

# Respiratory syncytial virus and influenza surveillance in schoolchildren seen at a children's hospital over 2 months of the second semester of 2021

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## ABSTRACT

**Introduction.** Reporting of respiratory infections reduced during the COVID-19 pandemic. The objective was to estimate the prevalence of respiratory syncytial virus (RSV) and influenza in schoolchildren seen at a children's hospital during the return to school.

**Methods.** Cross-sectional study of patients aged 3–18 years suspected of COVID-19 with a negative test for SARS-CoV-2 between August and October 2021. Participants were stratified by level of education. PCR was used to detect RSV and influenza.

**Results.** A total of 619 children were included: 234 in pre-school, 224 in primary and 161 in secondary school; 25.5% (158) tested positive for RSV (36.3% in the pre-school level versus 21% in primary and 16% in secondary school). Infection among adolescents was associated with school contact with symptomatic cases (OR 2.5; 95%CI 1–6.80;  $p = 0.04$ ). No case of influenza was detected.

**Conclusion.** RSV was isolated in one fourth of the study population, with a higher frequency in pre-school; among adolescents, it was associated with school contact with symptomatic cases. No case of influenza was detected.

**Key words:** respiratory syncytial virus, respiratory infections, COVID-19, education, influenza.

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## INTRODUCTION

Acute respiratory infections (ARIs) are the leading cause of morbidity and mortality in pediatrics; respiratory viruses are the main agents involved.<sup>1</sup> In March 2020, the World Health Organization declared the pandemic of coronavirus disease 2019 (COVID-19). To limit the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), social activities were restricted and control measures were strengthened, which affected the circulation of respiratory viruses worldwide.

During 2020 and 2021, influenza virus circulation remained below expectations across all regions of the world.<sup>2</sup> In South America, respiratory virus activity was also low, with the exception of SARS-CoV-2, which remained at moderate to high levels in all countries in the region.<sup>3-6</sup> In Argentina, clinical reports of influenza-like illness, bronchiolitis, and pneumonia in 2021 were lower than in the same period of previous years.<sup>7</sup>

Active surveillance of acute lower respiratory tract infections (ALRTIs) is a critical tool for the rapid detection of any increase in the number of cases, the identification of high risk groups, and the determination of characteristics of disease causing microorganisms.<sup>8</sup>

At Hospital de Niños Ricardo Gutiérrez (HNRG), a completely atypical virus circulation pattern was observed during 2020, marked by the absence of cases of respiratory syncytial virus (RSV) and influenza (IF) infections, with isolated cases of ALRTIs caused by rhinovirus (RV), adenovirus (AV), and parainfluenza (PIF).<sup>9</sup>

The objective of this study was to estimate the prevalence of RSV and IF in school children and adolescents seen at HNRG during 2 months of the second semester of 2021 in the context of the return to in-person activities.

## OBJECTIVES

### General objective:

To estimate the prevalence of RSV and IF in schoolchildren seen at a children's hospital.

### Specific objectives:

- To assess RSV and IF circulation in schoolchildren aged 3–18 years by level of education seen at a children's hospital.
- To describe the clinical and epidemiological characteristics of the study population by virus isolation.

## POPULATION AND METHODS

Study design: cross-sectional, prospective study.

Study period: 8-2-2021 to 10-4-2021.

Population: schoolchildren (3–18 years) seen at a children's hospital suspected of COVID-19.

Inclusion criteria: schoolchildren aged 3–18 years who met the definition of suspected COVID-19 case and had a negative result for SARS-CoV-2.

Sample selection: convenience, non-probabilistic sampling; the first 5 patients seen by age group by level of education were recruited.

### Definitions

Age groups and level of education:

- Pre-school education: 3–5 years
- Primary education: 6–12 years
- Secondary education: 13–18 years

**Clinical diagnosis:** based on the definition of suspected COVID-19 case established by the National Ministry of Health to date.<sup>10</sup>

**Viral diagnosis:** a polymerase chain reaction (PCR) test was used to detect RSV and IF using nasopharyngeal swabbing samples previously tested and negative for COVID-19, without the need to re-test the patient.

**Contact with COVID-19 case:** a person who has been within 1.5 meters of a confirmed case for more than 15 minutes and who has not used appropriate protective measures.<sup>10</sup>

**Contact with ARI case:** close school or family contact with a person presenting acute respiratory symptoms: nasal congestion, rhinorrhea, cough, fever, general malaise and/or odynophagia, without laboratory diagnosis.

### Clinical and epidemiological data collection

The following data were collected in the epidemiological card: demographic, clinical, and epidemiological data about the school,

compliance with control measures, and potential sources of infection.

### Sample size calculation

In the study period, approximately 50 children with a presumptive diagnosis of COVID-19 were seen per day, with a positivity of less than 10%. Based on these data, 5 patients per level of education per day were included for 2 months and a minimum sample size of 148 subjects per group was calculated, with a 95% reliability level and an 80% power. The OpenEpi® software, version 3.01, was used for such calculation.

### Ethical considerations

Patients' privacy rights were warranted in all cases based on the ethical principles for medical research involving human subjects established by the World Medical Association Declaration of Helsinki. The patient informed consent form was not applicable in this study because data were collected from a routine epidemiological surveillance activity in the setting of National Law no. 15465/60.

### Statistical analysis

The sample was described using median and interquartile range for numerical variables and absolute number, percentage, and 95% confidence interval (CI) for nominal variables. Numerical variables were compared between 2 groups using Student's t test or the Wilcoxon rank-sum test; nominal variables were compared between 2 groups using the  $\chi^2$  test. The odds ratio (OR) with a 95% CI was used as a measure of association. A value of  $p < 0.05$  was considered statistically significant. The Epi Info 7® software was used for statistical analysis.

## RESULTS

### Characteristics of the population

A total of 619 patients aged 3–18 years, attending school, and with symptoms compatible with COVID-19 and a negative SARS-CoV-2 test were included. The prevalence of RSV was 25.5% (95% CI: 22.25–29.10). No case of influenza virus was detected.

The characteristics of the study population are described in *Table 1*.

Comorbidities were observed in 14.7% (91 cases); the most frequent ones were respiratory (77%). All cases were mild and none required hospitalization.

### Positivity by age group

The distribution of RSV cases by age group varied; prevalence almost doubled in the pre-school level of education compared to the other levels: 36.3% versus 21% in primary education and 16% in secondary education ( $p < 0.001$ ).

### Factors associated with RSV infection

Table 2 shows the variables analyzed by age group. In the group of adolescents, a statistically significant association was observed between RSV positivity and school contact with someone who had respiratory symptoms ( $p = 0.04$ ).

### DISCUSSION

In the context of the return to in-person activities and the advances in vaccination against SARS-CoV-2, it is necessary to maintain an active surveillance for respiratory viruses.

Several studies have shown a reduction in ARIs with an early end of seasonal outbreaks

of IF and RSV infection, as a result of restriction and lockdown measures, compared to previous seasons.<sup>11,12</sup>

In Argentina, the near absence of these viruses during the winter season of 2020 was remarkable. During 2021, according to official data, the reports increased compared to 2020, but they were fewer than in previous years, with isolated cases of adenovirus, parainfluenza, metapneumovirus, and influenza.<sup>7</sup>

The effect of school closures on ARI reduction is controversial. Data from the United States, where active RSV surveillance is in place, showed that re-opening schools was not associated with an increase in RSV infections.<sup>13</sup>

In 2021, in Tokyo, Japan, an unusually high number of viral infections was reported with the occurrence of RSV outbreaks after the COVID-19 pandemic, in different seasons and with a different trend compared to previous years.<sup>14</sup> Such variation has been observed in other regions,

TABLE 1. General characteristics of the study population (total and by level of education)

Variable	Total (n = 619) % (n)	Pre-school education (3-5 years) (n = 234) % (n)	Primary education (6-12 years) (n = 224) % (n)	Secondary education (13-18 years) (n = 161) % (n)	p value
Age (years) (median, IQR)	7 (4-13)	4 (3-4)	8 (7-9)	15 (14-17)	< 0.001
Female sex	51.7 (320)	53 (124)	47 (105)	56.5 (91)	0.15
Place of residence in CABA	74.7 (463)	72.7 (170)	76.8 (172)	75.1 (121)	0.34
Presence of comorbidities	14.7 (91)	13.2 (31)	16 (36)	14.9 (24)	0.69
Positive test for RSV	25.5 (158)	36.3 (85)	20.9 (47)	16 (26)	< 0.001
Presence of symptoms	100 (619)	100 (234)	100 (224)	100 (161)	0.95
Contact with a confirmed COVID-19 case	3.2 (20)	1.7 (4)	3.1 (7)	5.6 (9)	0.09
Contact with a symptomatic ARI case	1.6 (10)	2.5 (6)	0	2.5 (4)	0.05
Contact with a symptomatic case in the family	3.2 (20)	2.9 (7)	2.2 (5)	4.9 (8)	0.69
Contact with a symptomatic case in the same bubble	25.5 (158)	27.3 (64)	28 (63)	19.2 (31)	< 0.001

IQR: interquartile range; CABA: City of Buenos Aires; ARI: acute respiratory tract infection;

RSV: respiratory syncytial virus; COVID-19: coronavirus disease 2019.

Bubble: group of people in close contact due to family, emotional, work-related or educational ties.

TABLE 2. Factors associated with respiratory syncytial virus infection by age group

Variable	Pre-school education OR (95% CI); p	Primary education OR (95% CI); p	Secondary education OR (95% CI); p
Female sex	0.6 (0.4-1.1); 0.17	1.1 (0.58-2.1); 0.7	0.7 (0.3-1.6); 0.4
Presence of comorbidities	1.7 (0.8-3.8); 0.1	1.3 (0.5-2.9); 0.5	1.9 (0.6-5.5); 0.2
Contact with a confirmed COVID-19 case	0.5 (0.05-5); 0.5	0.5 (0.06-4.9); 0.6	2.4 (0.5-10.4); 0.2
Contact with a symptomatic ARI case	0.7 (0.1-4.3); 0.7	Not defined	4.8 (0.6-36); 0.09
Contact with a symptomatic case in the family	0.6 (0.1-3.6); 0.6	0.9 (0.03-7.8); 0.9	1.7 (0.3-9.4); 0.4
Contact with a symptomatic case in the same bubble	1.3 (0.6-2.5); 0.4	0.8 (0.4-1.8); 0.7	2.5 (1-6.8); 0.04

OR: odds ratio; CI: confidence interval; ARI: acute respiratory infection.

including the Americas and Australia, where substantial outbreaks of RSV infection were reported starting in the spring of 2021.<sup>6</sup>

This study shows that RSV caused 1 of 4 cases of ARI analyzed, and that it especially affected children in the pre-school level. The analysis of potential sources of infection showed that, in the group of adolescents, a statistically significant association was observed between RSV infection and school contact with someone who had respiratory symptoms. No case of influenza infection was detected.

This study has some weaknesses, such as the selection bias, its limited period, and the lack of investigation of other respiratory viruses. However, a strength of this study is that it was performed at a children’s hospital with vast experience in respiratory virus surveillance and with a reference virology laboratory, which contributed to early warning.

**CONCLUSION**

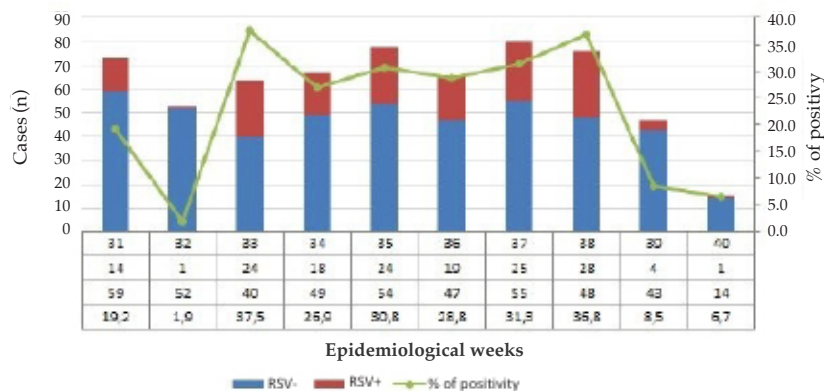
RSV was isolated in one fourth of samples from school children and adolescents seen at HNRG; the greatest impact was observed in children attending pre-school. Among adolescents, RSV infection was associated with a school contact with respiratory symptoms. No case of influenza virus was detected in the study period. ■

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FIGURE 1. Percentage of positive results for respiratory syncytial virus by epidemiological week



RSV: respiratory syncytial virus.

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