Screening for common respiratory viruses in pediatric outpatients 2 years after the onset of the COVID-19 pandemic

María B. Leone[a], Daniela A. Ponti[a], María N. Fernández Berengeno[a], Nicolás A. Grisolía[a], Valeria P. Aprea[a], María L. Yazde de Puleio[a], Alejandra Svartz[a], Emilce Haleblian[a]

ABSTRACT

Introduction. During 2020, circulation of other respiratory viruses was lower than usual. Most likely, as mitigation measures for coronavirus disease 2019 (COVID-19) were modified, their prevalence in 2021 may have increased.

Objective. To estimate the prevalence of common respiratory viruses among patients aged 0–5 years seen at the Emergency Department of a children's hospital in the City of Buenos Aires.

Methods. Cross-sectional study of 348 patients consulting for suspected COVID-19 in whom SARS-CoV-2 infection was ruled out and routine screening for common respiratory viruses was performed.

Results. Respiratory syncytial virus (RSV), a common respiratory virus, was identified in 40% of patients. Age younger than 2 years was an independent predictor of RSV (odds ratio [OR]: 4.15; 95% confidence interval [CI]: 2.46–6.99).

Conclusion. In the study population, 40% of patients suspected of COVID-19 in whom SARS-CoV-2 infection was ruled out had RSV infection.

Key words: *SARS-CoV-2, respiratory syncytial virus, respiratory infection.*

http://dx.doi.org/10.5546/aap.2022.eng.264

To cite: Leone MB, Ponti DA, Fernández Berengeno MN, Grisolía NA, et al. Screening for common respiratory viruses in pediatric outpatients 2 years after the onset of the COVID-19 pandemic. *Arch Argent Pediatr* 2022;120(4):264-268.

a. Hospital General de Niños Pedro de Elizalde, City of Buenos Aires, Argentina.

E-mail address:
María B. Leone: beluleone@hotmail.com

Funding: None.

Conflict of interest: None.

Received: 1-19-2022
Accepted: 3-31-2022

INTRODUCTION

Acute respiratory infections (ARIs) still show a seasonal pattern, with an increase in cases during the winter season[1] and are a cause of morbidity and mortality.

The coronavirus disease 2019 (COVID-19) pandemic, which began in 2020,[2] altered the usual circulation pattern of other respiratory viruses (ORVs) commonly involved in seasonal ARIs: respiratory syncytial virus (RSV), influenza A and B, parainfluenza 1, 2, and 3, adenovirus, and metapneumovirus.

Until epidemiological week (EW) 42 of 2019, the National Health Surveillance System had reported that ORVs were identified in 36.3% of cases.[3] During 2020, virus circulation decreased to 7.3%.[4]

Most likely, the implementation of non-drug mitigation measures had an impact on such circulation reduction. With the return to in-person activities, it is probable that the circulation of ORVs increased again in 2021.

The primary objective of this study was to estimate the prevalence of ORVs among outpatients seen at a children's hospital with suspected COVID-19 in whom infection was ruled out by negative polymerase chain reaction (PCR).

Our secondary objective was to explore the existence of an association between the characteristics of the study sample and the presence of ORVs.

MATERIALS AND METHODS

This was a cross-sectional, analytical study. The study included male and female patients aged 0–5 years who consulted the Emergency Fever Unit, a device designed to assist cases suspected of COVID-19 according to current regulations[5] in place at Hospital General de Niños Pedro de Elizalde between August 1st and September 30th, 2021. Asymptomatic children screened by institutional protocol and patients in whom hospitalization was indicated were excluded.

Age, associated symptoms (fever, cough, odynophagia, respiratory distress, headache, myalgia, diarrhea, vomiting and/or rhinitis), duration of symptoms greater or less than 24 hours, presence of comorbidities (chronic lung disease, obesity, diabetes, rheumatic, heart, kidney or immune disease, and cancer) were recorded.

Samples were obtained by nasopharyngeal swabbing and processed at the local laboratory within 24 hours of collection using an indirect immunofluorescence (IIF) virus panel for RSV, influenza A and B, parainfluenza 1, 2, and 3, adenovirus, and metapneumovirus. SARS-CoV-2 was ruled out by reverse transcription polymerase chain reaction (RT-PCR).

A convenience sample was used that included 10 samples entered consecutively each day of the week. Considering a 3.36% positivity for ORVs as reported in the national Epidemiological Bulletin corresponding to EW 26 of 2021,[6] and a maximum number of 560 samples to be analyzed in the study period, it was estimated that 187 patients were sufficient to demonstrate such prevalence with a margin of error of 2%.[7] A stratified sampling by age group was performed,[8] according to the usual distribution of consultations registered at the hospital. Thus, the sample was distributed as follows: 0–2 year-old group (60%) and 3–5 year-old group (40%). Only one case per family group was included, considering the first analyzed sample of the group.

Ethical considerations

The study was approved by the hospital's Ethics Committee (Protocol no. 5436-2021). The informed consent was requested to and obtained from each participant's parent or legal guardian.

Statistical analysis

Continuous variables were expressed as median and interquartile range (IQR 25–75) because data did not have a normal distribution (Shapiro-Wilk test) and categorical variables were described as frequency of occurrence and/or percentage. The χ^2 test was used to assess statistically significant differences between categorical variables. A multiple logistic regression model was developed to answer the secondary objective, which included the predictor variables that showed statistical significance in the univariate model and, as response variable, the presence of ORVs. A 5% type I error and an 80% power were estimated. Results are shown together with the 95% confidence interval. The Rstudio® software, version 3.6, was used.[9]

RESULTS

A total of 348 individuals were enrolled; 4 were left out due to database errors.

Participants' median age was 2.4 years (IQR 25-75: 2.39); 63% were 0–2 years old and 37%, older than 2 years; 52% were females. A comorbidity was present in 16% of participants; the most common one was recurrent wheezing.

TABLE 1. *Characteristics of the study population as per identification of respiratory syncytial virus*

Sample characteristics	Respiratory syncytial virus		*p* value
	Negative (n = 139)	Positive (n = 205)	
Female sex (%)	46.8	56	0.13
Presence of comorbidities (%)	14.6	16.5	0.64
Days elapsed between symptom onset and medical consultation	3.00 (2.00–4.00)	3.00 (2.00–4.00)	0.88
Age (years)	3.03 (1.53–4.20)	1.62 (0.90–2.58)	< 0.01*
Fever (%)	72.2	69.8	0.72
Cough (%)	83.4	89.2	0.18
Rhinorrhea (%)	79	84.2	0.29
Gastrointestinal symptoms (%)	20.5	27.3	0.18
Odynophagia (%)	16.1	6.5	0.012**
Headache (%)	6.8	1.4	0.039**
Respiratory distress (%)	18	28.1	0.039**

Categorical variables are expressed in percentages (%). Percentages were estimated for the total number of cases by sub-group. Continuous variables are reported as median and interquartile range 25–75.

* Highly significant difference ($p < 0.01$).

** Statistically significant difference ($p < 0.05$).

RSV: respiratory syncytial virus.

The median time from symptom onset to consultation was 3 days (IQR 25–75: 2 days); 50% sought care in the first 48–72 hours; 30%, after 72 hours; and the rest, in the first 24 hours.

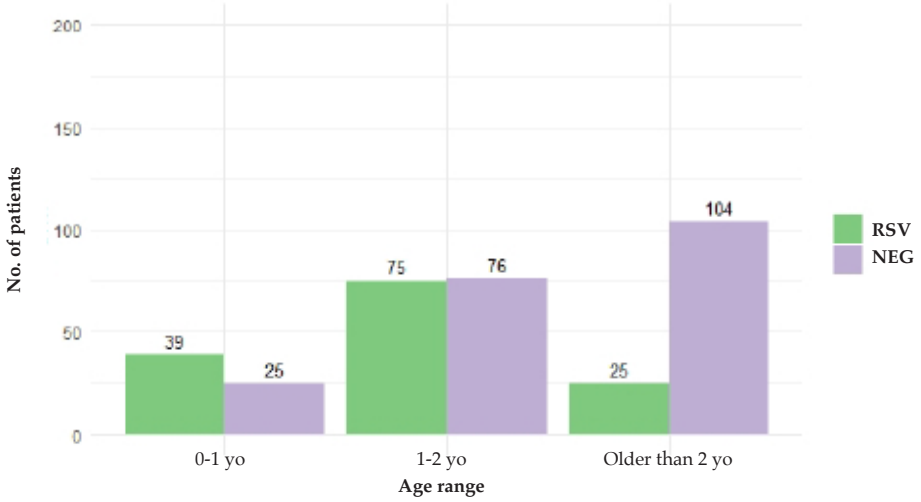
The most frequent symptoms were cough (85%), rhinorrhea (81%), and fever (71%) (*Table 1*).

In relation to common respiratory viruses, ORVs were identified in 139 patients (40%) (95% CI: 35%–46%). RSV was detected in all cases. When comparing RSV patients with those in whom no virus was identified, the former had respiratory distress more frequently (p: 0.039) and age younger than 2 years ($p < 0.001$) (*Figure 1*). The presence of odynophagia and headache was more frequent among patients in whom no virus was identified (p: 0.012 and 0.039, respectively). No significant differences were observed in relation to other variables (*Table 1*).

The analysis of the sample by age range showed that patients between 0 and 2 years old had respiratory distress more often; older patients had odynophagia and headache (*Table 2*).

A multivariate model showed that the population aged 0–2 years had a higher risk for RSV infection (OR: 4.15; 95% CI: 2.46–6.99). The rest of the co-variables did not show statistical significance when included in the model (*Figure 2*).

FIGURE 1. *Frequency of RSV detection by age range*



NEG: negative; RSV: respiratory syncytial virus.

TABLE 2. *Characteristics of the study population by age range*

Sample characteristics	Age range		*p* value
	0–2 years old (n = 215)	Older than 2 years (n = 129)	
Female sex (%)	51.2	53.5	0.76
Presence of comorbidities (%)	13.6	18	0.30
Days elapsed between symptom onset and medical consultation	3.00 (2.00–4.00)	3.00 (2.00–4.00)	0.95
Fever (%)	72.1	69.8	0.74
Cough (%)	84.7	87.6	0.55
Rhinorrhea (%)	81.9	79.8	0.75
Gastrointestinal symptoms (%)	26	18.6	0.15
Odynophagia (%)	7.9	19.4	0.003*
Headache (%)	2.8	7.8	0.064
Respiratory distress (%)	26.5	14.7	0.016*

Categorical variables are expressed in percentages (%). Percentages were estimated for the total number of cases by sub-group.
Continuous variables are reported as median and interquartile range 25–75.
* Statistically significant difference ($p < 0.05$).

DISCUSSION

The Ministry of Health has observed that there was a significant reduction in ORVs in 2020[4] compared to 2019.[3] This may be the result of non-drug mitigation measures as a strategy for the prevention of SARS-CoV-2 infection.

In this study, the prevalence of ORVs was 40% in children suspected of COVID-19 but in whom SARS-CoV-2 tests were negative. Compared to the values recorded in 2020 (7.3%),[4] the increase was considerable but similar to what was reported in 2019 (36.3%),[3] suggesting a return to usual epidemiological figures. Although it would be reasonable to note that the study population differs in terms of clinical characteristics, the exclusion of patients with COVID-19 in both reports allows us to emphasize the reported changes in the trend. This study used the same detection techniques as those reported by the Ministry of Health.[3,6]

These findings are consistent with reports made in similar epidemiological conditions, which indicated an increase in prevalence after the return to school.[10,11] In Argentina, this was already reported among hospitalized patients in the winter of 2021,[12] although few studies have been conducted in outpatients.

A novelty of our study is that it reports on the prevalence of ORVs in outpatients. The gradual return to usual epidemiological patterns is clear, coinciding with the decrease in the circulation of SARS-CoV-2; however, this pattern could be modified due to the emergence of new variants.

Another strength was our attempt to find an association between the characteristics of the study population and the presence of infections due to ORVs. The higher frequency of odynophagia and headache in patients in whom ORVs were not detected and the greater presence of respiratory distress in those with RSV infection stand out. Most of the patients had respiratory symptoms such as rhinorrhea (81%) and cough (86%), so we do not consider that there are any biases in this regard. When these variables were introduced in the multivariate model, only the 0–2-year-old group maintained a statistically significant association in relation to the occurrence of RSV infection.

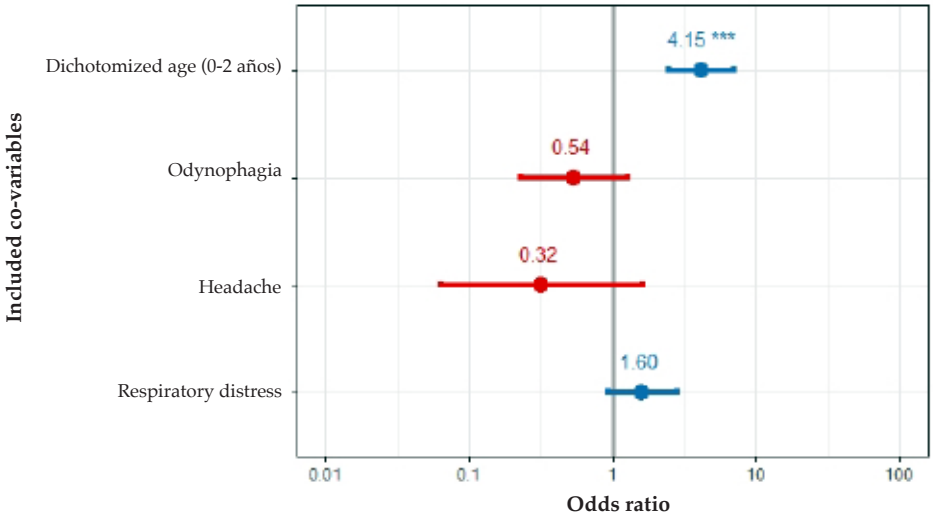
A limitation of this study was its limited period (EWs 31–38). However, the prevalence of RSV is consistent in both value and period of development with what has been reported nationally.[6]

It is possible that RSV infection in subjects with SARS-CoV-2 infection may have been underestimated. Notwithstanding this, co-infection is rare (3.2–4.3%), even in the pediatric population (2–8.2%).[13,14]

CONCLUSIONS

We identified a 40% prevalence of RSV infection in children who consulted due to suspected COVID-19 but in whom SARS-CoV-2 infection was ruled out. RSV identification was more common in children younger than 2 years.

FIGURE 2. *Multivariate logistic regression, measure of association (odds ratio) between study variables and virus identification*



NEG: negative; RSV: respiratory syncytial virus.

REFERENCES

1. Argentina. Ministerio de Salud. Guía de Vigilancia de las Infecciones Respiratorias Agudas. 2020. [Accessed on: March 31st, 2022]. Available at: https://portal-coronavirus.gba.gob.ar/sites/default/files/Guia%20Vigilancia%20Infecciones%20respiratorias%20agudas.%2006-08.pdf
2. Organización Mundial de la Salud. Alocución de apertura del Director General de la OMS en la rueda de prensa sobre la COVID-19 celebrada el 11 de marzo de 2020. [Accessed on: March 31st, 2022]. Available at: https://www.who.int/es/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
3. Argentina. Ministerio de Salud y Desarrollo Social. Boletín Integrado de Vigilancia. 2019;469;SE42. [Accessed on: March 31st, 2022]. Available at: https://bancos.salud.gob.ar/sites/default/files/2020-01/boletin-integrado-vigilancia-n469.pdf

Argentina. Ministerio de Salud. Boletín Integrado de Vigilancia. 2020;518;SE42. [Accessed on: March 31st, 2022]. Available at: https://bancos.salud.gob.ar/sites/default/files/2020-12/biv_518_se_42.pdf

4. Argentina. Ministerio de Salud del Gobierno de la Ciudad Autónoma de Buenos Aires. Protocolo de manejo frente a casos sospechosos y confirmados de Coronavirus (COVID-19) en Pediatría. Versión 15 Agosto 2021. [Accessed on: March 31st, 2022]. Available at: https://www.buenosaires.gob.ar/sites/gcaba/files/id_19_-_protocolo_de_manejo_de_casos_en_pediatria_1.pdf
5. Argentina. Ministerio de Salud. Boletín Integrado de Vigilancia. 2021;568;SE38. [Accessed on: March 31st, 2022]. Available at: https://bancos.salud.gob.ar/sites/default/files/2021-10/biv_568_se_38.pdf
7. Statistics Canada. Estimation. In: Survey Methods and Practices. Otawa: Minister of Industry; 2010.Pages.119-50.
8. Statistics Canada. Sample Designs. In: Survey Methods and Practices. Otawa: Minister of Industry; 2010.Pages.87-118.
9. R Core Team. R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing; 2021. [Accessed on: March 31st, 2022]. https://www.gbif.org/es/tool/81287/r-a-language-and-environment-for-statistical-computing
10. Hussain F, Kotecha S, Edwards MO. RSV bronchiolitis season 2021 has arrived, so be prepared! *Arch Dis Child*. 2021; 106(12):e51.
11. Delestrain C, Danis K, Hau I, Behillil S, et al. Impact of COVID□19 social distancing on viral infection in France: A delayed outbreak of RSV. *Pediatr Pulmonol*. 2021; 56(12):3669-73.
12. Ferrero F, Ossorio MF, Rial MJ. The return of RSV during the COVID-19 pandemic. *Pediatr Pulmonol*. 2022; 57(3):770-1.
13. Zhang DD, Acree ME, Ridgway JP, Shah N, et al. Characterizing coinfection in children with COVID-19: A dual center retrospective analysis. *Infect Control Hosp Epidemiol*. 2021; 42(9):1160-2.
14. Kıymet E, Böncüoğlu E, Şahinkaya Ş, Cem E, et al. Distribution of spreading viruses during COVID-19 pandemic: Effect of mitigation strategies. *Am J Infect Control*. 2021; 49(9):1142-5.