

# Etiology, sociodemographic profile, and outcomes of patients with asthma hospitalized for severe acute respiratory illness (SARI) in Brazil from 2020 to 2022: an analysis of 83,452 hospitalizations

*Perfil etiológico, sociodemográfico e desfechos dos pacientes com asma internados por síndrome respiratória aguda grave (SRAG) no Brasil de 2020 a 2022: uma análise de 83.452 internações*

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## ABSTRACT

**Introduction:** Asthma is one of the most common chronic diseases affecting the Brazilian population. We aimed to determine the etiology, sociodemographic profile, and risk factors for death in patients with asthma hospitalized for severe acute respiratory illness (SARI) in Brazil from 2020 to 2022. **Methods:** We included all patients over 5 years of age registered in the Influenza Epidemiological Surveillance Information System (SIVEP Gripe) database of the Brazilian Ministry of Health from January 1, 2020 to July 21, 2022 hospitalized for SARI. Patients had to have a history of asthma and known outcomes. As exposures, age, sex, region of residence, ethnicity, and viral etiological agent were evaluated. The outcomes measured were admission to an intensive care unit, need for mechanical ventilation, and death. We used multilevel generalized linear mixed models to calculate the odds ratio between exposure and outcomes. **Results:** A total of 83,452 hospitalizations were included, of which 14,062 were children and adolescents and 69,390 were adults. Mortality increased with age, ranging from 0.6% in those aged 5-10 years to 33% in those over 60 years. In the pediatric population, living in the north and northeast regions (OR 2.14, 95%CI 1.41-3.24) and having between 10-20 years (OR 3.73, 95%CI 2.65-5.26) were associated with higher mortality. As for etiologic agents, only SARS-CoV-2 was associated with a higher risk of death (OR 5.18,

## RESUMO

**Introdução:** A asma é uma das doenças crônicas mais frequentes na população brasileira. O objetivo deste estudo foi determinar as etiologias, o perfil sociodemográfico e os fatores de risco para óbito entre pacientes com asma internados por síndrome respiratória aguda grave (SRAG) no Brasil entre 2020 e 2022. **Métodos:** A partir do banco de dados SIVEP-Gripe, incluímos todos os pacientes com idade maior que 5 anos registrados no banco de 01/01/2020 até 21/07/2022, hospitalizados por SRAG, com antecedente de asma e com desfechos conhecidos. Como exposições, foram estudadas a idade, sexo, região de moradia, etnia e agentes etiológicos virais isolados. Os desfechos foram internação em unidade de terapia intensiva, necessidade de ventilação mecânica e óbito. Para calcular a razão de chances entre exposição e desfechos, utilizamos modelos lineares generalizados mistos multinível. **Resultados:** Foram incluídas na análise 83.452 internações, sendo 14.062 crianças e adolescentes, e 69.390 adultos. A mortalidade aumentou com a idade, indo de 0,6% entre 5-10 anos para 33% nos maiores que 60 anos. Na população pediátrica, morar na região Norte e Nordeste e ter entre 10-20 anos foram associados a maior mortalidade (OR 2,14 IC95% 1,41-3,24 e OR 3,73 IC95% 2,65-5,26 respectivamente). Quanto aos agentes etiológicos, apenas o SARS-CoV-2 conferiu maior risco de óbito (OR 5,18 IC95% 3,62-7,42). Entre adultos, sexo feminino

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95%CI 3.62-7.42). Among adults, female sex (OR 0.87, 95%CI 0.83-0.9) and non-White ethnicities (OR 0.90, 95%CI 0.85-0.94) were protective factors against death. Older age groups, living in the north and northeast regions, and a diagnosis of COVID-19 were associated with higher mortality. **Conclusions:** There are important sociodemographic vulnerabilities in the outcomes of patients with asthma hospitalized for SARI, with higher mortality rates in the north and northeast regions, among adolescents in the pediatric age group, and among older adults. Furthermore, COVID-19 was one of the main infections associated with higher mortality.

**Keywords:** Asthma, COVID-19, severe acute respiratory syndrome, epidemiology.

e etnias não brancas foram protetoras (OR 0,87 IC95% 0,83-0,9 e OR 0,90; IC95% 0,85-0,94 respectivamente) para óbito. Faixas etárias mais avançadas, morar nas regiões Norte e Nordeste e o diagnóstico de COVID-19 foram associados a maior mortalidade.

**Conclusões:** Há importantes vulnerabilidades sociodemográficas nos desfechos das internações de pacientes com asma por SRAG, com maior mortalidade nas regiões Norte-Nordeste, entre adolescentes na faixa etária pediátrica e entre idosos nos adultos. Além disso, destaca-se o protagonismo da COVID-19 entre as infecções associadas a maior mortalidade.

**Descritores:** Asma, COVID-19, síndrome respiratória aguda grave, epidemiologia.

## Introduction

Asthma is one of the most common chronic diseases affecting the population in Brazil, with estimated prevalence rates between 9% and 13% in children and adolescents (C&A) and 4.4% in adults.<sup>1,2</sup> Although mortality has fallen dramatically since inhaled corticosteroids use has been introduced and widespread,<sup>3</sup> the number of deaths due to the disease has stabilized over the last decade in the country. In addition to the loss of lives, it highly burdens the health system and has an impact on society, both in the form of direct treatment costs and healthy years lost to the disease.<sup>4,5</sup>

From 2020, the epidemiological health scenario in Brazil and worldwide has been dominated by the emergence of COVID-19 and its aftermath. Since its onset, with the adoption of social distancing and barrier measures to the transmission of SARS-CoV-2, the pandemic has had a profound impact on the transmission dynamics of respiratory viruses, changing the seasonality and profile of the most common respiratory viral infections.<sup>6,7</sup> This global reality culminated in an outbreak of respiratory cases following the relaxation of isolation measures, especially in the pediatric age group.<sup>8,9</sup> Although chronic diseases increase the risk of poorer outcomes in COVID-19, recent studies show that controlled asthma alone does not increase the risk of hospitalization or death from the disease, and may even be a protective factor.<sup>10,11</sup> However, among asthma patients hospitalized for respiratory symptoms, the impact of viral infections on their outcomes is still unclear, especially considering the dynamic change in the epidemiology of viral transmission experienced in recent years.

During the 2009 influenza epidemic, the Brazilian Ministry of Health (MH) began to record all hospitalizations for severe acute respiratory syndrome (SARS), which became mandatory notification, making up the Sistema de Vigilância Epidemiológica da Gripe (SIVEP-Gripe, Influenza Epidemiological Surveillance Information System). With the emergence of COVID-19, the disease also became part of the SARS database, representing a valuable source for epidemiological studies on the evolution of hospitalizations for the syndrome, its etiology, and outcomes. This study aimed to analyze this domestic database to determine the etiologies, outcomes, and risk factors for death among patients with asthma hospitalized for SARI in Brazil from 2020 to July 2022.

## Methods

This study used data from the MH-SIVEP-Gripe database, which records cases of hospitalization for SARS in the country, a compulsory notification condition. The database records multiple pieces of information about each patient, including sociodemographic data, clinical presentation, comorbidities, etiological research, outcomes, among others. The MH defines SARS for notification purposes as patients with flu-like syndrome who show signs of severity, such as dyspnea/respiratory discomfort or persistent pressure or pain in the chest, or oxygen saturation below 95% on room air or cyanosis of the lips/face.<sup>12</sup>

This study included all hospitalized patients older than 5 years, registered in the database from 01/01/2020 to 07/21/2022, with a history of asthma (reported by the patient or family member), and known

outcomes. As exposures, we studied age (divided into age groups and then into C&A and adults), sex, region of residence, ethnicity, and the viral etiological isolated agents. We considered patients to be adults if they were older than 20 years, according to the World Health Organisation.<sup>13</sup> So as to maximize contrasts, the regions of the country were grouped into Northern (North and Northeast) and Southern (Midwest, Southeast and South) macro-regions, a common strategy in population studies.<sup>14</sup> Similarly, ethnic groups were divided into white and nonwhite (black, mixed race, indigenous people, and yellow). The most common viral agents reported were SARS-CoV-2, influenza, rhinovirus, and respiratory syncytial virus (RSV). We also used the variable “sample collection” to describe the percentage of patients who underwent etiological research, although the form does not describe for which agent the samples were collected. We described intensive care unit (ICU) admission, need for mechanical ventilation, and death as outcomes, although only death was studied in the multivariate analyzes.

Categorical variables were presented as frequencies and percentages. Chi-square was used in the initial tables to analyze the significance of differences between categorical variables. Multilevel mixed generalized linear models (GLM) were built to calculate the odds ratio (OR) and confidence intervals (95% CI) between exposure and outcome, considering the health care facility where the patient was cared for as a random effect. The multivariate analysis was adjusted for other variables with significant differences for the outcome studied, in different models for C&A and adults. It is important to emphasize that the multivariate analysis compared the effects of having a positive result for a given agent with the absence of a positive result for that agent, regardless of whether the test had been performed or not. Considering the discrepancies between age groups, the results for C&A and adults were reported separately.

The only significant loss of data among the sociodemographic variables studied was ethnicity: 17.3% of hospitalizations had no record of the patients' ethnicities. In order to preserve the reliability of the data, we decided not to perform multiple imputation techniques, so patients with missing ethnical data were excluded from the analyzes involving this variable, and ethnicity was not included as an adjustment variable in the multivariate models.

The chance of an alpha error occurring was set at 5%. The data was processed and analyzed using

STATA (Data Analysis and Statistical Software) version 17.

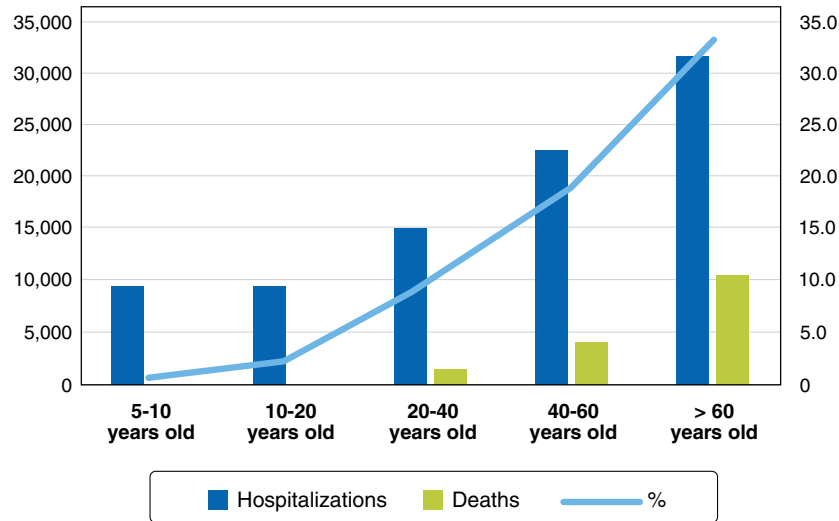
As this study used anonymized data taken from a repository available in the public domain, no approval from an ethics committee was required.

## Results

The analysis included 83,452 hospitalizations, of which 14,062 were C&A and 69,390 were adults. Most hospitalizations occurred in 2021 (47.6% in 2021, 42.4% in 2020, and 10% in 2022). As for the number of hospitalizations, a U-shaped curve can be seen, with a drop in the number among adolescents compared to children, followed by a gradual increase in the following age groups. Mortality showed a tendency to increase with increasing age: 0.6% between 5-10 years old, 2.3% between 10-20, 10% between 20-40, 18.9% between 40-60, and 33% in people over 60 (Figure 1).

Table 1 shows the sociodemographic characteristics, etiological agents, and outcomes in the pediatric age group, both in the general population studied and only deaths. The majority of children included were male, nonwhite, and from the South, Southeast, and Midwest regions. Among the sociodemographic characteristics, only to live in the North-Northeast region was associated with higher mortality ( $p < 0.001$ ). In addition, two-thirds of hospitalizations were among children, while most deaths were among adolescents, also a significant difference. Although more than 95% of the patients underwent an etiological investigation, less than 15% had a viral etiological isolated agent. SARS-CoV-2, the etiological agent of COVID-19, was the most frequent virus in this cohort (53.4% of isolated agents), especially among deaths (83%). Around a fifth of patients required ICU admission, and approximately 5% were intubated. Mortality among C&A was 1.2%.

Table 2 describes the sociodemographic characteristics, etiological agents, and outcomes among adults, including deaths. Contrasting with the pediatric age group, among adults admissions predominated among women and white patients, and the highest number of admissions was in the Southern macro-region. Men and living in the North and Northeast were associated with higher mortality ( $p < 0.001$ ). Most hospitalizations were among patients older than 60, as were most deaths. The majority of adults underwent viral testing, and more than half had



**Figure 1**  
 Number of hospitalizations, deaths, and death rate per age group among asthma patients hospitalized for severe acute respiratory syndrome (SARS) in Brazil between 2020-2022  
 Source: SIVEP-Gripe.

The X axis on the left represents the number of hospitalizations and deaths (bars); on the right, the death rate and each age group (line).

**Table 1**  
 Sociodemographic characteristics, etiological agents, and outcomes of children and adolescents with asthma hospitalized for severe acute respiratory syndrome (SARS) in Brazil between 2020 and 2022

Characteristics	Categories	General (N = 14,062) N (%)	Deaths (N = 163) N (%)	p
Region	North/Northeast	2,728 (19.4)	53 (32.5)	< 0.001
Sex	Male	7,664 (54.5)	78 (47.8)	0.086
Ethnicity	Nonwhite	6,402 (57)	83 (60.6)	0.395
Age	5-10	9,346 (66.5)	54 (33.1)	< 0.001
	10-20	4,716 (33.5)	109 (66.9)	
Sample collection	Collected	13,408 (95.3)	151 (92.6)	0.385
Etiological agent	Isolated	2,088 (14.8)	67 (41)	< 0.001
	SARS-CoV-2	1,115 (7.9)	56 (34.4)	
Rhinovirus	Positive	513 (3.6)	4 (2.4)	0.413
Influenza	Positive	264 (1.9)	5 (3.1)	0.260
RSV	Positive	158 (1.1)	1 (0.6)	0.534
ICU	Yes	2,946 (22.7)	101 (65.6)	< 0.001
Invasive ventilation	Yes	679 (5.3)	97 (65.5)	< 0.001

p value: results from Chi-square test.  
 RSV: respiratory syncytial virus, ICU: intensive care unit.

a viral agent isolated, and SARS-CoV-2 was the agent in most cases, both in the general population studied and among deaths (96.5% and 98.4% of viral agents isolated, respectively). Of the patients, one third were admitted to ICU and 18% required intubation. Mortality among adults was 23.5%.

Figures 2 and 3 show the results of the multivariate analyzes among C&A and adults, death as the outcome, and the different sociodemographic and etiological variables as the exposure. Adolescents have a risk of death almost 4-fold higher than children (OR 3.73; 95% CI 2.65-5.26), and residents in the North and Northeast regions die more than twice as often as patients living in other regions (OR 2.14; 95% CI 1.41-3.24). C&A with isolated SARS-CoV-2 also have a higher risk of death when compared to patients without this diagnosis (OR 5.18; 95% CI 3.62-7.42); this relationship is maintained in C&A in an analysis stratified by age group. Neither sex, ethnicity, nor a diagnosis of influenza, RSV, or rhinovirus were

related to death. However, among adults, women were protective, 13% less likely to die than men (OR 0.87; 95% CI 0.83-0.9), as were nonwhite ethnic groups (OR 0.90; 95% CI 0.85-0.94). Similar to pediatrics, older age groups and living in the North and Northeast regions were also risk factors. A diagnosis of COVID-19 increased mortality risk almost 3-fold (OR 3.01; 95% CI 2.66-3.41), an association that was maintained when broken down into age groups. Conversely, isolation from influenza, RSV, or rhinovirus was a protective factor.

## Discussion

This is the most comprehensive nationwide study to date on the epidemiology, etiology, and risk factors for death in asthma patients hospitalized for SARI. Using a population-based database, we included a large number of patients to show how these hospitalizations are distributed across the country and the impact of

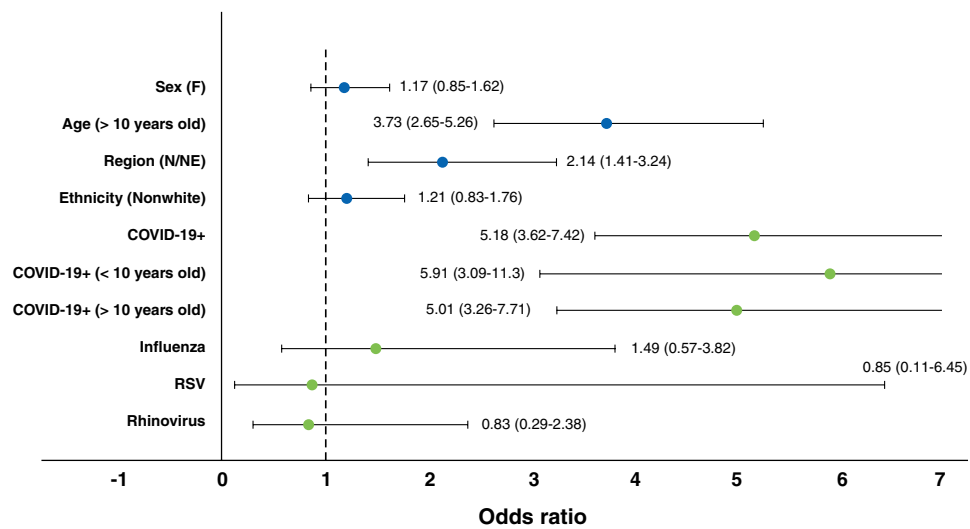
**Table 2**

Sociodemographic characteristics, etiological agents, and outcomes in adults ( $\geq 20$  years old) with asthma hospitalized for severe acute respiratory syndrome (SARS) in Brazil between 2020 and 2022

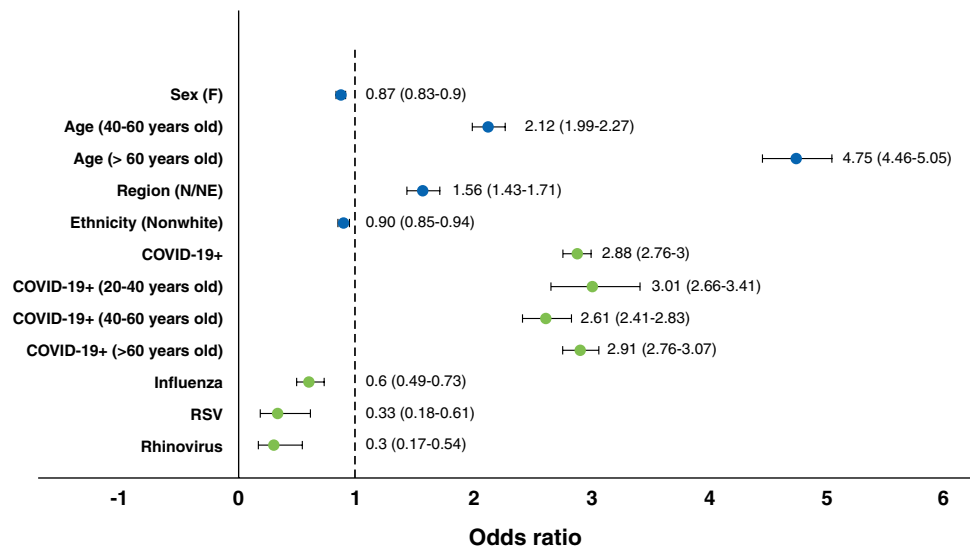
Characteristics	Categories	General	Deaths	p
		(N = 69,390) N (%)	(N = 16,284) N (%)	
Region	North/Northeast	10,949 (15.8)	3,121 (19.2)	< 0.001
Sex	Male	26,369 (38)	6,427 (39.5)	< 0.001
Ethnicity	Nonwhite	25,228 (43.7)	6,095 (43.6)	0.771
Age	20-40	15,050 (21.7)	1,511 (9.3)	< 0.001
	40-60	22,532 (32.5)	4,265 (26.2)	
	> 60	31,765 (45.8)	10,500 (64.5)	
Sample collection	Collected	65,942 (95)	15,513 (95.3)	0.028
Etiological agent	Isolated	34,856 (50.2)	10,645 (65.4)	< 0.001
SARS-CoV-2	Positive	33,640 (48.5)	10,478 (64.3)	< 0.001
Rhinovirus	Positive	192 (0.3)	14 (0.1)	< 0.001
Influenza	Positive	908 (1.3)	139 (0.8)	< 0.001
RSV	Positive	118 (0.2)	12 (0.1)	0.001
ICU	Yes	21,910 (33.4)	9,993 (65.6)	< 0.001
Invasive ventilation	Yes	11,439 (18.2)	7,810 (52.5)	< 0.001

p value: results from Chi-square test.

RSV: respiratory syncytial virus, ICU: intensive care unit.



**Figure 2**  
 Demographic and etiological factors related to mortality among children and adolescents with asthma hospitalized for severe acute respiratory syndrome (SARS) in Brazil between 2020-2022  
 Result of generalized linear mixed models, assuming hospital of admission as a random effect. Demographic factors adjusted relative to each other (except ethnicity). Ethnicity adjusted for sex and age group. Viral etiological factors adjusted for region and age group. Results expressed as odds ratios and 95% confidence intervals in brackets. Bars represent the confidence interval. RSV: respiratory syncytial virus.



**Figure 3**  
 Demographic and etiological factors related to mortality among adults with asthma hospitalized for severe acute respiratory syndrome (SARS) in Brazil between 2020-2022  
 Result of generalized linear mixed models, assuming hospital of admission as a random effect. Demographic factors adjusted relative to each other (except ethnicity). Viral etiological factors and ethnicity adjusted for sex, region, and age group. Results expressed as odds ratios and 95% confidence intervals in brackets. Bars represent the confidence interval. RSV: respiratory syncytial virus.



the region of residence, sex, and age group on the outcome of death. We also assessed SARS etiology based on viral isolation of the main respiratory viruses, demonstrating the prominence of COVID-19 in the period studied and the impact of SARS-CoV-2 on patient mortality. Considering that asthma has different predominant phenotypes in different age groups, our results were reported separately between C&A and adults, and are of interest to both pediatricians and clinicians. Our results point to a complex picture and shed light on the interaction between a history of asthma and acute infectious conditions, in the context of the dynamic epidemiological evolution that has characterized the COVID-19 pandemic.

It is important to bear in mind that although this study focused on patients with asthma, the criteria for hospitalization and inclusion in the database were not based on disease exacerbation, but on the presence of SARS criteria. While the entities often overlap, with the infectious condition triggering the asthma exacerbation, it is impossible to say that all patients had poorer respiratory functional parameters and/or bronchospasm. Thus, the infectious condition and the etiological agent play a key role in the evolution and outcome of the patient. It is known that patients with asthma generally have poorer outcomes in respiratory infections,<sup>15,16</sup> yet this trend was curiously not demonstrated in COVID-19.<sup>10,11,17</sup> Our sample showed a predominance of SARS-CoV-2 isolates, showing that this was the dominant infection during the study. Thus, patient outcomes are closely linked to COVID-19 outcomes in these groups.

The analyzes showed increasing mortality as age increased in asthma patients hospitalized for SARI, in both age groups. The difference in mortality between C&A and adults is striking, with a 55-fold increase when comparing the age endpoints. This behavior is to be expected, since it has been shown that older patients die more from asthma, as epidemiological studies conducted in the country using the SUS mortality registration systems have shown.<sup>18,19</sup> It has also been shown that advancing age is a risk factor for mortality from COVID-19, the predominant infection in the study population, both among C&A and adults.<sup>17,20</sup> It is therefore no surprise that age was also a risk factor for death in the study population.

Brazil is a continental country with enormous variability in access to health care and profound socioeconomic inequalities. Our data show higher mortality among patients living in the North and Northeast regions, in both age groups, and adjusted

for sex and age group. This inequality probably reflects the difficulty of access and the poorer health conditions that residents of the North and Northeast face. Social determinants of health are closely related to asthma prevalence and outcomes. A large American population study, including more than 1,500,000 C&A with asthma, showed a significant association between living in poorer regions and both emergency room visits and hospitalizations for asthma (OR 1.06 95% CI 1.01-1.12 and OR 1.1 95% CI 1.03-1.17 respectively, in adjusted models).<sup>21</sup> Similarly, socioeconomic factors are also related to poorer COVID-19 outcomes, as 2 Brazilian studies have shown. The first study included 5,857 C&A with COVID-19 and showed that living in more developed towns reduced the chance of mortality with the disease by nearly 75%.<sup>17</sup> The second study focused on the adult population, including 228,196 patients hospitalized for the disease, and showed that living in the North and Northeast regions of the country increased the chance of death more than 2-fold (OR 2.76 and 2.05 respectively).<sup>22</sup>

The association between asthma and viral infection is complex and appears in different instances throughout life. In the first few years, the vast majority of wheezing episodes occur in the context of a viral infection, especially RSV and rhinovirus.<sup>23</sup> The latter has already been recognized as an important risk factor for developing asthma.<sup>24</sup> Viral infections are among the most frequent triggers of attacks in patients already diagnosed with asthma, with rhinovirus predominating as the etiological agent.<sup>24,25</sup> Despite high rates of etiological research, our study showed a low rate of positive results, especially in children. This result may be associated with the fact that the majority of etiological investigations in the period probably corresponded to SARS-CoV-2, a less important agent in the pediatric age group when compared to adults, a population that showed a much higher rate of positive results.

The main limitations of this study are due to the fact that it used a secondary database, so important biases should be considered. Firstly, the diagnosis of asthma was reported by patients or family members, with the scrutiny of the practitioner who filled in the notification form, and no standardized approach of proof. This self-reporting approach is common in large epidemiological studies, and it has been shown that reliance on medical diagnosis can underestimate the prevalence of asthma in the population.<sup>1</sup> In addition, it is impossible to guarantee that all cases of SARI have been reported, and there may have been a

selection for more severe cases, thus leading to a bias in the proportion of negative outcomes in the study population.

In the multivariate analyzes, the effects of the etiological agents compared patients with the positive agent with those without the positive agent, not including whether they had been tested or not. This conservative approach may have underestimated the size of the effects, since not all untested patients were actually negative. A selection bias may also exist for testing agents, with more severe patients more likely to be tested. In addition, the availability of tests also differs between agents: while there is greater availability of tests for COVID-19, testing for RSV and rhinovirus depends on more advanced and not so easily available tests, which has an impact on the rates of detection reported. Therefore, the proportions of etiological diagnosis should be interpreted in light of these limitations.

Ethnicity was not recorded for more than 17% of the hospitalizations included, and this loss of data was proportionally greater in the North than in the South (21.5% vs. 16.5%,  $p < 0.001$ ). As patients with no ethnic data were excluded from analyzes of the effect of ethnicity on mortality, a higher proportion of patients from the Northern macro-region were excluded. Considering that living in the Northern macro-region represented a risk factor for mortality in both age groups, the protective effect of ethnicity among adults may have been overestimated and the result of a bias.

This nationwide analysis of asthma hospitalizations highlighted demographic vulnerabilities, with higher mortality in the North-Northeast regions, among adolescents in the C&A age group, and among older adults in the adult age group. In addition, COVID-19 is the leading cause of infections associated with mortality. Population measures should therefore be targeted at the groups most at risk to protect the population with asthma.

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