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Severe Acute Respiratory Syndrome in Children Treated at a Pediatric Referral Hospital in Brazil during the COVID-19 Pandemic

Síndrome Respiratória Aguda Grave em Crianças Atendidas em Hospital Pediátrico de Referência no Brasil Durante a Pandemia de COVID-19

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ABSTRACT

Background - Although we have accumulated knowledge along with the pandemic, there are still gaps, including the impact of seasonal conditions of SARS-CoV-2 and other respiratory viruses.

Methods - A retrospective cohort study that aimed to describe the etiological diagnosis and compare the clinical presentation and outcomes of children with Severe Acute Respiratory Syndrome (SARS).

Results – 1,027 children diagnosed with SARS were evaluated. In 926 (90.2%) children who collected RT-PCR Covid, 2.3% had a positive result. A total of 365 (35.4%) of the children underwent collection for Viral Panel exam, with identification of the etiology in 28%. There was a statistically significant difference in the age of patients infected with RSV and other viruses. The length of hospital stay was statistically different (p:0.006) when comparing groups of rhinovirus with COVID or RSV.

Conclusion - This study is a pioneer in conducting large-scale testing for respiratory viruses in pediatric patients during the pandemic and contributes to the knowledge about the etiology of SARS in childhood, and this disease's relationship with the seasonality of respiratory viruses.

Keywords: Respiratory virus; SARS-CoV-2; SARS.

RESUMO

Introdução - Embora tenhamos acumulado conhecimento ao longo da pandemia, ainda existem lacunas, incluindo o impacto do SARS-CoV-2 no comportamento sazonal de outros vírus.

Métodos - Estudo de coorte retrospectivo que teve como objetivo descrever etiologia e comparar a apresentação clínica e os desfechos de crianças com Síndrome Respiratória Aguda Grave (SRAG).

Resultados – Foram avaliadas 1.027 crianças com diagnóstico de SRAG. Em 926 (90,2%) crianças que coletaram RT-PCR Covid, 2,3% tiveram resultado positivo. Um total de 365 (35,4%) das crianças coletaram Painel Viral, com identificação de etiologia em 28%. Houve diferença estatisticamente significativa na idade dos pacientes infectados pelo VSR e outros vírus. O tempo de internação foi estatisticamente diferente (p:0,006) ao comparar os grupos de rinovírus com COVID ou VSR.

Conclusão - Este estudo é pioneiro na realização de painel viral em larga escala em pacientes pediátricos durante a pandemia e contribui para o conhecimento sobre a etiologia da SRAG na infância, e a relação desta doença com a sazonalidade e circulação dos vírus respiratórios.

Palavras-chave: Vírus respiratórios; SARS-CoV-2; SRAG.

INTRODUÇÃO

Acute respiratory infection (ARI) is a major cause of morbidity and mortality worldwide. Most of these pathologies occur by viruses infection. The variety of viruses that infect the respiratory tract is considerable, and the overlapping symptoms make the differential diagnosis a difficult task. Respiratory syncytial virus (RSV), influenza, and human coronavirus (HCoV) are common viruses identified in children. They have clinical manifestations ranging from mild upper respiratory infections (URIs) to severe lower respiratory tract infections (LRTIs) (WALD, SCHMIT e GUSLAND, 2021). Specific diagnosis relies almost entirely on laboratory investigation (QU, 2020; PEDRAZA e ARAÚJO, 2017).

Since December 2019, the world has passed an outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The response to the pandemic triggered a considerable change in overall human behavior, with social distancing measures. As respiratory viruses such as influenza, RSV and SARS-CoV-2 share similar routes and means of transmission, these great social efforts to prevent the spread of SARS-CoV-2 also affected the epidemiology of influenza and RSV (CASTRO, 2020).

Although we have accumulated knowledge about the behavior of this virus and the disease along with the pandemic, there are still gaps in knowledge, including the impact of seasonal conditions of SARS-CoV-2 and other common childhood respiratory viruses infections and transmissions. This study aimed to describe the effect of seasonality on the dynamics of virus dissemination and clinical presentation, regarding symptoms, hospitalization, morbidity, and mortality of infected children.

METHODS

This is a retrospective cohort carried out at the João Paulo II Children's Hospital (HIJPII), in Minas Gerais, Brazil. The hospital offers free public health care services, and it was the reference for the hospitalization of pediatric patients suspected of COVID-19 during the 2020 pandemic. Surveillance was carried out on all children between ages 0 and 18 treated ate HIJPII with a severe acute respiratory syndrome (SARS) from January 2020 to December 2020.

By studying medical records, we had access to patient information: age, sex, symptoms, immunological status, travel history, or contact with a suspected case, results of imaging and viral research, treatment, as well as clinical outcomes.

According to definitions by the Ministry of Health of Brazil, the diagnosis of SARS was considered for patients with flu-like illness accompanied by at least one severity criterion: dyspnea, respiratory distress, O2 saturation < 95%, worsening of clinical conditions of preexisting diseases, hypotension, respiratory failure(BRASIL, 2020).

The etiological diagnosis was made using the following tests: a molecular test for SARS-CoV-2, a rapid serological test for Influenza or RSV, and Respiratory Viral Panel. The viral panel included the investigation of Metapneumoviruses, Bocaviruses, Parainfluenza 1, 2, and 3, Adenovirus, Influenza A and B, and Respiratory Syncytial Virus (RSV). The investigation of Rhinoviruses was also included, starting in October.

Data Analysis

The qualitative variables were displayed as absolute and relative frequencies, and the quantitative variables as average ± standard deviation. The associations between qualitative variables were evaluated with chi-square or Fisher's exact tests, used when the expected frequency was less than five. Kruskal-Wallis test had used to compare groups or Dunn's test for multiple comparisons. To analyze the data, version 4.0.0 of the R program (R Foundation for Statistical Computing, Vienna, Austria) had used, and the significance level adopted was 5%.

Ethical issues

The Ethics in Research Committees from HIJPII approved all procedures conducted in this study.

RESULTS

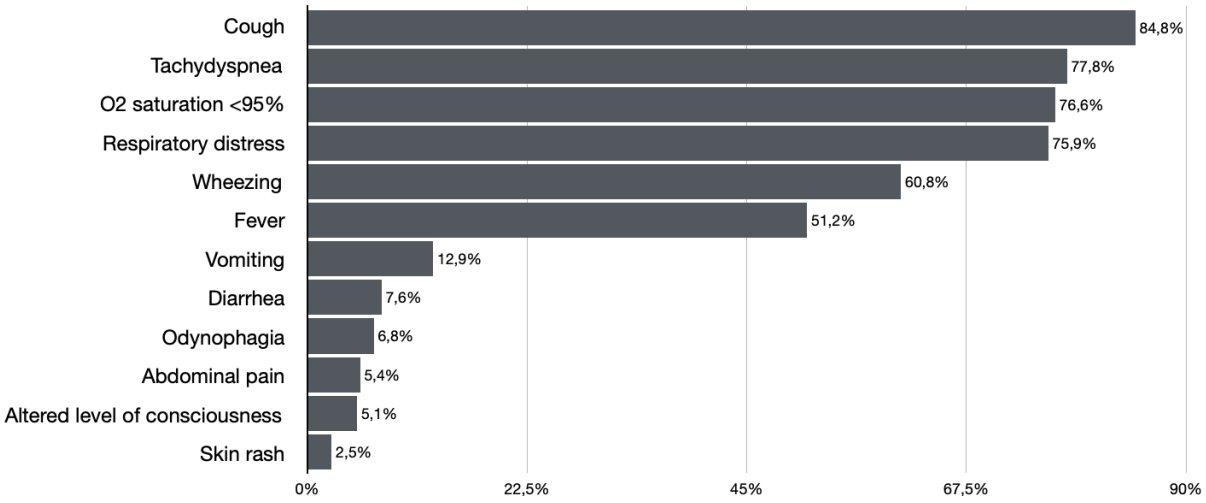
During the cohort period, 1.027 children were diagnosed with SARS, with a predominance of males (54.1%) and a median age of 39 months, as described in Table 1. In total, 134 (13%) patients had a history of contact with a symptomatic respiratory case in the 14 days preceding the onset of symptoms. About 314 (30.6%) had no comorbidity.

Among the group of patients with underlying diseases considered a risk factor for unfavorable disclosure, there was a predominance of asthma (29.6%), wheezing infant (15.4%), chronic neurological disease (9.9%), prematurity (4.7%), and Sickle Cell Anemia (4.1%).

963 (93.8%) of the cases were of community origin, and 64 (6.2%) started after 72 hours of hospitalization due to another diagnosis with a possible origin's nosocomial. Only 376 (36.6%) of the patients had a record of immunization against Influenza related to the 2020 seasonality.

As shown in Graph 1, the most prevalent clinical findings were cough (84.8%), tachydyspnea (77.8%), desaturation (76.6%), and wheezing (77.8%). Fever was present in 51.25% of patients. Gastrointestinal symptoms, rash, and odynophagia had found to be less prevalent.

Graph 1 - Clinical findings among children hospitalized with the severe acute respiratory syndrome (SARS), HIJPII, January 2020 to December 2020. (n= 1027)



Fonte: Teixeira et al, 2022.

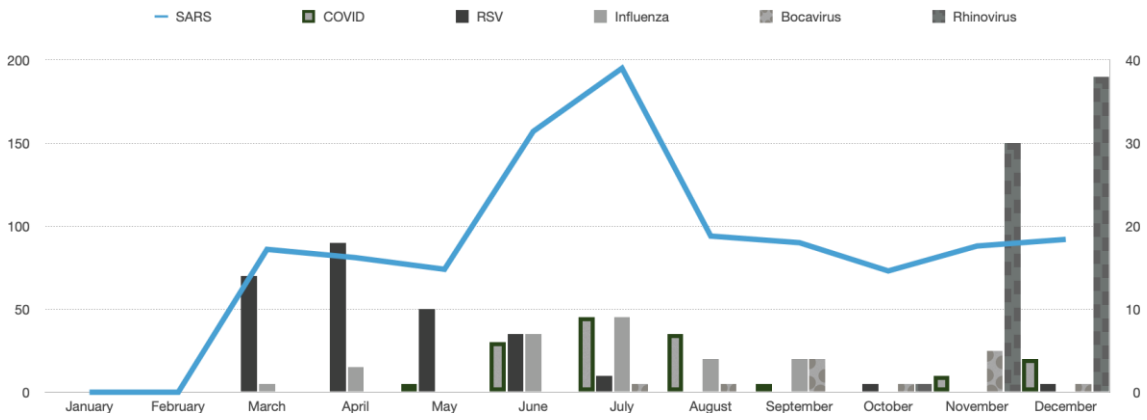
About 825 children needed to use ventilatory support. Of these patients, 84.2% required only oxygen therapy, provided in 566 (68.6%) cases by nasal catheter and 115 (13.9%) by face mask with reservoir. In total, 48 (5.8%) patients used non-invasive ventilation, and 86 (10.4%) required invasive mechanical ventilation.

A total of 926 (90.2%) children collected Covid RT-PCR, with a positive result in 30 (3.2%) of the tests performed. Of the 64 patients with possible nosocomial infection, 2 (3.1%) tested positive for Covid by RT-PCR.

Rapid Influenza and RSV tests had performed on 575 (56%) and 267 (26%) patients, respectively, with a positive rate of 5% and 19.8%. A total of 365 (35.4%) of the children underwent viral panel collection for sentinel investigation of respiratory viruses. And an etiological agent was identified in 28% of them.

Among the 1027 patients evaluated, six had two respiratory viruses identified simultaneously in the tests performed. One of them was positive for Influenza and Covid, one positive for Rhinovirus and Covid, and four positive for Rhinovirus and Bocavirus. There was a higher incidence of RSV during March, April, May, and June, coinciding with autumn. June, July, and August were the months with the highest institutional incidence of COVID, coinciding with the peak incidence of Influenza. At the end of October, began the introduction of Rhinovirus testing. So there was a high identification rate of this etiological agent among the children tested.

Graph 2 - SARS incidence by etiologic agent per month in children with the severe acute respiratory syndrome (SARS), HIJPII, January 2020 to December 2020.



Fonte: Teixeira et al, 2022.

Chest radiography had performed in 560 (54.4%) patients, has been described as unchanged in 193 (34.5%) of cases and with interstitial infiltrates in 198 (35.4%). Images of consolidation (12%), hyperinflation (6.1%), atelectasis (5.2%) and pleural effusion (1.1%) were described. Chest tomography had performed in only 3% of patients.

The median hospitalization of patients due to SARS was three days (2 – 7). 13 (1.3%) patients died due to respiratory symptoms or secondary complications. The descriptive characteristics of children with severe acute respiratory syndrome are summarized in Table 1.

Table 1 – Descriptive characteristics of children with the severe acute respiratory syndrome (SARS), HIJPII, January 2020 to December 2020.

	n (%)
Gender, male	556 (54,1)
Age, months, median (IQ25-75)	39,0 (13,5 – 77,5)
Length of stay, median (IQ25-75)	3,0 (2,0 – 7,0)
Regional Health Unit	
Belo Horizonte	919 (89,5)
Other cities	101 (9,8)
No information	7 (0,7)
Epidemiology	
Travel history	5 (0,5)
Contact with suspicious case	134 (13,0)
Risk factors	
None	314 (30,6)
Asthma and wheezing infant	462 (45,0)
Chronic neurological disease	102 (9,9)
Prematurity	48 (4,7)
Sickle Cell Anemia	42 (4,1)
Other chronic lung diseases	34 (3,2)
Cardiovascular diseases	23 (2,2)
Other	52 (5,1)
Nosocomial infection	64 (6,2)
Influenza vaccine (2020)	376 (36,6)
Antibiotic use	378 (36.8)
ICU admission	267 (26.0)
Oxygen therapy	825 (80.3)
Nasal cateter	566 (68.6)
Face mask	115 (13.9)
Non invasive ventilation	48 (5.8)
Mechanical ventilation	86 (10.4)
Chest X-ray	660 (64.2)
Normal	193 (34.5)
Interstitial infiltrate	198 (35.4)
Consolidation	67 (12.0)
Hyperinflation	34 (6.1)
Atelectasis	29 (5.2)
Pleural effusion	9 (1.6)
Chest CT	31 (3.0)

Death	13 (1.3)

Fonte: Teixeira et al, 2022.

The comparison of the epidemiological profile, clinical and imaging manifestations, and outcomes of patients positive for Covid, Influenza, Rhinovirus, and RSV, was summarized in Table 2. These analyses excluded those with positive results for more than one virus.

Table 2: Comparison of variables between variables of children with severe acute respiratory syndrome (SARS), HIJPII, January 2020 to December 2020. (n = 175)

	COVID (n=30)	**Influenza** (n=29)	**Rhinovirus** (n=68)	**RSV** (n=53)	**Valor-p**[Q]
Age, months, median (IQ25-75)	48.0 (19.0 – 86.0)	21.0 (8.0 – 55.0)	38.5 (17.8 – 70.0)	5.0 (3.0 – 8.0)	<0,001[K]
Length of stay, median (IQ25-75)	6.0 (3.0 – 11.0)	3.0 (3.0 – 8.2)	3.0 (2.0 – 4.0)	5.0 (3.0 – 8.0)	0,006[K]
Influenza vaccine (2020)	12 (40.0)	14 (48.3)	38 (55.9)	4 (7.5)	<0,001
Clinical findings					
Fever	22 (73.3)	16 (55.2)	33 (48.5)	34 (64.2)	0,133
Cough	20 (66.7)	28 (96.6)	60 (88.2)	51 (96.2)	< 0,001
Odynophagia	4 (13.3)	2 (6.9)	5 (7.3)	0 (0.0)	0,096
O2 saturation < 95%	17 (56.7)	22 (75.9)	54 (79.4)	48 (90.6)	0,004
Wheezing	11 (36.7)	17 (58.6)	51 (75.0)	34 (64.2)	0,001
Tachydyspneia	19 (63.3)	21 (72.4)	55 (80.9)	48 (90.6)	0,016
Respiratory distress	17 (56.7)	22 (75.9)	51 (75.0)	44 (83.0)	0,079
Diarrhea	6 (20.0)	2 (6.9)	4 (5.9)	5 (9.4)	0,173
Vomiting	6 (20.0)	3 (10.3)	10 (14.7)	6 (11.3)	0,607
Abdominal pain	4 (13.3)	1 (3.4)	1 (1.5)	0 (0.0)	0,014
Rash	3 (10.0)	0 (0.0)	2 (2.9)	0 (0.0)	0,034
Change in the level of consciousness	2 (6.7)	1 (3.4)	2 (2.9)	2 (3.8)	0,895
ICU admission	11 (36.7)	9 (31.0)	10 (14.7)	22 (41.5)	0,014
Oxygen therapy	19 (63.3)	24 (82.8)	53 (77.9)	47 (88.7)	0,079
Nasal cateter	10 (33.3)	14 (48.3)	48 (70.6)	30 (56.6)	0,001
Face mask	5 (16.7)	4 (13.8)	5 (7.3)	2 (3.8)	0,277
Mechanical ventilation	3 (10.0)	1 (3.5)	0 (0,0)	6 (11.3)	0,023
Non invasive ventilation	1 (3.3)	6 (20.7)	0 (0,0)	9 (17.0)	0,002
Chest X-ray	11 (36.7)	17 (58.6)	23 (33.8)	38 (71.7)	<0,001
Normal	3 (10.0)	7 (24.1)	9 (13.2)	16 (30.2)	0,873
Interstitial infiltrate	2 (6.7)	6 (20.7)	5 (7.3)	12 (22.6)	0,695
Consolidation	2 (6.7)	3 (10.3)	3 (4.4)	3 (5.7)	0,705

Hyperinflation	1 (3.3)	1 (3.4)	4 (5.9)	1 (1.9)	0,183
Atelectasis	1 (3.3)	0 (0.0)	2 (2.9)	3 (5.7)	0,791
Death	2 (6.7)	0 (0.0)	0 (0.0)	0 (0.0)	0,053

Fonte: Teixeira et al, 2022.

There was a significant difference in the age of patients with positive results for VRS and other viruses. There was a relevant difference in length of stay between patients with positive results for rhinovirus and COVID. In addition, between patients with positive results for rhinovirus and VRS. Abdominal pain and exanthema were more prevalent in patients with Covid, while cough, hisses, and desaturation were less frequent findings when compared to the other viruses. Patients diagnosed with RSV were less frequently vaccinated against Influenza and had more episodes of tachydyspnea. Rhinovirus patients used oxygen therapy through a nasal catheter more often and had lower demand for intensive care support. There was no statistically significant difference between the lethality of the diagnosed viruses.

DISCUSSION

The new coronavirus causes severe respiratory disease in some individuals. In the same way as the outbreaks caused by two other human respiratory coronaviruses that emerged in the last two decades (SARS-CoV, MERS-CoV) (WALD, SCHMIT e GUSLAND, 2021).

Early literature reported the incidence of COVID-19 pneumonia were more common in male and associated it with a higher level of ACE2 expression in this gender (QU, 2020). However, our study showed an insignificant difference in the disease incidence between genders. Although reports of differences in severity according to age have been inconsistent, some have noted increased risk in the first year of life and others during adolescence. In our study, there was a significant predominance of children under two years of age. Part of this result may have been influenced by the fact that the hospital's emergency room attends to children up to 12 years of age. The patients between 12 and 18 years are received at the institution only through direct referral to hospitalization.

A synthesis of publications from China, Italy, Spain, and the United States showed that children represented a minority (< 2%) of the patients who presented with clinically recognized symptoms of SARS-CoV-2 (WALD, SCHMIT e GUSLAND, 2021). The

infection in most children is mild, with a substantial proportion (5–21%) being completely asymptomatic and another large group having symptoms of an usual viral upper respiratory infection.

The proportion of children with severe illness is 1–6%, even with the recent recognition of the pediatric multisystem inflammatory syndrome. Fortunately, fatalities have been infrequent, and most, but not all, children who have died have had severe comorbidities (WALD, SCHMIT e GUSLAND, 2021). We observed only two deaths in hospitalized children infected with Covid-19 (6% of cases). Comorbidities were present in the two cases. Oliveira et al. describe the clinical outcomes and risk factors for death in 11,613 hospitalized children and adolescents with laboratory-confirmed SARS-CoV-2 infection in Brazil. Death from COVID-19 was observed in 7.5% of the patients and was associated with age, indigenous ethnicity, poor geopolitical region, and pre-existing medical conditions. Disparities in health care, poverty, and comorbidities can contribute to magnifying the burden of COVID-19 in more vulnerable and socioeconomically disadvantaged children and adolescents in Brazil (OLIVEIRA, 2021).

Fever and nonproductive cough are the most common children's symptoms (nearly 50%). But, rhinorrhea, fever alone, or mild gastrointestinal symptoms such as abdominal pain, diarrhea, and vomiting also had observed (WALD, SCHMIT e GUSLAND, 2021). Our data showed that common COVID-19 symptoms included fever, coughs, dyspnea, and fatigue; in our study, fever is a frequent clinical manifestation of COVID-19 pneumonia, which is similar to the other reports (QU, 2020).

There are no respiratory manifestations that differentiate infections caused by SARS-CoV-2 from any other community-acquired respiratory virus, such as a respiratory syncytial virus (RSV), influenza, or parainfluenza. This fact will present a principal challenge in future respiratory seasons. It will be essential to identify cases and trace contacts, requiring systematic laboratory diagnosis in all children with minor respiratory symptoms. In our study, the presence of abdominal pain and rash were associated with COVID-19. These findings suggested, when present, the possibility to increase the diagnostic suspicion.

The median length of hospital stays for patients diagnosed with COVID was six days, similar to that found in patients with RSV. There was also no statistically significant

difference between the length of stay of patients diagnosed with influenza. Although children are relatively less affected than adults, the data reinforces that COVID-19 can generate demand for hospital care like other respiratory viruses in the age group analyzed.

In terms of imaging findings, we found that at least 34,5% of the patients had a regular chest x-ray. Other studies have shown that most pediatric patients have no alterations observed on chest x-ray (HOANG, 2020). In a similar number of children, it observed interstitial infiltrates and consolidations among the radiographic findings. Although there are articles that summarize the clinical or CT characteristics of COVID-19 pneumonia, the available data remained insufficient and generalized (QU, 2020).

Covid x Influenzae x RSV

Fever, cough, and rhinorrhea are the most common symptoms in children infected with the influenza virus (WALD, SCHMIT e GUSLAND, 2021). In our study, a lower prevalence of cough was observed in patients with a confirmed diagnosis of COVID-19. Although that, no direct association of these symptoms with influenza was found. Influenza-associated hospitalization morbidity, and mortality rates are highest among children younger than two years old and individuals with certain high-risk conditions such as asthma, diabetes, hemoglobinopathies, immunosuppression, and neurodevelopmental disorders (WALD, SCHMIT e GUSLAND, 2021). The findings of the evaluated cohort confirm data from the literature. We observed a significant predominance of patients under two years hospitalized with SARS-CoV-2. Among the comorbidities, are patients with underlying respiratory and neurological conditions.

Curiously, COVID-19 cases in infants and children are rare. Recent studies reported children under the age of 10 to correspond for only 1% of the COVID-19 cases in China. These children have a milder infection. It could happen because children have altered mechanisms that regulate the interaction between the immune system and respiratory system. In comparison to COVID-19 pneumonia, the incidence of influenza pneumonia was significantly higher in children in our study.

Varela et al. described that SARS-CoV-2 was detected in 49/298 (16.4%) study participants in Brazil. The percentage of weekly detection of SARS-CoV-2 varied from 0.0% to 43.8% in children from May to July. 99.5% of the samples were processed for Flu A, Flu B, and RSV, and resulted in negative. They have initially expected that

COVID-19 frequencies should increase significantly during the fall and winter months. That the usual patterns of community spread of RSV and influenza A and B would likely change due to public health measures taken to reduce transmission of COVID-19. Interestingly, a striking absence of these two usually prevalent pathogens was observed in that cohort of symptomatic subjects (VARELA, 2021).

In USA, Asia, and Europe, several public health measures aiming to prevent the rapid spread of COVID-19 have started mainly at the end of the winter season. The findings of concomitant viral infections in these communities may have been influenced by a natural decline in the incidence of RSV and influenza. Recently, however, an unprecedented drop in hospitalization due to RSV had registered in Alaska (NOLEN, 2021). Wu *et al* also observed that, during the COVID-19 pandemic in China, there was a decreasing trend in influenza reports early in 2020, in contrast with two spike waves observed in the previous year (WU, 2022). In Switzerland, SARS-CoV-2 completely replaced the seasonally circulating community-acquired respiratory viruses within three weeks of the pandemic (LEUZINGER, 2022). This finding raises the hypothesis of a possible competition pattern among respiratory viruses.

Another possible explanation for lower influenza rates could be heightened awareness due to the pandemic, with a subsequent increase in influenza vaccination numbers. However, Influenza vaccination rates were 88.8% for the target population, similar to historical values in Brazil (VARELA, 2021).

The respiratory syncytial virus is the most common cause of acute LRTI and subsequent hospitalizations in children less than one year. Most infants with RSV infection will have symptoms isolated to the upper respiratory tract, although 20–40% will develop LRTI. Overall, 1–3% of all infants less than one year of age will require hospitalization due to RSV-related LRTI, the majority during the first six months of life. The respiratory syncytial virus has the highest symptomatic incidence, hospitalization rate, and mortality rate for children less than five years of age, especially for those two years or less, compared with the available data for influenza and coronavirus (WALD, SCHMIT e GUSLAND, 2021).

Data on hospitalization for bronchiolitis in children under one year obtained by DATASUS from January 2016 to June 2020 revealed 167,870 cases during this period,

observing a significant reduction in 2020 (CASTRO, 2020). It noticed an annual increase in the incidence of hospitalizations for bronchiolitis from 2016 to 2019. And the sharp drop coincided with the implementation of measures of social distancing. The analysis showed a reduction of more than 70% in hospital admissions for bronchiolitis in children under one year of age, considering annual and geographic variations (FRIEDRICH, 2021). The Covid-19 pandemic arrived in Brazil in February 2020, just before autumn in the southern hemisphere, between March and September. Pandemic control measures, such as social distancing and restriction of non-essential services, began in mid-March. One of the measures was the suspension of in-person school activities.

Varela et al. also found a significant reduction in hospitalized cases number with acute viral bronchiolitis in Brazil, with hospital admissions for infants 85% lower than in the previous years. Schools and daycare centers remained closed from March 2020 to August 2021. These measures can be associated with these observed and significantly lower transmission levels for both influenza and RSV (VARELA, 2021).

Other Respiratory Viruses

The role of viruses that trigger other respiratory illnesses remains unclear for human metapneumovirus (hMPV), bocavirus (HBoV), and other agents. Whereas other viral pathogens, this association is more well defined. Human Rhinoviruses (HRV) account for 35% of infection-related asthma episodes, followed by the respiratory syncytial virus (RSV) and influenza viruses (FLU) (CASTRO, 2020).

HRV that was the most prevalent viruses detected, could not have a well-defined circulation profile, since the tests did not include the entire period studied. We consider that, despite an unprecedented study of great importance for the assessment of viral seasonality, our results were influenced by the fact that we could not standardize the testing of all the viruses available in the viral panel for all patients. The exam's availability and the laboratory's testing capacity determined this limitation. And it contributed to the fact that we had a considerable percentage of children still without etiological identification.

Finally, considering that some viral agents are susceptible to the colonization of the airways, such as rhinovirus or bocavirus, we also need studies that can assess whether

under what circumstances the detection of viral nucleic acids in an individual implies an active infection, especially in situations where two or more viruses are detected.

CONCLUSION

The current study is the first to perform large-scale testing of respiratory viruses in pediatric patients during the Covid pandemic, conducted in the southwest region of Brazil. Furthermore, this study adds important information regarding the spreading dynamics of high burden respiratory viruses during a period of effective public health measures. The low incidence of RSV and influenza, in contrast with SARS-CoV-2, should be considered in the development of guidelines for antiviral treatment of influenza or the prevention of RSV with monoclonal antibodies.

REFERENCES

BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. Guia de Vigilância Epidemiológica. Emergência de Saúde Pública de Importância Nacional pela Doença pelo Coronavírus 2019 [recurso eletrônico]. Brasília, 2021.

CASTRO, Italo A. Circulation profile of respiratory viruses in symptomatic and asymptomatic children from Midwest Brazil. **Brazilian Journal of Microbiology**, n. 51, p. 1729-1735, 2020.

FRIEDRICH, Frederico. Early impact of social distancing in response to Covid-19 on hospitalizations for acute bronchiolitis in infants in Brazil. **Clinical Infectious Diseases**, v. 72, n. 12, p. 2071-2075, 2021.

HOANG, Ansel. COVID-19 in 7780 pediatric patients: a systematic review. **EClinicalMedicine**, 2020.

LEUZINGER, Karoline. Epidemiology of SARS-CoV-2 Emergence Amidst Community-Acquired Respiratory Viruses. **The Journal of Infectious Diseases**, v. 222, n. 8, p. 1270–1279, 2022.

NOLEN, Leisha D. Impact of social distancing and travel restrictions on non–coronavirus disease 2019 (non–COVID-19) respiratory hospital admissions in young children in Rural Alaska. **Clinical Infectious Diseases**, p. 2196-2198, 2021.

OLIVEIRA, Eduardo A. Clinical characteristics and risk factors for death among hospitalised children and adolescents with COVID-19 in Brazil: an analysis of a nationwide database. **The Lancet Child & Adolescent Health**, p. 559-568, 2021.

PEDRAZA, Dixis F.; ARAÚJO, Erika M. Hospitalizations of Brazilian children under fiver years old: a systematic review. **Epidemiologia e Serviços de Saúde** , v. 26, p. 169-182, 2017.

QU, Jiajia. Clinical characteristics of COVID-19 and its comparison with influenza pneumonia. **Acta Clinica Belgica**, v. 75, p. 348-356, 2020.

VARELA, Fernanda H. Absence of detection of RSV and influenza during the COVID-19 pandemic in a Brazilian cohort: likely role of lower transmission in the community. **Journal of global health**, 2021.

WALD, Ellen R.; SCHMIT, Kathryn M.; GUSLAND, Daniele Y. A pediatric infectious disease perspective on COVID-19. **Clinical infectious Disease**, p. 1660-1666, 2021.

WU, Di. Positive effects of COVID-19 control measures on influenza prevention. **International Journal of Infectious Diseases**, v. 95, p. 345-346, 2022.