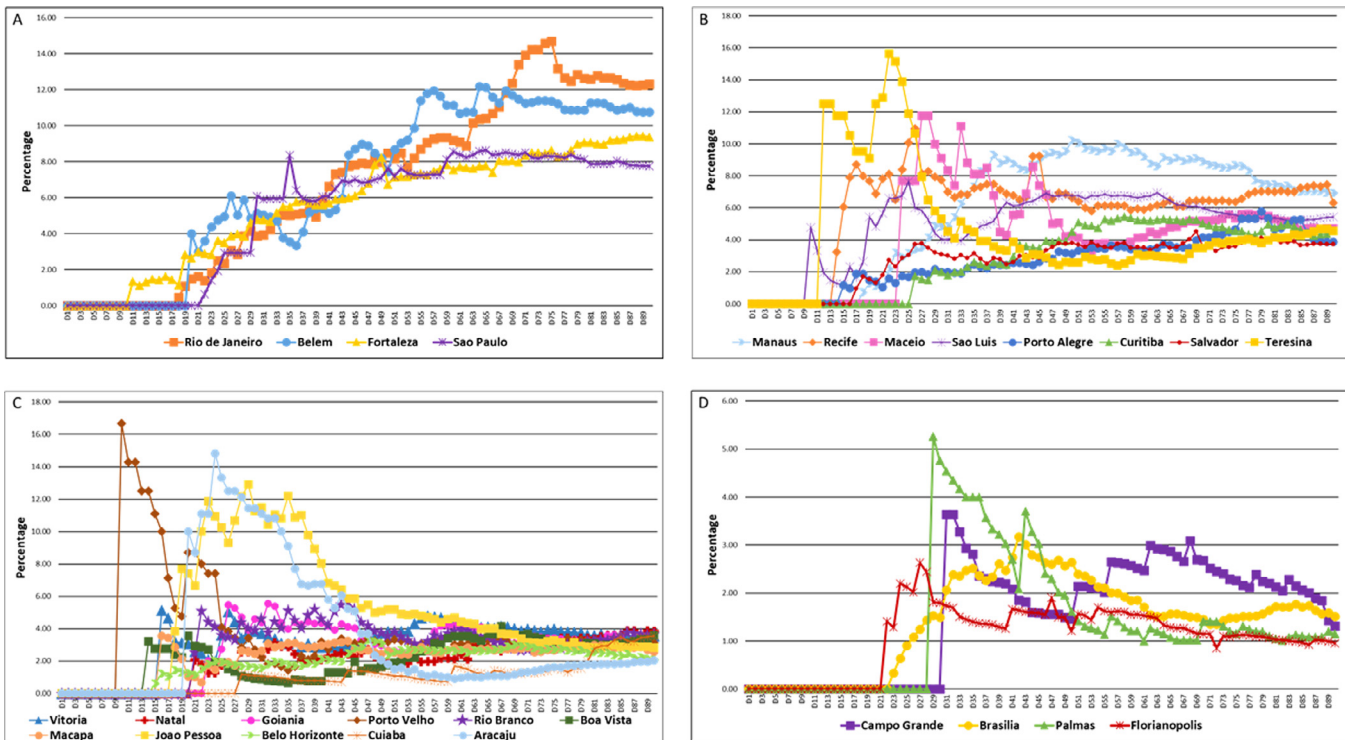


Fig. 6. Case fatality rate (%) by COVID-19, according to D1 to D90, in each group of cities in Brazil.

Correlation of relevant variables (Table 3) available in the data bank (IBGE, 2019) showed that the IR on D90 was positively correlated with the time interval between the appearance of the first case of disease in the country and first case in the observed cities ( $r = 0.514, p = 0.006$ ). By contrast, the IR and MR on D90 were negatively correlated with the variable measuring the time interval be-

tween the first case reported in each city and first recorded death [ $r = -0.592 (p = 0.001)$  and  $r = -0.522 (p = 0.005)$ , respectively]. The CFR on D90 was positively correlated with the demographic density of the city ( $r = 0.427, p = 0.026$ ). No other correlation was attributed to the city gross domestic index or the city human development index.

**Table 2**

Mortality rates of COVID-19 on D30, D60 and D90 in the state capitals of Brazil and comparison of ratios from D30 to D90 (arranged in decreasing order of ratio 90/30).

	D30	D60	D90	Ratio 60/30	Ratio 90/30
Belem	5.36	286.05	1171.67	53.38	218.63
Maceio	1.96	54.96	347.42	28.00	177.00
Rio de Janeiro	5.66	99.72	603.52	17.63	106.71
Boa Vista	5.01	135.27	468.42	27.00	93.50
Porto Velho	5.7	107.64	500.43	19.00	88.33
Sao Paulo	3.59	82.44	288.4	22.95	80.32
Cuiaba	0.18	0.91	13.97	5.00	77.00
Rio Branco	7.37	125.21	471.38	17.00	64.00
Salvador	3.83	48.04	234.65	12.55	61.27
Natal	3.39	21.49	190.02	6.33	56.00
Teresina	5.78	46.25	256.69	8.00	44.40
Manaus	20.62	316.57	702.78	15.36	34.09
Recife	19.44	252.17	656.85	12.97	33.78
Fortaleza	32.22	389.23	1069.18	12.08	33.19
Aracaju	6.09	19.79	194.82	3.25	32.00
Joao Pessoa	0.99	7.66	28.18	7.75	28.50
Brasilia	2.32	11.28	65.00	4.86	28.00
Macapa	15.89	149.01	403.32	9.38	25.38
Vitoria	22.09	154.65	499.87	7.00	22.63
Sao Luis	39.42	407.95	657.25	10.35	16.68
Goiania	3.30	15.17	53.43	4.60	16.20
Curitiba	2.59	15.00	32.07	5.80	12.40
Palmas	3.34	10.03	40.12	3.00	12.00
Belo Horizonte	2.39	11.15	26.67	4.67	11.17
Porto Alegre	4.04	11.46	29.65	2.83	7.33
Florianopolis	5.99	11.98	15.97	2.00	2.67
Campo Grande	0.00	0.45	0.89	NA	2.00*

NA: not applicable;

\* No deaths by COVID-19 were registered in Campo Grande until D30; the ratio was calculated only between D60 and D90.

**4. Discussion**

The descriptive approach used here was designed on a case-by-case basis since the first report of infection on February 25, 2020, of a Brazilian man coming from Italy with symptoms of COVID-19 by the end of the period dedicated to the Carnival party. We emphasize that he may not be the initial case of infection in Brazil because it is possible that the virus was already present but went undetected [9].

Despite the alert of the federal government that the virus was present in more than 53 countries [10], spreading rapidly and accompanied by a huge death toll, no local or state administration decided to refrain from the festivities. The virus might have entered the country, and transmission was accelerated some time during the festival. Cases of infection detected within an interval from ten to 25 days are compatible with a spread with the occurrence of waves two to three disease incubation periods long, confirmed by the inclusion of only ten cities in the first quartile and exclusion of cities from the north region. The virus took approximately the same period (30 days) to spread from Wuhan to the entire country [11].

It took ten days to detect the first case in Rio de Janeiro, indicating that underdiagnosed cases might have occurred. Salvador (16 days to detect) and Recife (17 days), two famous cities for their Carnival

parties, probably had independent introductions of the virus, not necessarily as a secondary spread from Sao Paulo or Rio de Janeiro, but from the many national and foreign visitors attending the festivities. International flights arrived in Sao Paulo, Rio de Janeiro, Salvador, Recife, Brasilia, Fortaleza, Belem and Manaus, but the Amazon region of Brazil was the last area involved with the epidemic; international traveling alone was probably not the key route of virus spread. During February and March, airports in Belem and Manaus reached more than 17,000 passengers [12]. A similar conclusion was obtained by phylogenetic analysis of the circulating virus in Brazil [13].

The observation period of 90 days of the epidemic leveled the time difference to spread to cities located geographically distant, demographically variable, with different cultural habits, social behavior, temperatures and humidity among other variables. The 27 urban conglomerates included 25% of the country inhabitants [8].

Importantly, the virus was identified by December 2019, almost 60 days before entering Brazil. The cities recorded the first deaths by COVID-19 with large differences in time and, most importantly, in their preparedness to fight against the epidemic. The first ten cities reporting cases of COVID-19 showed deaths occurring from nine to 27 days, evidence of differences in qualified medical services and medical preparedness and inability to manage the epidemic, despite international and national warnings; however, this situation was not unique to Brazil [14].

Two markers showed clear differences in cities handling the epidemic: the period (in days) from the start of the epidemic to the sharp increase of the IR (from D45 to D60) and the range of the values (from 70 to 1599/100,000) on D90. While Sao Paulo and Fortaleza showed the highest number of cases, the IR was three times greater in six different cities (Macapa, Porto Velho, Boa Vista, Rio Branco, Sao Luis and Vitoria) on D90.

The MR and CFR measured the major impact of the virus on the general population. The MR increased in most of the cities after D50. The CFR started the epidemic with an erratic curve reaching very high values but decreased in most cities by D90, except for Sao Paulo, Rio de Janeiro, Fortaleza and Belem, which showed a continuous upward trend on D90. This pattern should be further investigated to explain why these capital cities were completely different from the others.

Cities with a higher CFR (Belem, Fortaleza, Rio de Janeiro and Sao Paulo) were not among those with a higher IR but with the highest MR (except for Sao Paulo). The same situation was observed in China, where epidemic curves showed what might also be a mixed epidemic pattern [11,15,16].

Apparently, 90 days of the epidemic was insufficient to establish a successful protocol to treat sick persons, independent of the geographical region in the country. Special attention should be given to the CFR, which sharply declined in most cities, but this was not observed in Belem, Fortaleza, Rio de Janeiro and Sao Paulo (large cities with populations ranging from 1500,000 to 13,000,000 inhabitants) by D90, where there was an increasing trend since D25. The range of CRF (0.6% to 3.5%) for COVID-19 [15,17], is much lower than that of SARS and MERS [11] but shows a severe impact in handling the disease; whatever effort was performed, it did not decrease CRF. This marker is useful to assess the capacity of the local and state health systems to rapidly solve emergencies and reduce damage during the epidemic and to as-

**Table 3**

Correlation of the incidence, mortality and case fatality rates with relevant variables associated with the spread of SARS-CoV-2.

	Incidence		Mortality		Case Fatality	
	R	p value	r	p value	r	p value
Demographic density	-0.164	0.414	1.184	0.359	0.427	0.026
City gross domestic product (per capita 2017)	0.096	0.633	0.177	0.376	0.037	0.856
City human developmental index (2010)	-0.028	0.888	0.269	0.175	0.289	0.144
Time interval between the first case in the country and first case in the State capital	0.514	0.006	0.154	0.444	-0.283	0.153
Time interval between the first case in the State capital and first registered death	-0.592	0.001	-0.522	0.005	-0.282	0.155

sess the dynamics of transmission and health system preparedness. However, no value is definitive because the necessary rate components have not yet been fully defined and prevalence studies remain inconclusive [6,18,19].

The increase in the CFR was directly associated with population density. Preventive measures were imposed on most cities, but they did not show a positive effect in relation to the maintenance of sick people. The effect of social distancing and other procedures reported in 10 countries [20] and in Brazil [13] showed controversial and challenging results to measure. The economic power of a city and development and well-being of the inhabitants did not show a correlation, in contrast to what was shown in Fortaleza regarding the human developmental index and incidence of COVID-19 [21]. Variables, including temperature and humidity influencing virus dissemination, show conflicting results in Brazil [22] and elsewhere [23]. People's movements, including traveling, migration [24] or religious gatherings [25], must be further investigated in the epidemiology of SARS-CoV-2.

The reproduction number (R) in Sao Paulo and Rio de Janeiro for the early period of the epidemic was approximately one [13], but a huge ratio of growth (D90/D30) of the epidemic was observed in both cities (63.06 and 33.55, respectively). After D50, an explosive dissemination of the virus occurred, despite the intervention efforts of the entire country around March 12–23, 2020. A clear contrast between the epidemic modeling and the actual values was observed. Although modeling is a useful tool, actual values observed are essential.

Modeling the epidemic has been a constant task [26], but simpler epidemiological data should be pursued to obtain actual information, such as prevalence and incidence rates [6,15,27–29]. Time will be necessary to clarify the mechanisms that control the differences in the epidemic observed in Brazil and globally, including the long-term duration and continuous spread of the virus for more than a year. Individuals with and without severe comorbidities [11,30], different immunological responses and strategies to control the virus require investigation to bring assertive answers, including continuous waves of spread [31]. The reemergence of the virus will depend greatly on the present epidemic. Seroepidemiological studies consistently show that approximately 10% of the general population becomes infected; this infection rate is troubling as there are not enough immune individuals to establish herd immunity and consequent virus containment, which commonly requires 70% or more of the population to be immune to be effective [32]. Seroepidemiological information must be produced on a large scale for SARS-CoV-2 [5]. Notably, low seroprevalence rates are found for MERS-CoV in Saudi Arabia [33] and SARS-CoV-2 in Switzerland [29], Spain [27], and three areas of the USA (Los Angeles [28], Atlanta [34] and Indiana [35]) before the present vaccination efforts.

Although the endemic respiratory betacoronaviruses SARS-CoV-1 and MERS were eradicated following explosive epidemics [36], the future epidemiological behavior of SARS-CoV-2 remains unknown. Different scenarios are proposed, but they are speculative [26]. The three viruses are adapting to humans, and SARS-CoV-2 might be eradicated as well. The appearance of different strains [37] is a new sign of virus adaptation that requires good surveillance, good data collection, laboratories for a rapid diagnosis and administrators that elicit rapid decisions [38] to complement the vaccination program.

Errors in handling the epidemic are clearly observed and carry a significant toll to the continuous spread of the virus among the population. Important questions remain pending regarding transmission, the role of symptomatic infected persons in the epidemic, and other epidemiological markers after the definition of appropriate values. Underestimates due to the unknown number of asymptomatic cases, absence of mass testing and precarious health system access are misleading to calculate the epidemiological rates. Although clinical data, laboratory diagnosis and prophylactic vaccines have been rapidly developed, descriptive epidemiological information is influenced by virus biology, geographic location, social habits, cultural practices and other variables, making the agent behave somewhat differently in each setting.

## Author contributions

SSL and RI conceived, designed and acquired the data and performed statistical analysis. SSL, RI, ACRV, MOGI, LFAM and MAFQ performed the analysis and interpreted the data, drafted the first manuscript and critically revised the final version of the manuscript. All the authors approved the final manuscript.

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## Ethical approval

not required.

## Declaration of Competing Interest

None of the authors have any conflict of interest to report.

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