ORIGINAL ARTICLE

EPIDEMIOLOGICAL STUDY OF CHILDREN AND ADOLESCENTS AFFECTED BY SEVERE ACUTE RESPIRATORY SYNDROME IN THE COVID-19 PANDEMIC

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Highlights: (1). Children under one year old are more susceptible to SARS caused by the respiratory syncytial virus. (2). Children and adolescents have a low incidence of death from SARS. (3). Knowledge of the viral epidemiology in this population guides care.

PRE-PROOF

(as accepted)

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EPIDEMIOLOGICAL STUDY OF CHILDREN AND ADOLESCENTS AFFECTED BY SEVERE ACUTE RESPIRATORY SYNDROME IN THE COVID-19 PANDEMIC

ABSTRACT

Objective: To describe the epidemiological profile of respiratory viruses and the clinicoepidemiological characteristics of children and adolescents who were hospitalized with acute respiratory impairment in the period of the COVID-19 pandemic. **Methods:** This is a transversal descriptive study. The population of the study is comprised of children and adolescents aged between 0 and 18 years old who were hospitalized in the intensive care unit (ICU) and in the infirmary with acute respiratory impairment presenting with ate least 1 symptom, such as fever, even if just reported, cough, sore throat, dyspnea, O2 saturation < 95% or respiratory discomfort, diarrhea, and vomiting in the period from March 20, 2020 to December, 2021. **Results**: In the studied period, 95 individuals were eligible, predominantly males (50.5%) with comorbidities (58.2%). The most prevalent symptom was dyspnea (80%). Hospitalization in the ICU represented 53.6% of the cases, and 40% of the cases required noninvasive ventilatory support. Oseltamivir use was observed in 54.7% of the sample, and 28.4% of imaging exams evidenced pulmonary infiltrate; 98.8% of the cases evolved to full recovery. The most prevalent virus was the respiratory syncytial virus (RSV). **Conclusion:** The importance of knowledge of the current epidemiology regarding respiratory viruses in this population contributes to an assertive clinical practice and guides care to the target public in question, as well as to measures for blocking and mitigating the risks of unfavorable outcomes.

Keywords: SARS-Cov-2; Respiratory syncytial virus; Severe acute respiratory syndrome; Pediatrics; Hospital infection control program.

INTRODUCTION

The COVID-19 pandemic became the main public health problem in the world, devastating the population and causing millions of deaths, with ~ 38,048,773 notified cases and 704,470 deaths in Brazil up to the 47th Epidemiological Week of 2023. However, the disease did not present the same impact in the pediatric population, since most affected children were asymptomatic or oligosymptomatic[1].

Although COVID-19 has not had a great impact on the pediatric population, children and adolescents present higher susceptibility to viral respiratory infections due to their anatomy, physiology, and immunity, with severe acute respiratory syndrome (SARS) being the main unfavorable outcome, since it may have significant impacts in the short and long term on the health of children and adolescents, such as contributing to lung damage, chronic respiratory complications, extended hospitalization, and impacting on morbimortality[2].

According to data presented by Sivep-Gripe (2002)[1], until August 2021, approximately 89,826 children and adolescents between 0 and 14 years old were hospitalized in the ICU with SARS due to SARS-Cov-2 and other viruses, which represents a 17% increase in relation to the whole previous year.

Due to the relevant increase in the number of cases, to the identification of new SARS-Cov-2 variants, to the scarcity of special prevention and control measures aimed at children and adolescents, and to the low vaccination rates in the pediatric population, studies of this disease in this group are increasingly more relevant[3].

In this sense, the aim of the present study is to describe the epidemiological profile of respiratory viruses and the clinicoepidemiological characteristics of children and adolescents who were hospitalized with acute respiratory impairment during the period of the COVID-19 pandemic.

METHODS

This is a transversal descriptive study. The study population consists of children and adolescents between 0 and 18 years old who were hospitalized in the ICU and in the infirmary with acute respiratory impairment presenting with at least 1 symptom, such as fever, even if only reported, cough, sore throat, dyspnea, O2 saturation < 95%, respiratory discomfort, diarrhea, and vomiting in the period between March 2020 and December 2021.

The present research was approved under opinion number 5,141,068 and under CAAE 52428621.7.0000.5269 on December 2, 2021. A Free and Informed Consent Form

(FICF) and an Informed Consent Form were submitted to all individuals who were eligible for the research.

Data were extracted from the compulsory SARS notification forms of a child and adolescent care reference public hospital in the state of Rio de Janeiro, Brazil, using the EPI INFO 3.5.4 software of the Núcleo Hospitalar de Epidemiologia (NHE, in the Portuguese acronym).

The inclusion criteria were hospitalized children and adolescents, with a compulsory SARS notification form with laboratorial discharge criteria. The exclusion criteria were individuals > 18 years old and notifications with clinical, clinicoepidemiological, and clinical imaging discharge criteria.

The analyzed variables were: age, stratified into < 1 year old; between 1 year old and 1 year, 12 months, and 29 days old; preschool, between 2 and 5 years old; school, between 6 and 9 years old; preadolescent, between 10 and 11 years old; and adolescent, between 12 and 18 years old; males and females; basal diseases, which were stratified into comorbidities, chronical conditions including liver, lung, cardiac, renal, hematological, and immunological diseases, and without comorbidities, signs, and symptoms; antiviral use; ventilatory support; imaging exam; hospitalization in the ICU or in the inpatient unit; clinical outcome of the patient, either recovery or demise; and isolated virus.

The methodology used for the performance of the viral panel was real-time polymerase chain reaction (RT-PCR) through the collection of oropharynx and/or nasopharynx swab, according to the Centers for Disease Control and Prevention (CDC) protocol for respiratory viruses (CDC, Atlanta, GA, USA).

The descriptive analysis was based on the exploration of the frequency of the variables in Microsoft Excel 2010 (Microsoft Corporation, Redmond, WA, USA). The produced information was described in tables and was confronted with the existing literature.

RESULTS

During the studied period, 268 compulsory SARS notification forms were analyzed, of which 115 were from 2020 and 171 from 2021. However, after applying the inclusion and exclusion criteria and the FICF and the ICF, 95 individuals remained eligible.

Among these 95 individuals, the most prevalent virus was the respiratory syncytial virus (RSV), which was isolated in 36 cases (37.8%), followed by influenza A (22 cases; 23.1%) and parainfluenza 2 (22 cases; 23.1%), adenovirus (15 cases; 15.7%), SARS-Cov-2 (11 cases; 11.5%), parainfluenza 1 (7 cases; 7.3%), parainfluenza 3 (3 cases; 3.1%), and influenza B (1 case; 1%). There was no circulation of the parainfluenza virus 4 (Table 1).

Table 1. Distribution of circulant respiratory viruses concomitant of the SARS-Cov-2 pandemic. Rio de Janeiro, Brazil, 2022.

VIRUS	***n***	**%**
RSV	36	37.8
Influenza A	22	23.1
Parainfluenza 2	22	23.1
Adenovirus	15	15.7
SARS-Cov-2	11	11.5
Parainfluenza 1	7	7.3
Parainfluenza 3	3	3.1
Influenza B	1	1.0
Parainfluenza 4	0	0

Abbreviation: RSV, respiratory syncytial virus.

Source: The authors.

A total of 18 (18.9%) coinfections were identified: adenovirus + parainfluenza (*n* = 1), influenza A + adenovirus (*n* = 1), RSV + parainfluenza (*n* = 8), influenza A + RSV (*n* = 3), influenza A + parainfluenza (*n* = 1), adenovirus + RSV (*n* = 2), influenza A + SARS-Cov-2 (*n* = 1), and 1 triple infection with influenza A + influenza B + adenovirus (Table 2).

Table 2. Distribution of coinfections. Rio de Janeiro, Brazil, 2022.

COINFECTION	*n*
Adenovirus + parainfluenza	1
Influenza A + adenovirus	1
Influenza A + parainfluenza	1
Influenza A + SARS-Cov-	1
Influenza A + influenza B + adenovirus	1
Adenovirus + RSV	2
Influenza A + RSV	3
RSV + parainfluenza	8

Abbreviation: RSV, respiratory syncytial virus.
Source: The authors.

The distribution of the variables of individuals with SARS was analyzed. In this analysis, the different age groups were stratified according to the purposes of the study, being divided into < 1 year old; between 1 year old and 1 year, 12 months, and 29 days old; preschool, between 2 and 5 years old; school, between 6 and 9 years old; preadolescent, between 10 and 11 years old; and adolescent, between 12 and 18 years old.

Thus, the most prevalent age was < 1 year old (*n* = 55; 57.8%), followed by children between 1 year old and 1 year, 12 months, and 29 days old (*n = 16*; 16.8%); preschool children (*n* = 11; 11.5%); school children (*n* = 5; 5.2%); preadolescents (*n* = 3; 3.1%); and adolescents (*n* = 5; 5.2%) (Table 3).

Table 3. Distribution of age groups. Rio de Janeiro, Brazil, 2022.

AGE	*n*	%
< 1 year old	55	57.8
1 year old to 1 year 12 months 29 days old	16	16.8
Preschool	11	11.5
School	5	5.2
Preadolescent	3	3.1
Adolescent	5	5.2

Source: The authors.

There was a predominance of male patients, comprising 50.5% of the sample, with females comprising 49.5%. The subjects were divided into those with comorbidities (*n* = 49; 58.2 %), chronic conditions including liver, lung, cardiac, renal, hematological, and immunological diseases, and those without comorbidities (*n* = 45; 47.3%).

Regarding the observed symptoms, the patients evolved with dyspnea (*n* = 76; 80%), cough (*n* = 71; 74.7%), respiratory discomfort (*n* = 66; 69.4%), fever (*n* = 58; 61.0%), O2 saturation < 95% (*n* = 49; 51.5%), vomiting (*n* = 11; 11.5%), diarrhea (*n* = 5; 5.2%), and sore throat (*n* = 4; 4.2%) (Table 4).

Table 4. Distribution of symptoms. Rio de Janeiro, Brazil, 2022.

SYMPTOM	*n*	%
Dyspnea	76	80.0
Cough	71	74.7
Respiratory discomfort	66	69.4
Fever	58	61.0
O2 saturation < 95%	49	51.5
Vomiting	11	11.5
Diarrhea	5	5.2
Sore throat	4	4.2

Source: The authors.

Out of these individuals, 51 (53.6%) were admitted to the ICU and 44 (46.6%) to the infirmary, of which 26 (27.3%) required invasive mechanical ventilation, 38 (40.0%) required noninvasive mechanical ventilation, 24 (25.5%) did not require ventilatory support, and the SARS compulsory notification form was filled as unknown in 7 (7.3%) cases (Table 5).

Table 5. Distribution of ventilatory support. Rio de Janeiro, Brazil, 2022.

VENTILATORY SUPPORT	***n***	%
Invasive mechanical ventilation	26	27.3
Noninvasive mechanical ventilation	38	40.0
Did not require mechanical ventilation	24	25.2
Not informed	7	7.3

Source: The authors.

Regarding treatment, 54 (54.7%) patients received an antiviral, oseltamivir, sold under the brand name Tamiflu, 42 (44.2%) did not use an antiviral, and 1 (1.0%) was not reported. In the imaging exam 27 (28.4%) patients presented with pulmonary infiltrate, 2 (2.1%) with consolidation, 14 (14.7%) with mixed image, 20 (21%) with normal image, 11 (11.5%) did not undergo imaging examination, and 21 (22.1%) were not reported (Table 6).

Table 6. Distribution of imaging exams. Rio de Janeiro, Brazil, 2022.

IMAGING EXAM	***n***	%
Pulmonary infiltrate	27	28.4
Not reported	21	22.1
Normal	20	21.0
Mixed image	14	14.7
Did not undergo exam	11	11.5
Consolidation	2	2.0

Source: The authors.

Out of this population, 94 (98.8%) children and adolescents recovered and 1 (2.1%) died.

DISCUSSION

Our study corroborates the literature, which states that the RSV is the most prevalent virus, having maintained this pattern during the SARS-Cov-2 pandemic. A study conducted in Russia with 1,560 individuals with the objective of analyzing the etiology of respiratory infections in children and adolescents aged from 0 to 15 years old during a period of 4 years (2013–2017) also identified the RSV as the most prevalent virus[4-5]. This high prevalence of the RSV is due to its characteristic of high transmissibility and high hospitalization rates. It is a virus that circulates worldwide, being responsible for annual surges, affecting mainly children.

A Spanish study[6] described that the influenza type A virus is more predominant than influenza type B, corroborating our study, in which the influenza B virus represented 1% of the cases. The influenza A virus presents a higher capacity to cause epidemics and pandemics; the H1N1 and H3N2 subtypes are the influenza A variants that are most adaptable to humans and are responsible for common colds and flus, being easily transmitted between people.

Regarding the parainfluenza virus, the highest incidence reported in the literature is of parainfluenza 3; however, this variant was not observed in the present study, in which parainfluenza 2 was prevalent. Circulation of parainfluenza 4 was not observed; studies report a low frequency of its circulation, with this variant being rarely the cause of severe infections[7].

A total of 18 coinfections was detected, with the RSV being involved in the majority of cases. The RSV is frequently associated with viral coinfections, which may be due to its characteristic of high transmissibility and to its prevalence during the fall and winter, which are also periods of seasonality of other viruses, increasing the opportunities of exposure to multiple viruses, facilitating the occurrence of coinfections[8].

Coinfection by the SARS-Cov-2 virus with other respiratory viruses is frequently reported in the literature. The relationship between influenza and SARS-Cov-2 was one of the most cited in studies, particularly in the beginning of the pandemic[9]. In the present study, there was only one coinfection (influenza A + SARS-Cov-2). The repercussion of COVID-19 in this population in the short and long term includes multisystem

inflammatory syndrome in children (MIS-C), an association of Kawasaki disease (KD) with COVID-19, as well as physical, social, emotional, and learning impacts, including signs and symptoms that may be persistent and incapacitating. In this regard, postacute and long-term sequelae of SARS-Cov-2 are defined when clinical abnormalities persist 12 weeks after the onset of acute COVID-19 and cannot be justified by other conditions, being called long COVID. A very well-defined characterization regarding the persistence of the symptoms and sequelae of COVID-19 does not exist yet; however, there is evidence that children present them in a similar way as adults in this situation[10].

When analyzing the data on age groups, it becomes evident that hospitalization due to pneumonia is more frequent in children < 1 year old, a time of life marked by immature immunity and exposure to potential agents that cause viral infections[5, 11-12].

There was no significant difference in the occurrence of SARS according to the gender of the individuals, although a relative predominance is observed in male children and adolescents due to their susceptibility to respiratory infections due to their unfavorable anatomy[11-12].

There is an increased risk of death in individuals with previous comorbidities, such as pneumopathies and cardiopathies, which evidences the relationship between comorbidities and an unfavorable outcome. These pre-existing conditions compromise the function of these organs, making them more susceptible to the difficulties of dealing with the additional stress caused by the infection[5-13].

According to the literature, the classic symptoms of SARS are dyspnea/respiratory discomfort or pressure/persistent pain in the thorax or oxygen saturation < 95% in ambient air or cyanosis; in children, there may also be nose flaring, intercostal retraction, dehydration, and inappetence. In our research, the prevalence of dyspnea, cough, and respiratory discomfort was observed. Although fever and cough are associated with less severe cases such as flu syndrome, a significant presence of these symptoms was observed in the present study.

The percentage of patients admitted in the ICU was higher than that of those admitted in the infirmary; however, there was a prevalence of requirement of noninvasive ventilatory support. In contrast, in the study conducted in the pediatric hospital of

Joinville, state of Santa Catarina, in the southern region of Brazil, with 93 children and adolescents with viral pneumonia, only 3.2% of the patients required invasive mechanical ventilation, and 80% of admissions were in the normal ward[15]. One of the factors that may have contributed to this finding is the vulnerability of the study population; in our casuistry, male patients < 1 year old with comorbidities were the population that stood out. According to this profile, admission to the ICU is justified, differently from the compared study.

The radiological pattern found in the literature was interstitial infiltrate, which is in line with our study, which has also evidenced its prevalence. Although it is difficult to differentiate between viral infections by means of radiological exams, hyperinflation and pulmonary infiltrate are considered the gold standard[16].

Oseltamivir was the main drug of choice, considering that it is indicated in cases of clinical suspicion, independently of the collection of material for laboratory examination, starting early on, until 48 hours after the onset of symptoms, due to the benefits it presents, such as reduced hospital stay and lower risk of readmission[16-19].

Of the 35,891 (69.26%) children and adolescents notified with SARS to the Ministry of Health, 1,816 (3.50%) died[20], which is a low incidence, in line with that observed in our study, in which the mortality rate was of 2.1%, despite the severity of the cases.

As limitations of the present study, we cite that only hospitalized children and adolescents took part of the research, which makes it impossible to extend the results to children and adolescents who did not require hospitalization. Tests for the identification of bocavirus, rhinovirus, and metapneumovirus were not performed; the inclusion of these viruses in the present research could result in a higher prevalence of coinfections. We emphasize the importance of studies encompassing longer periods, with a larger number of individuals and ampliation of the viral panel, which shall enable a comparison of the results, besides the acquisition of further knowledge regarding the behavior of the viral agents that circulate concomitantly of the SARS-Cov-2. As a strength of the present study, we point out its relevance to public health, having an impact in the advancement

of knowledge in health care of children and adolescents, since viral infections have a great impact in the morbidity and mortality of this population.

CONCLUSION

It has been concluded that the clinicoepidemiological profile of children and adolescents affected by SARS in the SARS-Cov-2 pandemic in the studied scenario was that of individuals < 1 year old, males, and with comorbidities. Dyspnea stood out among the symptoms, as pulmonary infiltrate did in the imaging exams and oseltamivir as the drug of choice. The requirement of admission to the ICU with noninvasive ventilatory support prevailed, with cure as the main outcome. The RSV was the most prevalent virus in this population.

The importance of knowledge on the current epidemiology regarding respiratory viruses in this population contributes to an assertive clinical practice and guides care for the target public in question, besides contributing to measures of blocking and to the mitigation of the risks for unfavorable outcomes.

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