

Severe Acute Respiratory Syndrome caused by New Coronavirus (COVID-19) and *influenza* viruses in Brazil: Descriptive analytical observational retrospective study

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ABSTRACT

The World Health Organization monitors diseases that can spread rapidly, including infections that may result in severe acute respiratory syndrome. New coronavirus and influenza are etiological agents capable of causing SARS. This is a descriptive-analytical observational retrospective study based on secondary data extracted from epidemiological bulletins (EB) from weeks 01 to 48, the Ministry of Health on COVID-19 and Influenza virus, consulted until November 28, 2020. The Ministry of Health received the first notification of a confirmed case of COVID-19 in Brazil on February 26, 2020. From February 26 to November 28, 2020, 6,314,740 cases and, 172,833 deaths from COVID-19 in Brazil were confirmed. The highest mortality rate was observed in the Midwest region (98.9 / 100 thousand inhabitants). The pandemic has already a high rate of serious morbidity and mortality in older adults and is higher than in the influenza pandemic. In Brazil, the numbers have increased and there are already cases of re-infection shared by some health centers. We cannot think that other pandemics will not occur, we must learn from this experience and prepare ourselves with new tests, adequate stocks of personal protective equipment, and, the capacity for intensive care.

Keywords: Sick, Infection, Health Public, New coronavirus, Influenza.

1 INTRODUCTION

The World Health Organization monitors diseases that can spread rapidly, including infections that may result in severe acute respiratory syndrome (SARS) [1, 31].

Severe Acute Respiratory Syndrome (SARS) is caused by Influenza, Coronavirus, and other etiologic agents, such as respiratory syncytial virus, Parainfluenza, and Adenovirus, which infect the upper respiratory tract [2]. The Patients have a flu-like condition, associated with dyspnea or tachypnea (respiratory rate equal to or above 20 incursions per minute), or hypoxemia, with oxygen saturation (SpO₂) <95%, on environmental [3].

COVID-19 has spread worldwide [1]. Until November 10, 2020, 55,928,327 COVID-19 cases and 1,344,003 deaths have been confirmed worldwide. In the Region of the Americas, 15,259,486 people, who were infected with the new coronavirus, recovered in the same period [4].

In Brazil, the surveillance for SARS was created in 2009, due to the Influenza pandemic. The system, initially limited to notifying those affected by Influenza viruses in the country, has improved and incorporated the monitoring of other respiratory viruses, increasing the scope of surveillance. With COVID-19 beginning and, the detection of community transmission in the country, the protocol began including the test to identify the New coronavirus, being incorporated into the surveillance network for Influenza and other respiratory viruses [5].

In Brazil, 521,090 cases of SARS, have been reported this year, 285,628 (54.8%), with positive results for some respiratory virus, 161,303 (31.0%) with negative results, and, approximately 42,369 (8.1%), awaiting laboratory results [6].

Among positive cases, 0.4% were associated with Influenza A virus, 0.2% with Influenza B, 0.4% with a respiratory syncytial virus (RSV), and, 97.7% were associated with SARS CoV-2. The total number of hospitalizations or deaths in SIVEP-Flu, regardless of symptoms, is 841,405 cases, with a current estimate of 887,196 [6].

The number of deaths caused by SARS in Brazil is in the risk zone, with high numbers of cases. It is estimated that 131,315 deaths caused by SARS, have occurred, ranging from 130,449 to 132,545 until the end of week 4 [6]. Among positive cases, 0.2% were caused by Influenza A, 0.1% were caused by Influenza B, 0.1% were caused by a respiratory syncytial virus (RSV) and, 99.3% were caused by SARS-CoV-2. According to the international definition of SARS, the total number of reported deaths, was 87,716, with an estimate of 88,053 [6].

After the above, the objective of this study was to describe patients hospitalized for SARS-COVID-19 and SARS-Influenza virus in Brazil, correlating epidemiological, demographic, and comorbid characteristics until Epidemiological Week (EW) 48 of 2020.

2 METHODOLOGY

This is a descriptive-analytical observational retrospective study based on secondary data extracted from epidemiological bulletins (EB), among weeks 01 to 48, the Ministry of Health on COVID-19 and Influenza virus, Other sources of official information were also used, such as the websites of the World Health Organization (WHO), Pan American Health Organization (PAHO) and, the Epidemiological Surveillance Guides to complement the information.

For the description of the epidemiological profile of confirmed cases the variables used for the research, such as age, sex, and risk factor, were used. On the website of the Brazilian Ministry of Health, the data are presented on a consolidated basis, with a total omission of the identity of the subjects associated

with them. For this reason, the study was conducted without the project having to be analyzed by an Ethics in Research Committee.

Statistical analysis

The Shapiro-Wilk test was performed, determining the distribution of mortality according to age and sex, then the non-parametric Odds Ratio (OR) test was applied, comparing the number of deaths by COVID-19 to the number of deaths from Influenza, considering age and sex as interfering with results. Likewise, the number of deaths in the southwest region was compared to other regions in Brazil. A) The evaluated hypotheses if age and sex are factors that interfere in mortality; B) the number of deaths from COVID-19 is higher than the number of deaths from Influenza; C) the number of deaths in the southwest of Brazil is higher than the other regions; individuals 60 years of age or older are more likely to die from COVID-19 and influenza. For the acceptability of the hypotheses, a significance limit of 5% was considered ($p\text{-value} = 0.05$). The analyzes were performed with the aid of the software BioEstat® 5.3 and STATA® 16.0.

3 RESULTS

The Ministry of Health received the first notification of a confirmed case of COVID-19 in Brazil on February 26, 2020. From February 26 to November 28, 2020, 6,314,740 cases and, 172,833 deaths from COVID-19 in Brazil were confirmed. The highest mortality rate was observed in the Midwest region (98.9 / 100 thousand inhabitants). The Southeast and Northeast Brazil regions had the highest numbers of confirmed cases (2,197,965) and deaths (78,920); confirmed cases (1,627,547) and deaths (44,411), respectively (Table 1).

Table 1 Confirmed cases, deaths, incidence / 100 thousand inhabitants, and Mortality / 100 thousand inhabitants by COVID-19 in Brazil

Location	Confirmed cases	Deaths	Incidence / 100mil hab.	Mortality /100mil hab.
Covid-19				
Brazil	6,314,740	172,833	3004.9	82.2
South	957,482	16,619	3194.2	55.4
Midwest	763,593	16,118	4685.5	98.9
Southeast	2,197,965	78,920	2487.2	89.3
Northeast	1,627,547	44,411	2851.8	778
North	768,153	16,765	4167.7	91

The number of deaths in the Southwest region showed superiority when compared to the South, it presented $OR = 2.10$ ($2.07-2.14$, $p < 0.0001$). The other regions were Midwest with $OR = 1.72$ ($1.69-1.75$, $p < 0.0001$) and North with $OR = 1.66$ ($1.64- 1.69$, $p < 0.0001$), with that, the number of deaths in

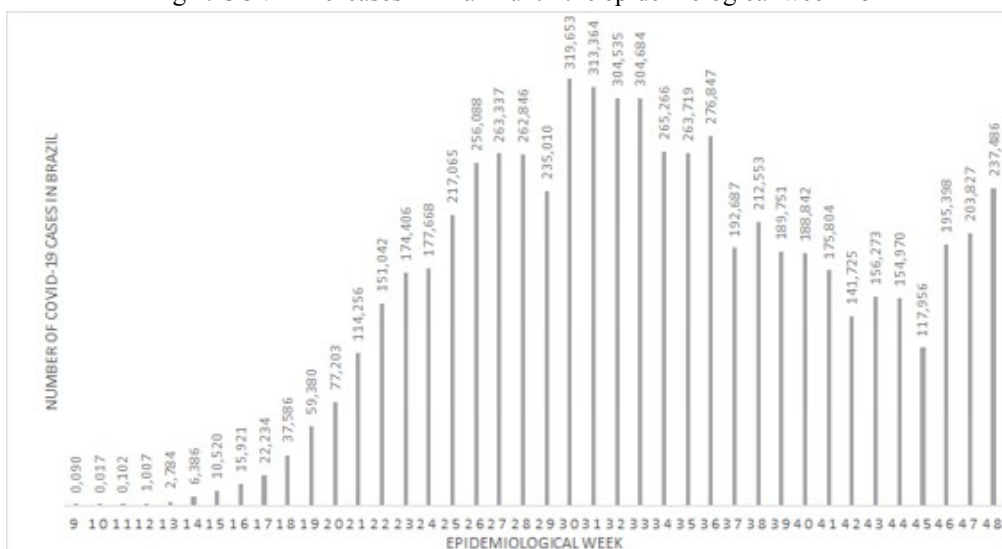
Southwestern Brazil, presented approximately twice as much when compared to the other regions (Table 2).

Table 2 Deaths by COVID-19: superiority of the southwest region over the other regions of Brazil

Region	OR (CI95%)	p-value
South	2.10 (2.07-2.14)	<0.0001
Midwest	1.72 (1.69-1.75)	<0.0001
Northeast	1.32 (1.31-1.34)	<0.0001
North	1.66 (1.64-1.69)	<0.0001

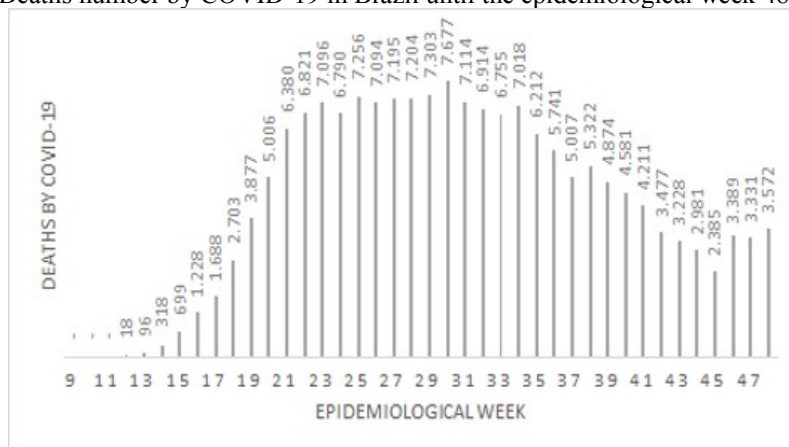
During EW 25, the number of cases was 217,065 cases, remaining above 200,000 cases until EW 36 (263,847). The peak during this period was at EW 30 (319,653 cases). After, there was a reduction to EW 45 (117,956); however, from EW 46 to EW 48, there was a further increase in the cases (Figure 1).

Fig 1. COVID-19 cases in Brazil until the epidemiological week 48



The peak of COVID-19 deaths, occurred at EW 30 (7,677). From EW 38 to EW 45 (2,385), there was a gradual reduction in the death number. From EW 46 to EW 48, there was a small increase in deaths cases from COVID-19 (Figure 2)

Fig 2. Deaths number by COVID-19 in Brazil until the epidemiological week 48



In Brazil, 219,437 cases of SARS, were hospitalized until EW 48 in 2020 and, registered in the Influenza Epidemiological Surveillance Information System. The total hospitalized SARS cases with onset of symptoms notified among the EW 01 and the EW 48, (217,713) were confirmed for COVID-19 and, 1,724 were confirmed for Influenza. The deaths total number varies according to the age group, with a prevalence of the plus 60 age group for COVID-19 and Influenza. The male gender is predominantly affected by the corona and influenza viruses (Table 3).

The mortality distributions of COVID-19 and Influenza, segregated by age group, showed significant heterogeneity, qualifying the data as non-parametric. Highlighting the target of the investigation, data on deaths from COVID-19 and Influenza pointed to p-value= 0.00. Likewise, the total sample pointed to COVID-19 p-value= 0.00 and to Influenza p-value= 0.04 (Figure 3)

Fig 3. COVID-19 and Influenza: Sample distribution with segregation of the total deaths and survivors

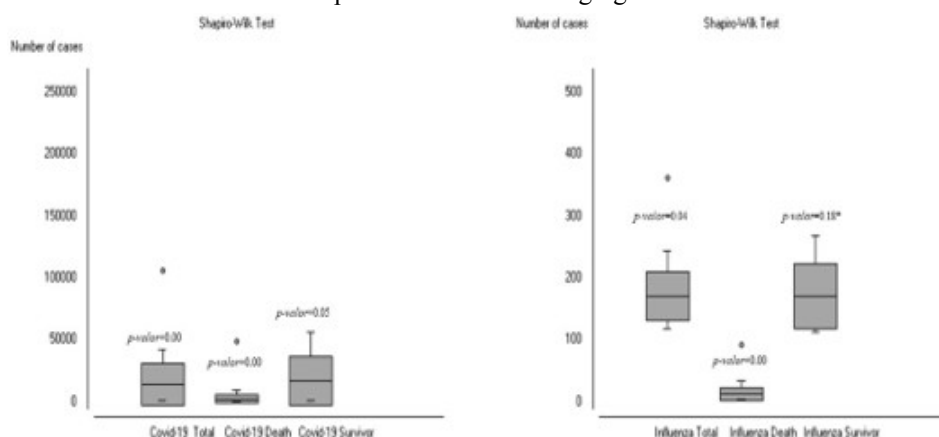


Table 3 Hospitalizations and deaths number by SARS caused by COVID-19 and Influenza virus

Variables	Hospitalizations by SARS							
	Covid-19		Influenza		Deaths COVID-19		Influenza Deaths	
	Absolute Number	%	Absolute Number	%	Absolute Number	%	Absolute Number	%
<2	1,238	0.56	244	14.15	124	0.18	5	2.62
2 to 4	547	0.25	139	8.01	19	0.02	3	1.57
5 to 9	542	0.25	157	9.11	32	0.04	4	2.2
10 to 19	1,358	0.62	119	6.9	165	0.3	7	3.66
20 to 29	7,718	3.54	174	10.1	704	1.04	15	7.85
30 to 39	23,115	10.6	206	11.9	2,486	3.68	16	8.37
40 to 49	34,972	16.1	157	9.11	5,393	7.99	16	8.37
50 to 59	42,636	19.58	167	9.9	9,657	14.3	33	17.28
60 +	105,587	48.5	361	20.9	48,905	72.46	92	48.17
Gender								
Male	129,039	59.2	872	50.6	41,168	60	98	51.3
Female	88,639	40.7	850	49.3	26,307	39	93	48.7
ignored sex	35	0.1	2	0.1	15	0.1	0	0
General Total	217,713	100	1,724	100	67,490	100	191	100

Comparisons between COVID-19 and Influenza, according to age and sex, showed similarities in the chances of death. Only ages under two years, ten to 19, and 60 years or more had higher mortality due to COVID-19, respectively OR= 5.32 (2.15- 13.15) and OR= 2.52 (1.99-3.19). The comparison considering the sex factor showed greater efficiency of COVID-19 in causing deaths, male sex with OR= 3.70 (2.99-4.56) and the female sex with OR= 3.43 (2.76-4.26). When considering all ages and sexes, COVID-19 had approximately four more times deaths than Influenza, OR= 3.60 (3.10- 4.19) (Table 4)

Table 4 Deaths by COVID-19 compared with Influenza according to age and sex

Average age	OR (CI95%)	p-value
< 2	5.32 (2.15-13.15)	<0.0001*
2 to 4	1.63 (0.47-5.59)	0.6
5 to 9	2.40 (0.83-6.89)	0.14
10 to 19	2.21 (1.01-4.83)	0.05*
20 to 29	1.06 (0.62-1.81)	0.92
30 to 39	1.43 (0.85-2.38)	0.2
40 to 49	1.60 (0.95-2.69)	0.08
50 to 59	1.18 (0.81-1.74)	0.42
60 or more	2.52 (1.99-3.19)	<0.0001*
Gender		
Male	3.70 (2.99-4.56)	<0.0001*
Female	3.43 (2.76-4.26)	<0.0001*
All ages and sex	3.60 (3.10-4.19)	<0.0001*

The number of deaths by COVID-19 and Influenza is higher in the risk group aged 60 or older, deaths by COVID-19 in this group, indicated 24 times more than the number of deaths in children aged two to four years and 14 times more than in children aged five to nine years. Influenza, considering the same risk group, presented several deaths, 16 times more, when compared to children under two years. The results point to a relationship between age and the number of deaths due to COVID-19 and Influenza, with greater aggressiveness than COVID-19 according to advancing age (Table 5).

Table 5 Odds Ratio values highlighting 60 years old or more concerning other ages

Deaths by Influenza		
Average age	OR (CI95%)	p-value
< 2	16.34 (6.53-40.88)	<0.0001
2 to 4	15.50 (4.82-49.86)	<0.0001
5 to 9	13.08 (4.71-36.29)	<0.0001
10 to 19	5.47 (2.46-12.17)	<0.0001
20 to 29	3.62 (2.03-6.47)	<0.0001
30 to 39	4.06 (2.31-7.12)	<0.0001
40 to 49	3.01 (1.70-5.32)	0.0001
50 to 59	1.38 (0.88-2.17)	0.18
Deaths by Covid-19		
Average age	OR (CI95%)	p-value
< 2	7.75 (6.43-933)	<0.0001
2 to 4	23.98 (15.17-37.90)	<0.0001
5 to 9	13.75 (9.62-19.66)	<0.0001
10 to 19	6.23 (5.29-7.34)	<0.0001
20 to 29	8.59 (7.94-9.29)	<0.0001
30 to 39	7.16 (6.85-7.47)	<0.0001
40 to 49	4.73 (4.58-4.88)	<0.0001
50 to 59	2.94 (2.87-3.02)	<0.0001

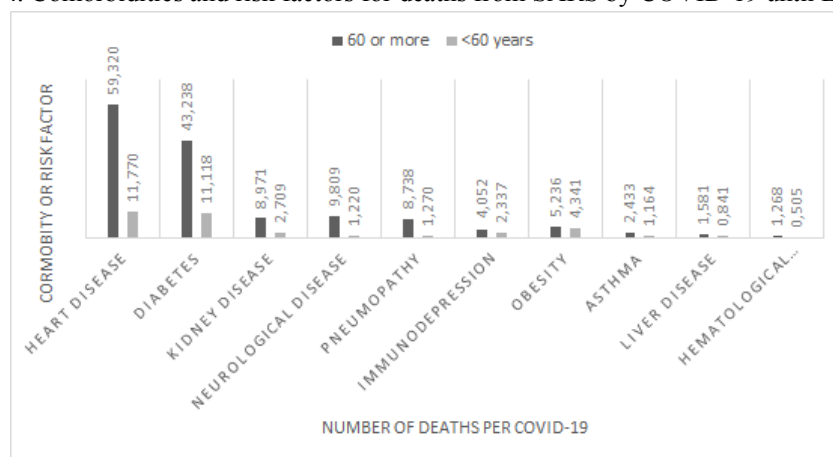
According to the data available by SIVEP, Gripe in the bulletin of EW 48, until November 28, 69,405 cases of deaths were caused by SARS. Of this total, 99.3% (68,919) were affected by the New coronavirus, 0.2% (138.8) patients were diagnosed with Influenza A, 0.1% (69.4) were found with Influenza B and, 0.1% (69.4) were caused by Respiratory Syncytial Virus (RSV) (Table 6).

Table 6 Deaths by Severe Acute Respiratory Syndrome caused by Influenza subtypes (A and B) and by COVID-19

SARS DEATHS BY RESPIRATORY VIRUSES									
YEAR	Influenza A VIRUS		Influenza B VIRUS		RESPIRATORY SYNCYTIAL VIRUSES		NEW CORONAVIRUS		TOTAL CONFIRMED
	Number Absolute	%	Number Absolute	%	Number Absolute	%	Number Absolute	%	
2020	138.8	0,2	69.4	0,1	69.4	0,1	68,919	99.3	69,405

Among the main comorbidities and risk factors associated with the risk of developing SARS by COVID-19, there are heart diseases (59,320) and diabetes (43,238). The least frequently associated risk factor was observed in hematological diseases (1,268). The number of deaths, due to SARS was predominantly observed in the age group 60 years or more, with comorbidities such as cardiopathic (11,770), diabetic (11,118), and kidney diseases (2,709). Hematological diseases had a lower frequency of deaths (505) (Figure 4).

Fig 4. Comorbidities and risk factors for deaths from SARS by COVID-19 until EW 48

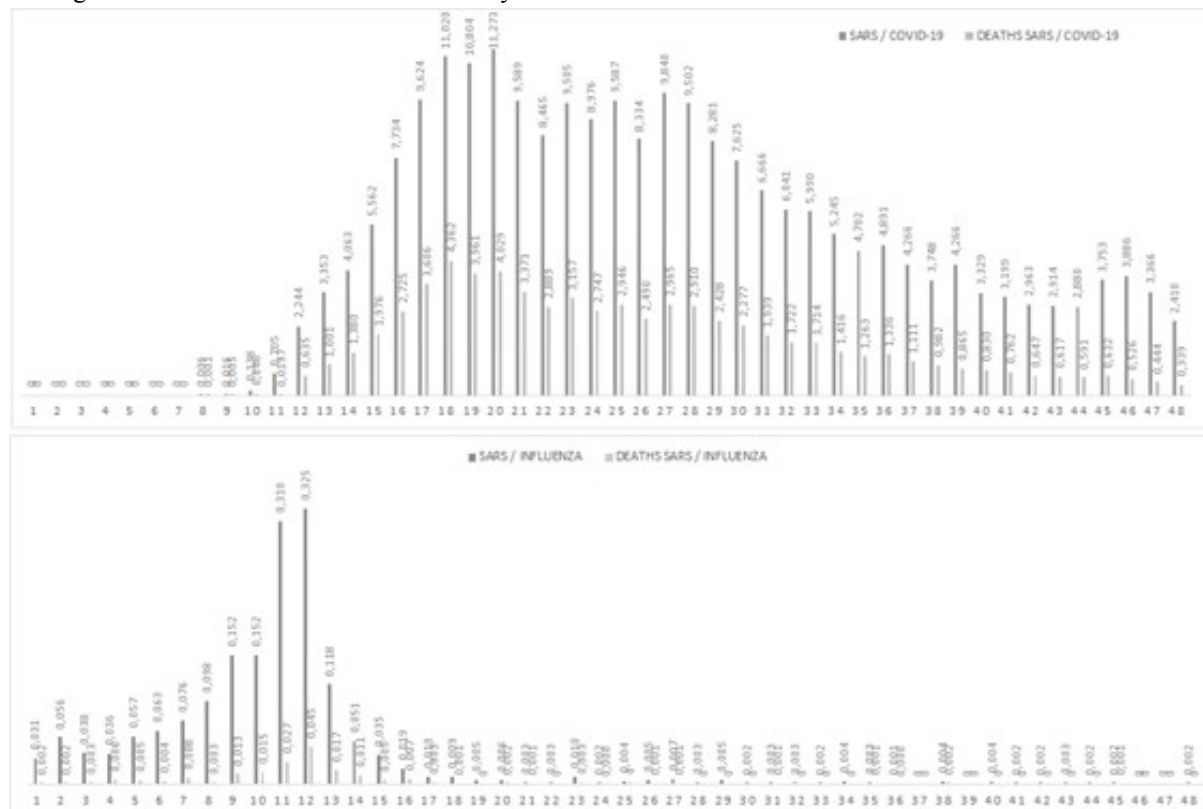


The profile of temporal evolution for SARS varied according to the etiological agent. The number of Respiratory Syndrome by COVID-19, had its prevalence between EW 12 (2,244) and EW 48 (2,410), keeping above 2,000 confirmed cases. During this period, the peak of cases occurred at EW 20 (11,273). The number of deaths over two thousand cases was observed between the EW 16 (2,725) and the EW 30 (2,277), later, until the last evaluation (EW 48), the number of deaths decreased, reaching 339 cases (Figure 5).

The number of respiratory syndrome cases caused by Influenza, occurred between EW 01 (31) and EW 15 (35), maintaining above 30 confirmed cases. Having the maximum number of confirmed cases in

EW 12 (325). The maximum number of confirmed deaths was in EW 12 (45). Among EW 17 (10) and EW 48, the number of cases of SARS, affected by Influenza, remained below ten reports and, the number of deaths in the same period remained below five reported cases (Figure 5)

Fig 5. Cases and deaths numbers caused by SARS-COVID-19 and SARS-Influenza in Brazil until EW 48



4 DISCUSSION

At the end of Epidemiological Week 48 of 2020, on November 28, 62,244,181 cases of COVID-19 in the world were confirmed. The United States ranks first on the list, with the highest number of accumulated cases, secondly, India, and Brazil occupies third place with the highest number of cases of COVID-19, then France and Russia, respectively. A total of 1,452,410 deaths by COVID-19 have been confirmed worldwide since November 28, and the United States was the country with the highest cumulative number of deaths, according to Brazil, India, Mexico, and the United Kingdom [4].

The results are shown in Table 1, the possibility to analyze the numbers of cases and deaths in Brazil and, the evolution of the pandemic across the different regions of Brazil. The incidence of cases was 3004.9 / 100 thousand inhabitants and, the mortality rate was 82.2 / 100 thousand inhabitants.

Around the world at the end of EW 48, the gross incidence coefficient was 7,985,348 cases for every 1 million inhabitants. The country with the highest incidence was Bahrain (50,920 cases / 1 million inhabitants), followed by the Czech Republic (48,431 / 1 million inhabitants), Qatar (48,065 / 1 million. inhabitants), Armenia (45,084 / 1 million inhabitants), the United States (40,013 / 1 million inhabitants) and Brazil is in 19th position with a coefficient of 29,933 / 1 million inhabitants [4].

Analyzing Table 1, the Southeast and Northeast Brazil regions, had the highest rate of cases due to COVID-19, but the Midwest and North regions, had the highest rate of deaths in Brazil. Currently, the population of Brazil has 210,147,125 people and has shown a great increase in the spread of the disease by country, since the first case was registered in February in São Paulo city.

The Southeast region of the country has a population that corresponds to 38.3% of the entire population, with the São Paulo State, being the most populous with 45,919,049 people. In the Northeastern region, about 25% of the Brazilian population lives, but the reported cases of the disease in this region, corresponding to 31.2% of the country. Even though it is the most populous region in Brazil, the incidence and lethality of COVID-19 in the Southeast, are 40% lower than in the North and, 50% less than in the Midwest [7,8].

Brazil began a period of cases number and deaths, a decline from COVID-19, which can be analyzed in Figures 1 and 2, which demonstrate this decline from EW 37 and show a decline peak in EW 45, but from then, the numbers started to increase again.

Brazilian researchers believe that this increase is due to the rather that people think that the pandemic was decreasing, due to the reduction of numbers and, began to leave their houses without any protection, people making agglomerations and, that they never had COVID-19, without wearing a mask and taking proper care. This scenario is perfect for virus proliferation [9].

Health surveillance agencies in Brazil, also recorded cases of patients with SARS during the COVID-19 pandemic, generating important information about the associated etiological and clinical patterns in the country during EW, as shown in Table 3.

Severe Acute Respiratory Syndrome causes a high rate of morbidity and mortality worldwide and, is causally linked to many different viral agents, such as Influenza A and B viruses, Parainfluenza viruses, Coronavirus spp., respiratory Syncytial viruses (RSV), Adenovirus spp. (AV) and Rhinovirus spp [10].

Data from the Centers for Disease Control and Prevention (CDC), between 2018 and 2019, show that the Influenza virus infected 35.5 million people, with 490,600 people hospitalized and, about 34,200 dying in the United States [11].

As shown in Table 6, in addition to the New coronavirus, Influenza A and B viruses were detected, as Syncytial viruses during WE 1 to 48, where the rate of the New coronavirus was much higher (99.3%). It is important to diagnose these viruses but distinguishing them (Influenza and SARS-CoV-2) is a challenge, due to the similarity in clinical signs and the way of contagion. The most common clinical symptoms for COVID-19, Influenza type A and Influenza type B demonstrated fever, cough, and coryza respectively, but it was less common among patients with COVID-19 [11].

Influenza and SARS-Cov-2 viruses cause respiratory diseases, with a wide range of people asymptomatic or with mild symptoms to severe symptoms, remembering that both viruses are transmitted by contact, contaminated droplets, surfaces, and, the basic number of reproduction R zero (R0) for COVID

- 19 (1.5–5.7), is more significant than Influenza (0.9–2.1), showing that the SARS-Cov-2 virus, can infect more people than the Influenza virus [12-16]

In the analysis made by Pormohammad et al. [11], the mortality rates were COVID – 19 (6.5%), Influenza types A (6%) and B (3%), and, the strain of the Influenza type A virus, presented among the subtypes; high mortality rates to H5N1 (42%) and, H7N9 (30%) subtype being more prevalent. They also demonstrated that the Influenza mortality rate was associated with different age groups. People aged ≥ 50 years old (12%) and, the highest rate when compared to other age groups, but the H5N1 subtype is fatal and, all age groups are at risk of death.

Estimates by region, the lethality rate, ranges from 0.6% to 7.2%, which is substantially higher than the mortality rate of 0.1%, for seasonal Influenza. However, may be overestimated cause of countries that prefer testing people with severe manifestations, who are at risk of death [17-20].

Comparing the mortality rate from other epidemics (SARS, MERS, and EBOLA), with the COVID-19 outbreak, at the end of the epidemiological week 9, the death rate from COVID-19, was much lower and overestimated (ranging from 1% to 3.4%) than SARS and MERS. However, the SARS outbreak contained 10% of the death rate, and, the MERS outbreak 34%. They also showed that the average (human-to-human) infection of COVID-19 is greater than MERS and seasonal Flu (COVID-19 1.5-3.5; MERS 0.42- 0.92; seasonal flu 1.3), with approximate intervals around infection rates like Ebola (1.5- 2.5) and SARS [3,21].

The risk of death among people infected with COVID-19 is higher according to age and comorbid diseases [17-22]. In children, the clinical manifestations of COVID-19, are milder compared to adults, but the risk has increased with a critical condition when the age is less than one year [23].

Zhou et al. [22] demonstrated that almost half of the patients (191), admitted had some comorbidities, such as hypertension (30%), diabetes (19%), and coronary disease (8%). Of this total of hospitalized patients, 54 did not survive, and, analyzing the percentage of these comorbidities, the rates are more significant (hypertension, 48%, diabetes 31% and, coronary disease 24%). The average age of all adult patients was 56.0 (46.0 - 67.0), with 38% women and 62% men and, they concluded that increasing age was associated with death in patients with COVID-19.

Data from figure 4, show comorbidities and risk factors for deaths from SARS by COVID-19, EW 48, did not present data on patients with hypertension, but present data of patients with diabetes (> 60 years - 59, 32%; <60 years - 11.77%) and coronary heart disease (> 60 years - 43.23%; <60 years - 11.18%). The numbers present a prevalence higher than the study mentioned previously. This expressive number could be due to the date that the samples were collected (December 2020), or because are people from a developing country.

For Malta et al. [24] developing countries are regions where most deaths from chronic non-communicable diseases occur. Approximately 1/3 of deaths occur in people less than 60 years old. All socioeconomic strata are vulnerable to chronic non-communicable diseases, but it affects more or generates more problems, as people who belong to socially vulnerable groups, with low education and low income.

The complications of these diseases, influence an increase in poverty for these individuals, as they become incapable, limited, and consequently reduce their productive force [24,25]. Due to non-communicable diseases, morbidity, and mortality, are public health problems in several countries and, are well rooted in Brazil, reflecting on the actual epidemiological transition scenario [25].

Advanced age, pre-existing cardiovascular disease, and, worsening pneumonia at the time of hospitalization, are some risk factors for cardiac events after pneumonia. In patients with Influenza and other viral infections, acute cardiac events and, unfavorable outcomes for coronary heart disease, are also associated [22-28].

Chan et al.,[29] described that age over 60 years and, the presence of comorbidities, are associated with a higher mortality rate and, the presence of diabetes mellitus and/or heart disease, which also had higher mortality, presenting severe adverse outcomes.

In another study that assessed risk factors in patients with COVID-19, a total of 54.1% of patients, had associated comorbidities and, the most common were hypertension, diabetes, cardiovascular disease, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease, carcinoma or chemotherapy and chronic renal failure with $p < 0.05$ [30].

The profile of temporal evolution for SARS as an association of COVID-19 and Influenza in Brazil varied according to the etiological agent (figure 5). The age distribution of critically ill patients is the main difference between SARS-CoV-2 and the influenza pandemic. There is an average variation in the lethality rate from each country, perhaps this is due to differences in the strategies for carrying out the tests.

5 CONCLUSION

The pandemic has already a high rate of serious morbidity and mortality in older adults and is much higher than in the influenza pandemic. In Brazil, the numbers have increased and there are already cases of re-infection shared by some health centers. Due to the country's economy, the population has left quarantine to be able to work and there are several entertainment events where the population has made agglomerations without social distancing, wearing a mask, and other security measures. Pending the vaccine, the government of Brazil has done its part and continues to publicize the care that the population must take, striving to slow down and limit the spread of the virus. Municipalities have been doing mass testing, and hospitals have supportive treatment currently available. We must be attentive to the strategies of Organs international health agencies, to guarantee support and the search for better guidelines in the control of events like this.

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