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Hospitalizations and deaths of children and adolescents with Severe Acute Respiratory Infection due to COVID-19 during the epidemiological year of 2020

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ABSTRACT

This study aimed to analyze the profile of hospitalizations and factors associated with the deaths of children and adolescents with severe acute respiratory infection (SARI) caused by SARS-CoV-2 nationwide. The study comprised 6,843 children and adolescents hospitalized in 2020 who tested positive for COVID-19, based on data from the Influenza Epidemiological Surveillance Information System. Sociodemographic and clinical profiles, hospitalization frequency, lethality and recovery rates were analyzed. The outcome was recovery or death. The 6,843 children and adolescents comprised 1.9% of SARI hospitalized cases (n = 563,051). Of these, 57.7% developed critical SARI and 90% survived. Comorbidities were present in 40.8%, especially asthma, immunodepression, and neurological and cardiovascular diseases. The main symptoms were fever, cough, dyspnea, respiratory distress, and low oxygen saturation. Among those with critical SARI, 91.4% died. There was a higher frequency of children, especially those under five years of age and of mixed ethnicity. The highest hospitalization frequency occurred in the Southeastern and Northeastern regions, the highest recovery rates in the Southeastern and Southern regions, and the highest lethality rates in the Northern and Northeastern regions. Deaths were associated with ages ranging from 12 to 19 and being under one year of age, living in the Northern and Northeastern regions, progression to critical SARI, and having immunosuppression and cardiovascular disease. In contrast, asthma was associated with lower death rates. The frequency of complications and mortality rates caused by SARS-Cov-2 in the pediatric population are relevant, as well as the severity of the epidemic in the social inequality context and the health services' frailty.

KEYWORDS: COVID-19. SARS-CoV-2. Severe acute respiratory syndrome. Hospitalization. Children. Adolescents. Pediatric.

INTRODUCTION

Infection by the novel coronavirus occurs in all age groups, however, it is known that adults and the elderly present higher morbidity when infected and, thus, more case reports when compared to children and adolescents. According to the Centers for Disease Control and Prevention (CDC), the pediatric population is believed to represent approximately 2 to 13% of all confirmed cases[1,2].

Worldwide, it has been noted that the vast majority of children present with mild clinical symptoms whereas moderate and severe symptoms are more common among adults. The reason for this is not yet completely clear. Some hypotheses for the lower infection rate of children by SARS-CoV-2 stem from the fact that

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their humoral and cellular immune systems are still developing, the immaturity of the angiotensin-converting enzyme 2 (ACE2) receptors in the respiratory epithelium of children, and the greater integrity of the endothelium and coagulation system. However, a small fraction of the pediatric population infected with the novel coronavirus requires hospitalization for developing the severe form of the disease and presenting with severe acute respiratory infection (SARI) as the presence of comorbidities increases the risk of complications[1-6].

Brazil is a large country with great socio-economic variety. It has been suggested that COVID-19 has a disproportionate effect on the most vulnerable, considering the frailty of health services, social inequalities, and increased risks of contagion and spread of respiratory infections in crowded environments, all these factors impacting the morbidity and mortality from the disease[7-10].

This study aims to increase the knowledge about the novel coronavirus in the pediatric population. It is known that SARS-CoV-2 presents high transmissibility, morbidity, and mortality rates worldwide. However, the knowledge regarding its effects on children and adolescents is still limited, which highlights the need for further studies. In this sense, this article aims to analyze the profiles of hospitalizations and factors associated with the deaths of children and adolescents diagnosed with SARI caused by COVID-19 in Brazil.

MATERIALS AND METHODS

A cross-sectional study with hospitalized children and adolescents who tested positive for COVID-19 on molecular biology testing (reverse transcriptase followed by quantitative polymerase chain reaction – RT-qPCR) with detectable results for SARS-CoV-2 was carried out, with the outcome being either death or recovery.

Secondary, non-nominal, nationwide data from the public domain Influenza Epidemiological Surveillance Information System (SIVEP-Gripe), available on the Ministry of Health website[11] and accessed on April 26, 2021, were used to include cases reported in 2020, between epidemiological weeks 01 to 53.

All child and adolescent patients classified as having SARI caused by COVID-19, with detectable RT-qPCR results and case closure criteria defined as laboratory-based, were included. Patients diagnosed by clinical, clinical-epidemiological or clinical-imaging criteria, patients without RT-PCR results or with inconclusive results, and patients with omitted data were excluded[1,2].

Individuals aged from zero to 11 years were considered to be children, while adolescents were considered to be those aged from 12 to 19 years. Children and adolescents with COVID-19 who presented at least one of the signs and symptoms, such as dyspnea, respiratory distress, low oxygen saturation (< 95%) under room air condition, and cyanosis, were classified as SARI cases. Those with SARI who required admission to the intensive care unit (ICU) or needed invasive or non-invasive ventilatory support were classified as critical SARI. COVID-19 infection was assumed when patients tested positive on the RT-qPCR test for SARS-CoV-2 infection[1,2].

The variables of interest were as follows: epidemiological week of first symptom onset; evolution (death and recovery); Brazilian region of residence and hospitalization; gender (male, female, and undetermined); age in years; self-reported ethnicity (Caucasian, African, Asian, Mixed, and Native); signs and symptoms; comorbidity; admission to ICU; and ventilatory support (invasive and non-invasive). For the analysis of factors associated with death, secondary variables were created and added based on the main ones, namely: age in years/age group and critical SARI.

For the descriptive analysis, measures of absolute and relative frequency, central tendency, and dispersion were calculated. The intra-hospital lethality rate was calculated as the total number of inpatient deaths was divided by the total number of hospitalized cases, multiplied by 100. The recovery rate was calculated as the total number of hospital discharges was divided by the total number of hospitalized cases, multiplied by 100. For the bivariate analysis, the Pearson's Chi-squared test was applied, while the crude Odds Ratio (OR) with a Confidence Interval (CI) of 95% and $p < 0.05$ was used as a measure of association, and the nonparametric Mann-Whitney's test was used for the comparison between medians.

Multivariate statistical analysis was performed using binary logistic regression, using the backward stepwise method (Wald), considering the number of independent variables obtained by the bivariate analysis ($p < 0.10$). The association measure used was the Adjusted Odds Ratio (AOR). Nagelkerke's R^2 and Hosmer–Lemeshow's tests were used to adjust the model. A hierarchical model was built in three blocks: the first block included sociodemographic data; the second block included disease severity and the presence of morbidity; and the third block included variables related to the identified morbidities. A p-value of < 0.05 was considered significant.

The SPSS (version 23.0, IBM, NY, USA), QGIS (version 3.20, Open-Source Geospatial Foundation, Delaware, USA), and Microsoft Excel (version 2016, Microsoft Corporation, Washington, USA) were the software used for data processing and analysis.

RESULTS

During the epidemiological weeks from 1 to 53 of the year 2020, a total of 563,051 SARI-hospitalized cases due to COVID-19 were reported, of which 10,850 cases included children and adolescents (1.9%). A total of 4,007 cases were excluded, consisting of the following: 709 cases that had been confirmed only by clinical, clinical-epidemiological, or clinical imaging criteria; 3,205 cases with undetectable, inconclusive, or no RT-qPCR result at the time of hospitalization; and 93 cases with missing data. Applying this study's inclusion and exclusion criteria, the records of 6,843 children and adolescents were analyzed, whose death and recovery rates were 10% (685), and 90% (6,158), respectively.

Regarding the age group, a higher frequency of children (5,123; 74.9%) was observed, with a median age of three years (Q1: 0.8; Q3: 12.0). The age groups were distributed as follows: under one year, 29.9% (2,046); aged from one to four years, 24.1% (1,649); aged from five to 11 years, 20.8% (1,423); aged from 12 to 14 years, 8.0% (547), and aged from 15 to 19 years, 17.1% (1,170).

A higher frequency of females (3,635; 53.1%) and of self-declared Mixed ethnicity (2,809; 53.1%) was observed. With regards to locality, most individuals lived in urban areas (5,755; 93.7%), 45.8% (3,135) of the hospitalizations occurred in the Southeastern region, 26.7% (1,827) in the Northeastern region, 11% (753) in the Southern region, 8.8% (602) in the Northern region, and 7.7% (526) in the Central-western region.

Most were classified as critical SARI (3,483; 57.7%) and progressed towards the recovery of their state of health (6,158; 90.0%). Comorbidities were present in 40.8% of patients (n = 2,793) and, in descending order, the most frequent were asthma, chronic neurological disease, immunodepression, and chronic cardiovascular disease.

Regarding the magnitude of SARI caused by COVID-19 among children and adolescents in different regions of Brazil (Figure 1), the Southeastern and Northeastern regions, however, presented the highest hospitalization

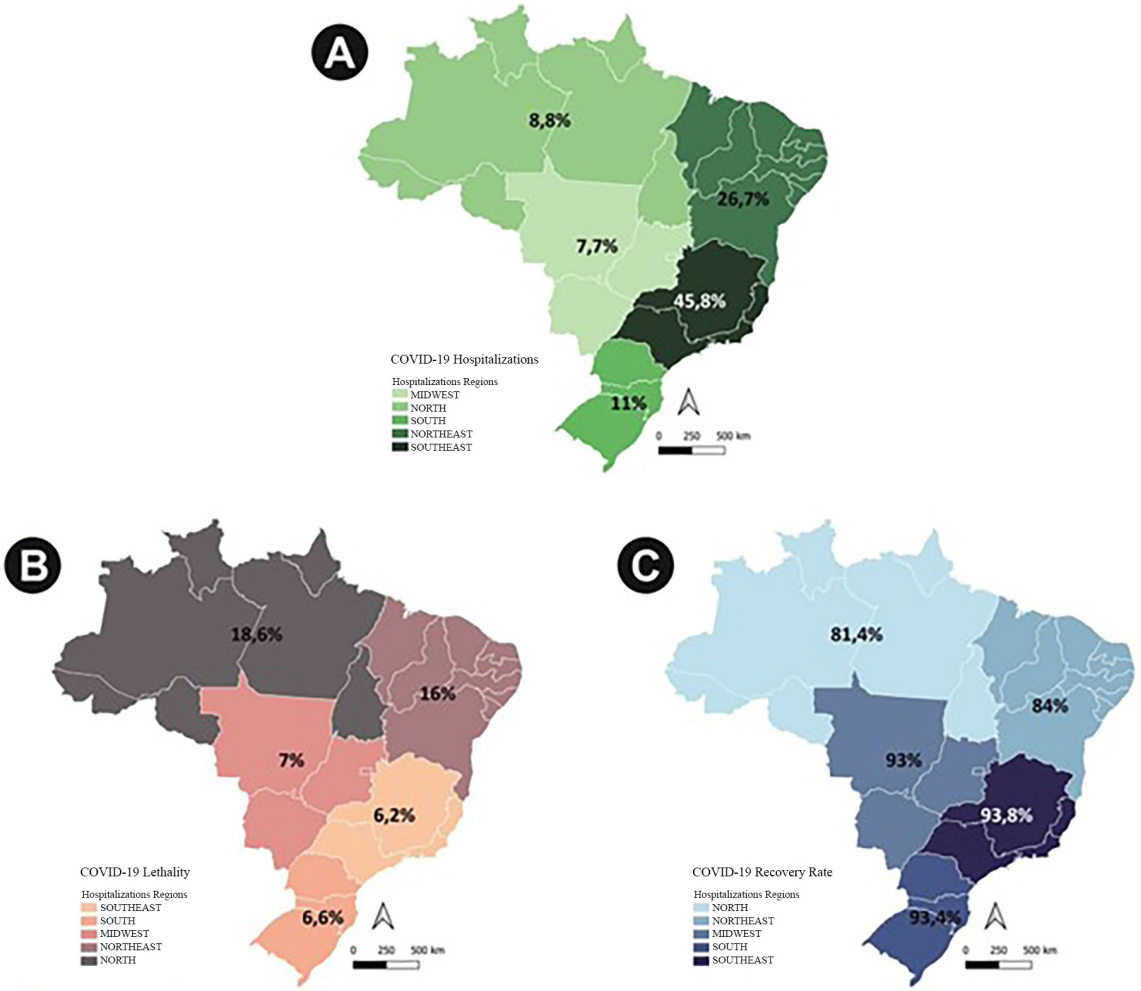

Figure 1 - Prevalence of hospitalizations, lethality and recovery rates of children and adolescents diagnosed with SARI caused by COVID-19, according to Brazilian regions. SIVEP-Gripe, 2020, Brazil (n = 6,843). Source: Brasil. Ministério da Saúde. DATASUS[11].

frequency (45.8% and 26.7%, respectively). Lethality rates were higher in the Northern and Northeastern regions (18.6% and 16%). In contrast, the recovery rates were predominant in the Southeastern (93.8%) and Southern (93.4%) regions.

The main signs and symptoms observed among the hospitalized children and adolescents, in decreasing order of frequency, were the following: fever (4,548; 73.9%), cough (3,953; 66.3%), dyspnea (3,401; 58.9%), respiratory distress (3,236; 56.9%), and low oxygen saturation (2,412; 43.9%). As presented in Figure 2, according to the outcomes of either recovery or death, the symptoms were as follows: a) among those who recovered from COVID-19, fever (74.0%), cough (67.1%), dyspnea (56.6%), and respiratory distress (54.3%); b) among those who died, respiratory distress (79.7%), dyspnea (78.6%), low oxygen saturation (73.9%), and fever (73.7%). It is noteworthy that the development of critical SARI occurred in 91.4% of the patients who died. Other symptoms such as anosmia, ageusia, fatigue, abdominal pain, and odynophagia were less frequent.

Based on the data in Table 1, of the patients who died compared to those who recovered, the distribution of deaths showed a higher concentration among the age groups under one year of age (35.5%) and adolescents aged 15 to 19 years (23.4%), among individuals of Mixed ethnicity (53.3%), rural residents (10.8%), and inhabitants of the Northeastern and Northern regions (42.6% and 16.4%, respectively). The median length of hospitalization was longer among the patients who died (7 days). Moreover, of the patients who died, a higher proportion of them presented critical SARI (91.4%) and comorbidities (64.8%), especially chronic neurological disease (12.7%), immunodepression (12.7%), chronic cardiovascular disease (10.8%), chronic kidney disease (4.5%), and chronic liver disease (1.8%). It should be noted that asthma was found in a higher proportion among the recovered patients (8.6%).

Table 2 presents the analysis results of the factors associated with death among the studied population: children under one year of age (OR = 1.806; p = 0.028); adolescents aged 12 to 14 years (OR = 2.039; p = 0.029) and adolescents aged 15 to 19 years (OR = 2.360; p = 0.001); residents of the Northern (OR = 3.100; p < 0.001) and Northeastern (OR = 2.523; p < 0.001) regions; cases classified as critical SARI (OR = 9.668; p < 0.001); and also the presence of immunosuppression (OR = 2.747; p < 0.001) and chronic cardiovascular disease (OR = 1.726; p = 0.028). However, asthma was considered a protective factor, and the death ratio was lower among the children and adolescents who had this comorbidity (OR = 0.318; p < 0.001).

It should be noted that, despite not being confirmed in the multivariate analysis, the mixed and native ethnicities had a higher chance of death in the bivariate analysis (OR = 1.689; p < 0.001 and OR = 6.204; p < 0.001, respectively).

DISCUSSION

This study aimed to analyze the profile of hospitalizations and the factors associated with the deaths of children and adolescents with SARI caused by SARS-CoV-2, nationwide, during a 12-month period.

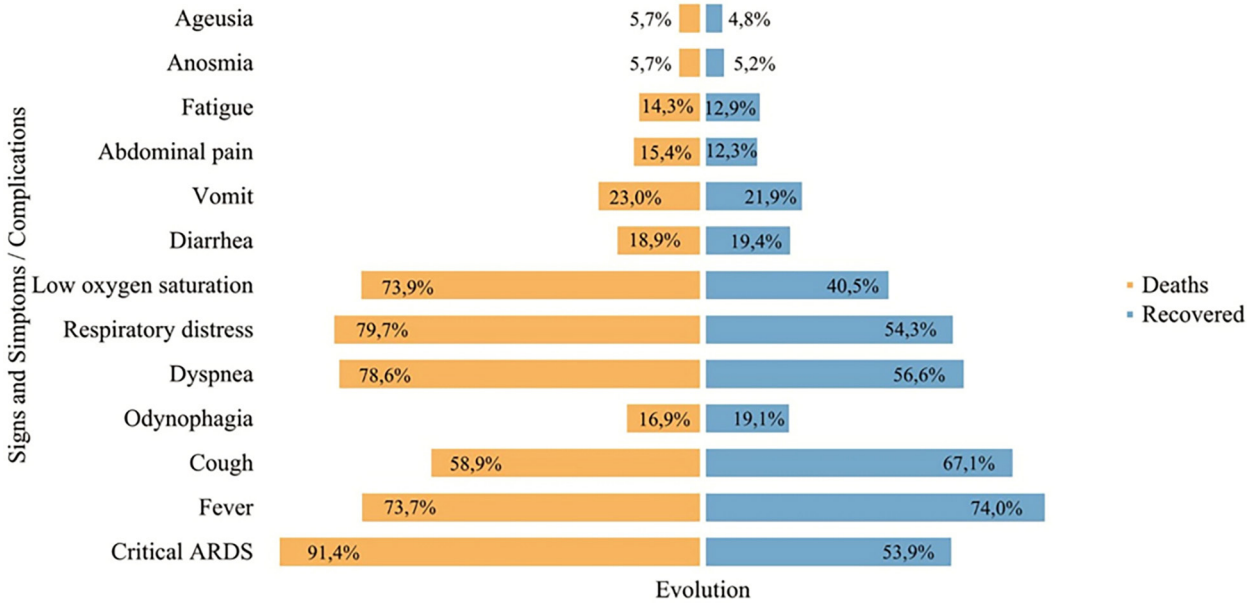

Figure 2 - Signs, symptoms, and complications according to the outcome of either death or recovery, among children and adolescents hospitalized with SARI caused by COVID-19. SIVEP-Gripe, 2020, Brazil (n = 6,843). Source: Brasil. Ministério da Saúde. DATASUS[11].

Table 1 - Development of hospitalized cases due to COVID-19 according to the children and adolescents' profiles. SIVEP-Gripe, 2020, Brazil (n = 6,843).

Profile	Deaths (n = 685)		Recoveries (n = 6,158)		p-value
	n or med	% or Q_1–Q_3	n or med	% or Q_1–Q_3	
Age (years)					< 0.001
< 1	243	35.5	1,805	29.3	
1–4	103	15.0	1,549	25.2	
5–11	105	15.3	1,318	21.4	
12–14	74	10.8	476	7.7	
15–19	160	23.4	1,010	16.4	
Gender					0.719
Female	325	47.4	2,881	46.8	
Male	359	52.4	3,276	53.2	
Self-declared ethnicity					<0.001
Caucasian	176	25.7	1,991	32.3	
African	20	2.9	213	3.5	
Asian	3	0.4	31	0.5	
Mixed	365	53.3	2,444	39.7	
Native	17	2.5	31	0.5	
Geographical residence area					<0.001
Urban	526	76.8	5,229	84.9	
Rural	74	10.8	265	4.3	
Peri-urban	3	0.4	45	0.7	
Country macro-region					<0.001
North	112	16.4	490	8.0	
Northeast	292	42.6	1,532	24.9	
South	50	7.3	705	11.4	
Southeast	194	28.3	2,941	47.8	
Central-west	37	5.4	490	8.0	
Critical SARS	560	91.4	2,923	53.9	< 0.001
Length of hospitalization (days)	7	2–20	5	3–11	< 0.001
Comorbidity	444	64.8	2,349	38.1	< 0.001
Asthma	23	3.4	527	8.6	< 0.001
Chronic neurological disease	87	12.7	316	5.1	< 0.001
Immunodepression	87	12.7	281	4.6	< 0.001
Chronic cardiovascular disease	74	10.8	212	3.4	< 0.001
Chronic hematological disease	29	4.2	141	2.3	0.539
Chronic lung disease	26	3.8	137	2.2	0.772
Diabetes Mellitus	23	3.4	128	2.1	0.975
Chronic kidney disease	31	4.5	83	1.3	< 0.001
Obesity	17	2.5	80	1.3	0.530
Down Syndrome	18	2.6	71	1.2	0.170
Chronic liver disease	12	1.8	28	0.5	0.009

SARI = severe acute respiratory infection; ICU = intensive care unit; SIVEP-Gripe = Influenza Epidemiological Surveillance Information System; n = absolute frequency; % = relative frequency; med = median; Q1 = 1st quartile (25%); Q3 = 3rd quartile (75%); SpO2 < 95% = Oxygen saturation lower than 95%; p-value from Pearson's Chi-squared test; the values refer to the total valid answers; missing data were disregarded.

Table 2 - Univariate and multivariate analysis of factors associated with the risk of progression towards death by COVID-19 in children and adolescents hospitalized with SARI caused by COVID-19, 2020, Brazil.

Variable	Crude OR			Adjusted OR		
	OR	CI 95%	p-value	AOR	CI 95%	p-value
Age (years)						
< 1	2.025	1.592–2.574	< 0.001	1.806	1.064–3.064	0.028
1–4	1.000	-	-	1.000	-	-
5–11	1.198	0.904–1.588	0.208	1.093	0.613–1.951	0.762
12–14	2.338	1.705–3.206	< 0.001	2.039	1.075–3.868	0.029
15–19	2.382	1.837–3.090	< 0.001	2.360	1.390–4.006	0.001
Self-declared ethnicity						
Caucasian	1.000	-	-	1.000	-	-
African	1.062	0.655–1.723	0.807	-	-	-
Asian	1.095	0.331–3.617	0.882	-	-	-
Mixed	1.689	1.398–2.042	< 0.001	-	-	-
Native	6.204	3.366–11.432	< 0.001	-	-	-
Geographical residence area						
Urban	1.509	0.467–4.872	0.492	-	-	-
Rural	4.189	1.266–13.862	0.019	-	-	-
Peri-urban	1.000	-	-	1.000	-	-
Country macro-region						
North	3.465	2.695–4.456	< 0.001	3.100	1.779–5.399	< 0.001
Northeast	2.889	2.385–3.500	< 0.001	2.523	1.666–3.821	< 0.001
South	1.075	0.780–1.483	0.659	1.435	0.857–2.401	0.169
Southeast	1.000	-	-	1.000	-	-
Central-west	1.145	0.795–1.648	0.467	0.926	0.458–1.869	0.829
Critical SARI	9.055	6.798–12.061	< 0.001	9.668	5.461–17.117	< 0.001
Comorbidity	2.987	2.533–3.523	< 0.001	-	-	-
Asthma	0.198	0.127–0.307	< 0.001	0.31	0.174–0.582	< 0.001
Chronic neurological disease	1.669	1.263–2.207	< 0.001	1.477	0.978–2.231	0.064
Immunodepression	1.979	1.492–2.625	< 0.001	2.74	1.763–4.280	< 0.001
Chronic cardiovascular disease	2.102	1.557–2.838	< 0.001	1.726	1.061–2.809	0.028
Chronic kidney disease	2.135	1.383–3.296	0.001	-	-	-
Chronic liver disease	2.426	1.218–4.833	0.012	-	-	-

SARI = severe acute respiratory infection; OR = Odds Ratio; CI = confidence interval; AOR = Adjusted Odds Ratio; Nagelkerke's R^2: 0.253; Hosmer–Lemeshow's test (adjustment quality): p = 0.934; Variables included in the multivariate logistic regression: 1st Block = age, ethnicity, geographical area, country macro-region; 2nd Block = critical SARI, morbidity; 3rd Block = asthma, chronic neurological disease, immunodepression, chronic cardiovascular disease, chronic kidney disease, chronic liver disease; Significant p < 0.05. Source: Brasil. Ministério da Saúde. DATASUS[11].

In 2020, children and adolescents comprised 1.9% of SARI-hospitalized cases due to COVID-19 in Brazil. It is noteworthy that, among the hospitalized children and adolescents, although 57.7% of them developed critical SARI, 90% survived. Moreover, in the present study, 40.8% had comorbidities, especially asthma, chronic neurological disease, immunodepression, and chronic cardiovascular disease.

The present study's findings are corroborated by other studies demonstrating that children and adolescents represent 2 to 13% of all confirmed COVID-19 cases and that most of them present less severe forms, although a significant number of hospitalized patients require intensive care, but with improved prognosis and lower occurrence of deaths when compared to the adult population[1,4,12-14]. An association exists between the severity of the disease and

the presence of comorbidities, such as immunodepression, cardiovascular diseases, and neuropathies, along with clinical manifestations, such as fever, dyspnea, and respiratory distress[1,10,15].

Recent evidence is available in the literature that the cellular ACE2 receptor and TMPRSS2 protease, required for SARS-CoV-2 entry into cells and tissue distribution, may differ between the pediatric and adult populations, and that in the former, ACE2 receptors are distinct in their configuration, concentration, or ability to bind to the virus. In addition, other viruses present in children's airway mucosa may limit SARS-CoV-2 replication by direct competition[12,13,16,17].

The main symptomatology found in hospitalized children and adolescents included fever, cough, dyspnea, respiratory distress, and low oxygen saturation. Other studies also report fever and cough as the most frequent symptoms, with the presence of some associated gastrointestinal symptoms[12,15,18]. When analyzing the patients who died, the main signs and symptoms found were respiratory distress, dyspnea, and low oxygen saturation. It should be noted that 91.4% of those who progressed to critical SARI died. Among the hospitalized patients, a significant number required ICU treatment, and there was an association between the severity of the disease and the presence of clinical manifestations such as fever, dyspnea, and respiratory distress[1,14,15]. The association of critical SARI with mortality or death risk should be highlighted and is explained by the need for ventilatory support or intensive care. Children and adolescents with more severe respiratory system impairment, septic shock, or organ dysfunction, with a consequent need for invasive or non-invasive ventilatory support and ICU admission, develop more severity and mortality[19].

When analyzing the hospitalization frequency, a higher occurrence was observed in the children's age group, especially those under five years of age and among those of self-reported Mixed ethnicity. Respiratory diseases are among the leading causes of hospitalizations for Brazilian children in the first five years of life, and Mixed ethnicity is frequent in the Brazilian population, especially those with low income. Thus, it is possible to suggest a disproportionate effect of COVID-19 among the most vulnerable, when considering social inequalities and the increased risks of contagion and spread of respiratory infections[7-10].

In this study, adolescents and children under one year of age presented a higher death rate when compared to the other age groups. Thus, despite the higher hospitalization frequency in children under five years of age, adolescents presented higher death rates, followed by children under one year of age. It is possible that the presence of comorbidities among adolescents hospitalized with COVID-19 is associated with greater severity and mortality from the disease. There is evidence that the occurrence of chronic diseases such as obesity, congenital heart disease, immunosuppressive diseases, and diabetes mellitus among adolescents may explain these findings[20-23]. In addition, the incidence of complications such as congenital heart disease and those related to prematurity may progress to death in children under one year of age[20]. A recent systematic review also associates a propensity for greater severity and mortality among children under one year of age and adolescents[24].

Although this study showed an association between death and ethnicity among the mixed and native groups in the bivariate analysis, this association was not confirmed after adjustment in the multivariate analysis. Missing data may have led to a study bias, as there seems to be an intertwining between race, social inequality and health care disparity, with a greater risk of unfavorable outcomes among patients from the poorest regions of the country and certain ethnic groups[25].

In our study, the comorbidities that remained associated with a higher death rate were immunodepression and chronic cardiovascular disease. The data found are supported by a recent systematic review, which associates propensity to greater severity or mortality among children under one year of age and adolescents, among those with cardiac or neurological conditions, with two or more comorbidities, and those with obesity[24]. Another study also converges in this sense and reports age and pre-existing comorbidities as the main risk factors[26]. In contrast, a study conducted in a tertiary care hospital in India found no associations between the presence of comorbidities in pediatric patients hospitalized with COVID-19 and disease severity, length of hospitalization, need for ventilation, or mortality. However, the authors report the small sample size and the retrospective design as limitations[18].

In this study, asthma was considered a protective factor, that is, death rates were lower among children and adolescents with this comorbidity. A case-control study identified asthma as a risk factor for hospitalization in children with COVID-19, but not as a risk factor for worse disease outcomes[27]. In this light, the literature provides mechanisms that justify asthma not being a risk factor for severity or mortality in patients with COVID-19. Some of the hypotheses would be that patients with asthma are under adequate disease control at the time of infection with SARS-CoV-2, that the presence of asthma upon hospitalization leads to differential care during hospital treatment, or that they were under corticosteroid treatment before becoming infected with SARS-CoV-2[1,5].

Furthermore, the reduced levels of ACE2 in the nasal and bronchial cells of atopic patients may explain the peculiarities in the immune response of atopic patients when exposed to SARS-CoV-2 infection[4,6].

In this study, regarding the Brazilian regions, the highest hospitalization frequency occurred in the Southeastern and Northeastern regions, the highest recovery rates occurred in the Southeastern and Southern regions, and the highest lethality rates occurred in the Northern and Northeastern regions. Furthermore, an association effect between living in the Northern and Northeastern regions and a higher death rate was shown. Regarding hospitalizations due to SARI in different Brazilian regions, a recent study assessed the participation of health units of different administrative spheres and showed the important role of the Brazilian public health system in the Northern and Northeastern regions, which is of paramount importance, especially for those living in economically disadvantaged situations[28]. Brazil is a continental-sized country with social inequalities, and the differences in rates of infection and mortality from COVID-19 emerge as a result of concurrent non-communicable diseases, social vulnerability, and the frailty of health services. The economically disadvantaged population is prone to sharing a household with more people and having comorbidities, which represent risk factors for the greater severity of COVID-19[10,29,30]. However, it is worth noting that even so, cases of SARS-CoV-2 infection are subject to underreporting[30]. A Brazilian study demonstrates the challenge of regionalized organization of health services during pandemics, especially when great distances are involved for patients, as observed in the Northern, Northeastern, and Central-western regions[31].

According to the 2016 Brazilian ICU Census, issued by the Brazilian Intensive Care Medicine Association, there are, on average, 2.84 pediatric ICU beds for every 10,000 pediatric residents in Brazil[32]. When analyzing the distribution of pediatric ICU beds by Brazilian region, the distribution is as follows: North 1.1; Northeast 1.60; Central-west 2.80; Southeast 4.07; South 3.22. It is also noteworthy that the number of pediatric ICU beds in the Southeastern region (2,296 beds; 52%) is already equivalent to the sum of the other Brazilian macro-regions. In addition, it is worth questioning the impact that access to health care in the Northern and Northeastern regions had on the higher lethality rates, especially in the inland cities, since 70% of the pediatric intensive care unit beds are located in the state capitals. It would also be interesting to consider, in addition to health care inequalities, the socioeconomic aspects and social vulnerability in these regions, since these can also impact the mortality rates[10,30,32].

Strengths and weaknesses of this study

Using a rich dataset covering children and adolescents nationwide, comprising 6,843 RT-qPCR-confirmed COVID-19 hospitalizations over a 12-month period, or 53 epidemiological weeks, this study has provided a profile of sociodemographic and clinical characteristics and the factors associated with mortality from the disease.

Some limitations in this study should also be acknowledged. Firstly, there are low data about epidemiological information on pre-existing comorbidities, as this information is not mandatory. On this basis, estimates from these variables should be interpreted with caution due to the potential underreporting bias. Secondly, these data do not enable analyzing the effects of intra-hospital quality of care from the perspective of physical infrastructure or human resources. And finally, the data only assessed the hospitalized population, not allowing inferences on the cases of COVID-19 that had no record of hospital admission.

Implications for clinical practice and health policies

Since the pandemic outbreak, concerns have been raised by health authorities regarding the collapse of health care systems and the shortage of clinical hospital and ICU beds for patients with moderate and severe forms of COVID-19. This study's findings suggest that, nationally, regional differences in the survival rates of hospitalized pediatric patients may be explained by geographic access to hospital and ICU beds.

From this study's results, it is possible to highlight the factors related to the Brazilian pediatric population that led to greater rates of intra-hospital death: age (12 to 19 years and less than one year old), the macro-region of residence in the country (Northern and Northeastern regions), the most severe clinical progression, which requires ventilatory assistance and/or ICU (critical SARI) and the presence of certain comorbidities (immunodepression and chronic cardiovascular disease). In contrast, asthma was associated with lower death rates, that is, it worked as a protective factor.

It is important to state that this study did not evaluate the effects of a novel SARS-CoV-2 variant, which caused a resurgence of cases and deaths in Brazil as of December 2020, nor the impact of COVID-19 vaccination, which started in January 2021 and whose impact deserves to be analyzed.

CONCLUSION

By using a dataset that includes children and adolescents nationwide, comprising 6,843 hospitalizations due to

COVID-19 confirmed by RT-qPCR testing in a 12-month period, or 53 epidemiological weeks, a profile of socio-demographic and clinical characteristics and factors associated with mortality from the disease was provided. Deaths were associated with age (12 to 19 years old and under one year old), the macro-region of residence in the country (Northern and Northeastern regions), more severe clinical progression requiring ventilatory assistance and/or ICU (critical SARI), and the presence of certain comorbidities (immunodepression and chronic cardiovascular disease). In contrast, asthma was associated with lower mortality rates, in other words, it worked as a protective factor.

Despite presenting lower hospitalization frequency and deaths than adults, the frequencies of complications and mortality from COVID-19 in the pediatric population are relevant. Furthermore, this study's findings expose the severity of the epidemic in the context of social inequality and fragility of health services, especially in impoverished areas, where the impact of the pandemic on mortality is pronounced. Thus, children and adolescents should not be neglected in the context of COVID-19 infection, and it is paramount to develop studies that clarify the mechanisms that influence COVID-19 mortality. Finally, the knowledge of the profile of children and adolescents hospitalized due to COVID-19 and the factors associated with deaths enables the direction of response actions for assisting this vulnerable population.

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