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Original Article

Severe acute respiratory syndrome by influenza and factors associated with death in older adults: a population study

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Abstract

Introduction: Influenza is characterized by an acute viral infection, which can lead to severe conditions and death, especially in vulnerable populations, such as older adults. Therefore, we sought to analyze cases of severe acute respiratory syndrome (SARS) due to influenza in older adults registered in Brazil and investigate the factors related to death due to this disease.

Methodology: This is a cross-sectional, population-based study that used secondary data from the Influenza Epidemiological Surveillance Information System (IESIS-Influenza). Older adults aged 60 years and above with laboratory diagnosis of influenza were included.

Results: A total of 3,547 older adults with SARS due to influenza were included, out of which 1,185 cases with death as the outcome were identified. Among older adults with death as the outcome, 87.4% were not vaccinated against influenza. The main risk factors for death were invasive ventilatory support use, intensive care unit admission, brown skin color and dyspnea ($p < 0.001$).

Conclusions: This study described the profile of older adults with SARS due to influenza in Brazil. Factors associated with death in this population were identified. Moreover, the need to encourage compliance with vaccination among older adults is evident in order to prevent severe cases and unfavorable outcomes related to influenza.

Key words: Influenza; death; risk factors; elderly; vaccine; infection.

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Introduction

Influenza is characterized by an acute viral infection of high transmissibility which attacks the respiratory tract several times throughout life and can generate mild or severe symptoms in affected individuals. Its transmission occurs through the respiratory tract, secretions such as droplets and aerosols, and contact with the mucosa. Severe cases may require hospitalization, and, in some cases, it can lead to death [1].

Older adults are more vulnerable to influenza, because, in addition to physiological changes related to age, there is the presence of comorbidities, which makes them more susceptible to mortality due to influenza and secondary infections [2]. Vaccine is the most efficient way of preventing influenza worldwide [3]. The influenza vaccine was included in the Brazilian vaccination schedule through the National Immunization Program (NIP) in 1999 and 2000. In 1999 the NIP aimed to immunize at least 70% of the adults who were ≥ 65 years of age and in 2000 they

aimed to immunize 70% adults ≥ 60 years of age. In 2008, the goal of vaccination coverage (VC) was 80%, and in 2017, 90% [4-6].

The VC goal was achieved in Brazil, and in 2018 influenza VC for older adults was on average 97%. VC was approximately 99% in 2019, and 100% in 2020 [5-8]. However, in 2021, the second year of the COVID-19 pandemic, the priority groups did not reach the VC goal. National coverage in older adults, was 70.9% and no state was able to reach the 90% goal for this group [9]. In addition, the data used to perform VC calculations may be outdated, since there are older adults who do not participate in vaccine campaigns annually [2,10,11]. Currently, the annual influenza vaccination campaign is underway in Brazil; however, compliance is low, and only 25.6% of eligible older adults have been vaccinated so far [12].

In general, influenza-associated deaths occur in individuals over 70 years old. Advancing age is considered a risk factor for developing severe acute respiratory syndrome (SARS). In 2019, until the epidemiological week 32 of 2019, Brazil registered 46% of deaths from SARS caused by influenza in individuals aged 60 years or older. Thus, SARS associated with influenza was the main risk factor for death [13]. Another study demonstrated that influenza causes 5% of deaths in older adults per year during winter in the United States, with vaccination being the most valid and competent way to prevent influenza in this population [14].

Given the above, it is concluded that the influenza has a high impact on morbidity and mortality among older adults. Therefore, the present study sought to analyze SARS cases due to influenza among older adults registered in Brazil and to investigate factors related to death due to this disease.

Methodology

Study design

This is a cross-sectional, population-based study that used secondary data from the Influenza Epidemiological Surveillance Information System (IESIS-Influenza). The INFLUD20-31-01-2022, INFLUD21-31-01-2022 and INFLUD22-31-01-2022 databases were made available by the Brazilian Ministry of Health (available at: https://opendatasus.saude.gov.br/dataset?tags=SRAG).

Selection criteria

Older adults aged ≥ 60 years, as standardized by the Brazilian Ministry of Health, with laboratory confirmation of influenza by real-time polymerase chain reaction (RT-PCR, given its high sensitivity and specificity), [15,16] and those with the case evolution (death yes or no) recorded were included in the sample.

Data collection

Data were obtained from IESIS-Influenza, a national system that records, monitors and makes available SARS-related data including respiratory pathogens such as influenza. The data used include all regions of Brazil, beginning in epidemiological week 8 (February 16 to February 22) of 2020 until epidemiological week 4 (January 23 to January 29) of 2022, and the final data collection was performed in February 2022.

To construct the database and obtain the sample that answered the study questions, the following protocol was used: full databases available on February 3, 2022 were used; records of individuals aged ≥ 60 years (536,540) with positive RT-PCR for influenza (4,816) were selected; and the cases with final evolution recorded (3,574) were filtered, since this was the outcome of interest (death yes/no). Next, the records with incomplete information were excluded, so that the proposed analysis would not be compromised. This resulted in a final sample of 3,547 cases.

The outcome investigated was death due to influenza (death/cure) in older adults. The factors associated (independent variables) with the primary outcome studied were those related to sociodemographic and clinical variables, signs and symptoms.

Ethical aspects

The data were extracted from a public secondary database which provides anonymized data in order to ensure that no participant can be identified. Therefore, all ethical precepts were complied with in accordance with Resolution 510 of the Brazilian National Health Council of April 7, 2016. This resolution outlines in the paragraph item II that research using publicly accessible information will not be registered by the Research Ethics Committee/Brazilian National Research Ethics Commission (REC/NREC), pursuant to Law 12,527 of November 18, 2011 [17]. Hence, the present study did not need to be reviewed by REC.

Data analysis

Data were analyzed by the softwares R version 4.1.1 and R Studio version 1.4.1106 (Integrated Development for R; RStudio, PBC, Boston, MA, United States), using the following packages: questionr, ResourceSelection, and pROC. Descriptive statistics

(absolute and relative frequencies) were used to present sociodemographic and clinical data. A bivariate analysis was performed using Fisher's exact test/Chi-square test, when appropriate, to identify the relationship between death due to SARS caused by influenza and the other variables studied. Logistic regression was performed with significant variables using the bivariate analysis in order to verify the association with outcome, and the Odds Ratio was estimated for each one. The significance level considered was $\alpha < 0.05$.

Results

The final sample consisted of 3,547 older adults with SARS due to influenza during the study period. Of these, 1,185 had death as outcome, recording a case fatality rate of 24.6% for this population group.

Among the older adults studied, there was a predominance of women (55.9%), completed elementary school (12.3%) and residence in urban areas (85.1%). It is noteworthy that 94% of older adults with SARS due to influenza required hospitalization, 28.3% of whom were in an Intensive Care Unit (ICU). More than 66% of individuals required ventilatory support, with invasive ventilatory support being used in 15.2% of cases (Table 1).

The most prevalent comorbidity was cardiovascular disease (46.1%), followed by diabetes (26.6%), chronic pneumopathy (11%), chronic neurological disease (6.5%), asthma (5.4%), and chronic kidney disease (4.4%). It is worth noting that 84.1% of the individuals reported not being vaccinated against influenza (Table 1).

Table 1. Description of sociodemographic and clinical characteristics of older adults with severe acute respiratory syndrome due to influenza, Brazil, 2022 (n = 3,547).

Characteristics	nº	%
Female	1983	55.9
Male	1564	44.1
Ethnicity/skin color		
White	162	4.6
Black	438	12.3
Yellow	192	5.4
Brown	174	4.9
Indigenous	75	2.1
Not informed/ignored	2506	70.7
Education		
No education/illiterate	162	4.6
First cycle of elementary school	438	12.3
Second cycle of elementary school	192	5.4
High school	174	4.9
University	75	2.1
Ignored	2506	70.7
Area of residence		
Urban	3019	85.1
Rural	175	4.9
Periurban	8	0.2
Not informed/ignored	345	9.7

Table 1 (continued). Description of sociodemographic and clinical characteristics of older adults with severe acute respiratory syndrome due to influenza, Brazil, 2022 (n = 3,547).

Characteristics	nº	%
Contact with birds, swine, other animals		
Yes	28	0.8
No	3517	99.2
Fever		
Yes	2030	57.2
No	1517	42.8
Cough		
Yes	2792	78.7
No	755	21.3
Sore throat		
Yes	592	16.7
No	2955	83.3
Dyspnea		
Yes	2509	70.7
No	1038	29.3
Abdominal pain		
Yes	103	2.9
No	3444	97.1
Fatigue		
Yes	699	19.7
No	2848	80.3
Oxygen saturation <95%		
Yes	2251	63.5
No	1296	36.5
Loss of smell		
Yes	57	1.6
No	3490	98.4
Loss of taste		
Yes	60	1.7
No	3487	98.3
Risk factors		
Yes	2745	77.4
No	802	22.6
Chronic cardiovascular disease		
Yes	1634	46.1
No	1913	53.9
Chronic hematologic disease		
Yes	30	0.8
No	3517	99.2
Chronic liver disease		
Yes	36	1
No	3511	99
Asthma		
Yes	190	5.4
No	3357	94.6
Diabetes		
Yes	942	26.6
No	2605	73.4
Chronic neurological disease		
Yes	232	6.5
No	3315	93.5
Other chronic lung disease		
Yes	389	11
No	3158	89
Immunodeficiency/immunosuppression		
Yes	84	2.4
No	3463	97.6
Chronic kidney disease		
Yes	156	4.4
No	3391	95.6
Obesity		
Yes	141	4
No	3406	96
Received flu vaccine		
Yes	563	15.9
No	2984	84.1

Table 2 summarizes the relationship between the case outcome (discharge/death) and the other variables studied, highlighting the following associations: ethnicity/skin color, education, fever, cough, sore throat, dyspnea, chronic neurological disease, received flu vaccine, used antiviral drug for flu, antiviral drug used, hospitalization, ICU admission, and ventilatory support use ($p < 0.001$). In addition to these, it is important to highlight the relationship between the case outcome and chronic kidney disease ($p = 0.025$) and loss of smell ($p = 0.046$).

Table 3 summarizes the association between the age of older adults with SARS due to influenza and the case outcome (discharge/death). It is worth noting that the group with the death outcome is older than the survivors, with the median being 3 years older, and the mean and the third quartile being two years older in the death group.

By adjusting a logistic model to estimate the risk of death, considering as covariates those significant in the bivariate analyzes (Fisher's exact, Chi square, and Mann-Whitney tests), it can be stated that brown older adults have almost 2 times higher chance of death due to influenza and those who report dyspnea are 1.5 times more likely to die. In addition, those with respiratory distress and oxygen saturation < 95% through the course of disease are 1.3 times more likely to die; having a chronic neurological disease increases the risk of death by 1.6 times; ICU admission increases the risk of death by 2.3 times; the need for invasive ventilatory support increases the risk of death by 8.8 times in older adults with SARS due to influenza; and for each 1-year increase in age, there is a 4% increase in the risk of death (Table 4).

On the other hand, those who have fever, cough, sore throat, obesity, need for hospitalization, normal chest x-ray result, atypical tomography appearance for COVID-19 and negative for pneumonia are less likely to die. We also highlight the identification of flu vaccine as a protective factor for the influenza case evolution to an unfavorable outcome (death) (Table 4).

Table 1 (continued). Description of sociodemographic and clinical characteristics of older adults with severe acute respiratory syndrome due to influenza, Brazil, 2022 (n = 3,547).

Characteristics	nº	%
Used antiviral drug for flu		
Yes	840	23.7
No	2707	76.3
Antiviral drug used		
Oseltamivir	789	22.2
Zanamivir	1	0
Other	17	0.5
Did not use/did not inform	2740	77.2
Hospitalization		
Yes	3333	94
No	214	6
ICU admission		
Yes	1005	28.3
No	2542	71.7
Ventilatory support use		
Yes, invasive	538	15.2
Yes, non-invasive	1816	51.2
No	1193	33.6
Chest x-ray		
Normal	114	3.2
Interstitial infiltrate	446	12.6
Consolidation	81	2.3
Mixed	78	2.2
Other	137	3.9
Not performed/not informed	2691	75.9
Type of sample collected		
Naso-oropharyngeal secretion	3252	91.7
Bronchoalveolar lavage	13	0.4
Post-mortem tissue	3	0.1
Other	228	6.4
Not informed	51	1.4
Type of influenza		
Influenza A	3430	96.7
Influenza B	110	3.1
Not informed	7	0.2
RT-PCR for influenza A - subtype		
Influenza A - H1N1	224	6.3
Influenza A - H3N2	1974	55.7
Influenza A - not subtyped	999	28.2
Influenza A - not subtypable	121	3.4
Inconclusive	34	1
Other	78	2.2
Not informed	117	3.3
RT-PCR for influenza B - subtype		
Victory	5	0.1
Yamagatha	3	0.1
Not performed	40	1.1
Inconclusive	3	0.1
Other	10	0.3
Not informed	3486	98.3
RT-PCR positive for another virus		
Yes	273	7.7
No	3274	92.3

ICU: Intensive Care Unit; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction.

Discussion

The study sample consisted of 3,547 older adults with SARS due to influenza in the period from 16 February 2020 (8th epidemiological week of 2020) to 29 January 2022 (4th epidemiological week of 2022), with a lethality of 24.6%, which made it possible to study and identify factors associated with death from this disease.

In the second half of 2021, cases of infection due to H3N2, an influenza A virus subtype, spread across Brazil and became an epidemic in several states, with an increase in cases and hospitalizations. One of the reasons for the spread of this infection is low VC against influenza, which reached 72.8% of the target population, when the goal was to have 90% of each priority population vaccinated. The other reason is the lack of understanding that the vaccine prevents, above all, hospitalization and death from happening [8].

Table 2. Association between outcome (discharge/death) and sociodemographic and clinical characteristics of older adults with severe acute respiratory syndrome due to influenza, Brazil, 2022 (n = 3,547).

Characteristics	Discharge n (%)	Death n (%)	*p* value
Female	1339 (56.7)	644 (54.3)	0.185#
Male	1023 (43.3)	541(45.7)	
Ethnicity/skin color			
White	1087 (46.0)	406 (34.3)	< 0.001#
Black	90 (3.8)	54 (4.6)	
Yellow	19 (0.8)	13 (1.1)	
Brown	705 (29.8)	530 (44.7)	
Indigenous	15 (0.6)	7 (0.6)	
Not informed/ignored	446 (18.9)	175 (14.8)	
Education			
No education/illiterate	92 (3.9)	70 (5.9)	< 0.001#
First cycle of elementary school	263 (11.1)	175 (14.8)	
Second cycle of elementary school	127 (5.4)	65 (5.5)	
High school	124 (5.2)	50 (4.2)	
University	60 (2.5)	15 (1.3)	
Ignored	1696 (71.8)	810 (68.4)	
Area of residence			
Urban	2042 (86.5)	977 (82.4)	0.016*
Rural	107 (4.5)	68 (5.7)	
Periurban	5 (0.2)	3 (0.3)	
Not informed/ignored	208 (8.8)	137 (11.6)	
Fever			
Yes	1419 (60.1)	611 (51.6)	< 0.001#
No	943 (39.9)	574 (48.4)	
Cough			
Yes	1964 (83.1)	828 (69.9)	< 0.001#
No	398 (16.9)	357 (30.1)	
Sore throat			
Yes	448 (19.0)	144 (12.2)	< 0.001#
No	1914 (81.0)	1041 (87.8)	
Dyspnea			
Yes	1585 (67.1)	924 (78.0)	< 0.001#
No	777 (32.9)	261 (22.0)	
Oxygen saturation <95%			
Yes	1447 (61.3)	804 (67.8)	< 0.001#
No	915 (38.7)	381 (32.2)	
Loss of smell			
Yes	45 (1.9)	12 (1.0)	0.046#
No	2317 (98.1)	1173 (99.0)	
Chronic neurological disease			
Yes	132 (5.6)	100 (8.4)	0.001#
No	2230 (94.4)	1085 (91.6)	
Chronic kidney disease			
Yes	91 (3.9)	65 (5.5)	0.025#
No	2271 (96.1)	1120 (94.5)	
Obesity			
Yes	104 (4.4)	37 (3.1)	0.066#
No	2258 (95.6)	1148 (96.9)	
Received flu vaccine			
Yes	414 (17.5)	149 (12.6)	< 0.001#
No	1948 (82.5)	1036 (87.4)	
Used antiviral drug for flu			
Yes	648 (27.4)	192 (16.2)	< 0.001#
No	1714 (72.6)	993 (83.8)	
Antiviral drug used			
Oseltamivir	612 (25.9)	177 (14.9)	< 0.001*
Zanamivir	1 (0.0)	0	
Other	13 (0.6)	4 (0.3)	
Did not use/did not inform	1736 (73.5)	1004 (84.7)	
Hospitalization			
Yes	2312 (97.9)	1021 (86.2)	< 0.001#
No	50 (2.1)	164 (13.8)	
ICU admission			
Yes	481 (20.4)	524 (44.2)	< 0.001#
No	1881 (79.6)	661 (55.8)	
Ventilatory support use			
Yes, invasive	116 (4.9)	422 (35.6)	< 0.001#
Yes, non-invasive	1400 (59.3)	416 (35.1)	
No	846 (35.8)	347 (29.3)	

Table 2 (continued). Association between outcome (discharge/death) and sociodemographic and clinical characteristics of older adults with severe acute respiratory syndrome due to influenza, Brazil, 2022 (n = 3,547).

Characteristics	Discharge n (%)	Death n (%)	*p* value
Chest x-ray			
Normal	97 (4.1)	17 (1.4)	< 0.001[#]
Interstitial infiltrate	304 (12.9)	142 (12.0)	
Consolidation	41 (1.7)	40 (3.4)	
Mixed	46 (1.9)	32 (2.7)	
Other	100 (4.2)	37 (3.1)	
Not performed/not informed	1774 (75.1)	917 (77.4)	
Type of sample collected			
Naso-oropharyngeal secretion	2197 (93.0)	1055 (89.0)	< 0.001[*]
Bronchoalveolar lavage	7 (0.3)	6 (0.5)	
Post-mortem tissue	0	3 (0.3)	
Other	124 (5.2)	104 (8.8)	
Not informed	34 (1.4)	17 (1.4)	
RT-PCR for influenza A - subtype			
Influenza A - H1N1	162 (6.9)	62 (5.2)	< 0.001[#]
Influenza A - H3N2	1265 (53.6)	709 (59.8)	
Influenza A - not subtyped	691 (29.3)	308 (26.0)	
Influenza A - not subtypable	80 (3.4)	41 (3.5)	
Inconclusive	25 (1.1)	9 (0.8)	
Other	65 (2.8)	13 (1.1)	
Not informed	74 (3.1)	43 (3.6)	
RT-PCR for influenza B - subtype			
Victory	5 (0.2)	0	0.289[*]
Yamagatha	2 (0.1)	1 (0.1)	
Not performed	28	12 (1.0)	
Inconclusive	2	1 (0.1)	
Other	4	6 (0.5)	
Not informed	2321	1165 (98.3)	
RT-PCR positive for another virus			
Yes	138 (5.8)	135 (11.4)	< 0.001[#]
No	2224 (94.2)	1050 (88.6)	
Notification year			
2020	262 (11.1)	120 (10.2)	0.352[#]
2021	657 (27.8)	312 (26.3)	
2022	1443 (61.1)	753 (63.5)	

[*]Fisher's exact test; [#]Chi-square test; ICU: Intensive Care Unit.

Table 3. Association between outcome (discharge/death) and age of older adults with severe acute respiratory syndrome due to influenza, Brazil, 2022 (n = 3,547).

Age	Discharge	Death	*p* value
Minimum	60	60	
First quartile	68	71	
Median	76	79	
Mean	76.38	78.73	< 0.001*
Third quartile	84	86	
Maximum	104	105	
Standard deviation	9,714	10,248	

[*]Mann-Whitney test.

Table 4. Logistic regression to estimate the risk of death from severe acute respiratory syndrome due to influenza in older adults, Brazil, 2022 (n = 3,547).

Characteristics	Odds Ratio	95% CI	*p* value
Intercept	0.162	0.074 - 0.353	< 0.001
Brown race	1.988	1.665 - 2.374	< 0.001
With fever	0.795	0.666 - 0.951	0.012
With cough	0.513	0.416 - 0.632	< 0.001
With a sore throat	0.761	0.595 - 0.969	0.028
With dyspnea	1.473	1.190 - 1.828	0.000
With respiratory distress	1.306	1.079 - 1.582	0.006
Oxygen saturation < 95%	1.283	1.046 - 1.574	0.017
With chronic neurological disease	1.665	1.196 - 2.310	0.002
With obesity	0.618	0.384 - 0.972	0.042
Received flu vaccine	0.720	0.563 - 0.917	0.008
Hospitalized	0.067	0.046 - 0.095	< 0.001
Admitted to ICU	2.261	1.855 - 2.753	< 0.001
Used invasive ventilatory support	8.778	6.814 - 11.377	< 0.001
Normal chest X-ray	0.407	0.218 - 0.722	0.003
Atypical tomography aspect for COVID-19	0.587	0.361-0.929	0.027
Negative tomography aspect for pneumonia	0.337	0.133-0.753	0.013
Age	1.040	1.031 - 1.049	< 0.001

ICU: Intensive Care Unit; CI: Confidence Interval.

That same year, in Brazil, the influenza vaccination campaign began in April and lasted until September, due to low compliance. Among the priority groups of the 2021 influenza vaccination campaign (children, health workers, pregnant women, postpartum women, indigenous people and older adults), 39.41 million people were vaccinated, when the target was to immunize 55.3 million. Only 67.98 million among the entire target population took the vaccine, compared to the 79.7 million needed to reach the target [12].

The trivalent influenza vaccine used in Brazil in 2021 features three types of virus strains in combination (A/Victoria/2570/2019 (H1N1) pdm09, A/Hong Kong/2671/2019 (H3N2) and B/Washington/02/2019 (B/Victoria lineage)), according to the Resolution 4.184 of October 15, 2020 of the Brazilian National Health Regulatory Agency (ANVISA) – RE [18]. During the study period, VC in 2020 exceeded 100%, and in 2021 the coverage was 70.9% [8,9]. Only 12.6% of the older adults in the study sample who had death as outcome were vaccinated. Thus, those who were not vaccinated account for a considerably larger portion of the group with an unfavorable outcome (87.4%). This fact reinforces the findings of Villaseñor *et al*., who studied a population in Mexico, and concluded that there was a lower frequency of death among vaccinated participants than among unvaccinated participants [19]. A Brazilian study carried out in the state of Santa Catarina in 2012 analyzed 3,282 reported cases of SARS, with a higher prevalence of confirmed cases among people aged 60 years and older. When analyzing the vaccination status of the cases studied, approximately 67% had not been vaccinated against influenza [20].

In a study by Lenzi *et al* [21], with a sample of 1,704 participants, 1,573 people did not receive the influenza vaccine, of which approximately 13% died. On the other hand, among the 131 people who received the vaccine, 5.3% had an unfavorable outcome. The findings of this study corroborate the results described previously, in which the mortality rate between groups (vaccinated and unvaccinated) is higher among those who are not vaccinated. This reinforces the importance of influenza vaccination campaigns, the demand for greater availability of doses, the expansion of eligible population, and above all, the importance of health education and proposition of new strategies in order to increase compliance with vaccination: a simple measure that considerably reduces morbidity, mortality, and costs to the public health system with treatment and hospitalization of severe cases.

In this study, there was a prevalence of older adults with brown skin color among those with a death outcome (44.7%), compared to those of other registered ethnicities. Lemos *et al*. [22] reported higher lethality of white individuals, although they had a higher sample proportion of brown skin color. The study by Cavalieri, Lime, and Traebert [20], which aimed to describe the epidemiological profile of influenza A in the state of Santa Catarina, did not find a statistical association between skin color and case notification.

Regarding literacy, our study shows a higher death rate among participants with complete the first cycle of elementary school (14.8%). In contrast, Lenzi *et al.* [23] concluded that individuals with no educational level were twice as likely to die due to influenza.

When analyzing the area of residence, 82.4% of older adults studied who had an unfavorable outcome lived in the urban area, which indicates that despite having easier access to health resources, including vaccination, it is necessary to elucidate the factors associated with death and non-compliance with vaccination.

The common symptoms of respiratory syndrome, such as fever, cough and dyspnea, had an incidence of 51.6%, 69.9% and 78%, respectively, among older adults with a death outcome. According to the study by Lenzi *et al*. [23], these symptoms increase the mortality rate, with dyspnea present in approximately 18% of deaths. These results support the findings of Rossetto and Luna [24] and Capitani *et al.* [25], where it was reported that these symptoms were the most identified in notified cases and their records.

Among the comorbidities analyzed, neurological disease and chronic kidney disease were related to death in older adults in the present study. In a study by Fahim *et al.* [26], lethality was higher in individuals aged 50 to 65 years and older, as 77% of patients who died due to influenza had a history of one or more chronic diseases, with a higher prevalence of diabetes (23.1%), followed by chronic obstructive pulmonary disease (5.8%), cardiovascular disease (4, 6%) and kidney and neurological disease (6.5%).

When comparing antiviral drug use, the present study showed that almost 84% of the population studied did not use this therapy, and 16.2% did, with Oseltamivir being the most frequently prescribed antiviral drug, which is the first therapeutic choice recommended by the protocols of the Brazilian Ministry of Health. Among older adults who used this therapy, a positive outcome (discharge) was more frequent (77.57%) than a negative one (22.43%). In literature, reports of the use of this antiviral drug are frequent, as shown by Cavalieri *et al*. [20], and Lenzi *et al*. [21]. The latter demonstrated an outstanding result

of low hospitalization rates when comparing treated and untreated cases with Oseltamivir.

There was a need for hospitalization in 86.2% of the sample, with the ICU being necessary in 44.2% of cases. Furthermore, ventilatory support use was frequent (more than 70%), and invasive ventilatory support was associated with death, increasing the risk of this outcome by more than 8 times. ICU admission was also associated with an increased risk of death. On the other hand, the need for hospitalization proved to be a protective factor, reducing the risk of death. This finding suggests that potentially serious cases were identified and treated, in order to reduce, in general, mortality in the group of hospitalized older adults.

The results of Rossetto and Luna [24], which describe the epidemiological profile of reported cases of pandemic influenza in 2009 and 2010 in Brazil, showed that there was 92.5% of hospitalization among the 2170 cases that died. In the study by Lenzi *et al.* [21], there was a higher percentage of deaths among hospitalized and unvaccinated patients. A study carried out in Spain showed mortality of approximately 79% of patients admitted to the ICU, and of these, 21% were 65 years old and older [27]. Araújo and his collaborators [28] analyzed SARS notifications in the state of Goiás, Brazil, and in 34.6% of the cases there were ICU hospitalizations due to respiratory syndrome and 19% of the patients died.

In the present study, the highest prevalence of death was among cases affected by the Influenza A - H3N2 virus (59.8%). A study by Shi *et al.* [29] showed peaks of Influenza A - H3N2 for four years in a row in northern China; however, at the peak of the flu in 2015-2016, this subtype circulated together with influenza A-H1N1, already in southern China, and the predominant virus was the A-H3N2 subtype. On the other hand, in the studies by Araújo *et al.* carried out in the state of Goiás [28], and in a study by Drăgănescu *et al.* carried out in Romania [30], the predominant etiology was the A-H1N1 virus. In mainland China, the influenza B virus (mainly the B-Victoria subtype) was identified as circulating in all years between 2005-2016, but with lower activity than influenza A [31].

Capitani *et al*. studied hospitalized patients in the Tuscany region of Italy and found a higher prevalence of the A-H3N2 influenza virus, thus supporting the findings of our study [25].

Lenzi and authors reported an increased risk of death due to influenza with age [23]. In their study, for each additional year of life, the risk of death increased by 5.5%. In the present study, there was a 4% increase in the risk of death for each year of age.

This study is extremely relevant for those in the area of epidemiology and public health, since it highlights the increase in influenza cases due to low population compliance with vaccination. It also demonstrates the importance of planning actions to promote and prevent diseases in the face of a pandemic, including the importance of adopting contingency plans and joint actions so that VC is achieved even in the presence of a health emergency.

This study has limitations since it deals with secondary data analysis, and data quality may be compromised, especially due to the heterogeneity and lack of standard in data registration in the IESIS-Influenza. It is important to highlight that there was a change in the SARS notification form for hospitalized patients during the period studied. The new data form included mandatory identification card and COVID-19 vaccine information. In addition, the notifier professionals experienced difficulty during 'peak' access times, especially during business hours, when it took a long time to load the registered information and consequently there was a greater risk of bias in the quality of the records

Conclusions

The results of this study summarized the profile of older adults with SARS due to influenza in Brazil and identified factors associated with death in the studied sample. Invasive ventilatory support use, ICU admission, brown skin color, pre-existing chronic neurological disease, dyspnea, respiratory distress, oxygen saturation < 95% and age stand out as risk factors. The influenza vaccine proved to be efficient in preventing death in 72% of the cases studied, thus it was essential for protecting this vulnerable population. Furthermore, these findings reinforce the importance of encouraging compliance with vaccination among older adults, in order to prevent severe cases and unfavorable outcomes related to influenza.

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