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Brief report

Acute bronchiolitis during the COVID-19 pandemic

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ABSTRACT

Introduction: The autumn and winter bronchiolitis epidemics have virtually disappeared in the first year of the COVID-19 pandemic.

Our objectives were characterised bronchiolitis during fourth quarter of 2020 and the role played by SARS-CoV-2.

Methods: Prospective multi-centre study performed in Madrid (Spain) between October and December 2020 including all children admitted with acute bronchiolitis. Clinical data were collected and multiplex PCR for respiratory viruses were performed.

Results: Thirty-three patients were hospitalised with bronchiolitis during the study period: 28 corresponded to rhinovirus (RV), 4 to SARS-CoV-2, and 1 had both types of infection. SAR-CoV-2 bronchiolitis were comparable to RV bronchiolitis except for a shorter hospital stay. A significant decrease in the admission rate for bronchiolitis was found and no RSV was isolated.

Conclusion: SARS-CoV-2 infection rarely causes acute bronchiolitis and it is not associated with a severe clinical course. During COVID-19 pandemic period there was a marked decrease in bronchiolitis cases.

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Bronquiolitis aguda durante la pandemia de COVID-19

RESUMEN

Introducción: La epidemia de bronquiolitis de otoño e invierno prácticamente desapareció durante el primer año de la pandemia de COVID-19.

Nuestros objetivos eran caracterizar la bronquiolitis durante el cuarto trimestre de 2020 y determinar el papel desempeñado por el virus SARS-CoV-2.

Métodos: Estudio multicéntrico prospectivo realizado en Madrid (España) entre los meses de octubre y diciembre de 2020, que incluyó a todos los niños ingresados con bronquiolitis aguda. Se recogieron los datos clínicos y se realizó una PCR múltiple para virus respiratorios.

Resultados: Se hospitalizó a treinta y tres pacientes con bronquiolitis durante el periodo del estudio: 28 correspondieron a rinovirus, 4 a SARS-CoV-2 y uno presentaba ambos tipos de infección. Las bronquiolitis por SAR-CoV-2 fueron comparables a las bronquiolitis por rinovirus, salvo por una estancia hospitalaria más corta. Se detectó una reducción significativa en la tasa de ingresos por bronquiolitis y no se aisló VSR.

Conclusión: Es raro que la infección por SARS-CoV-2 cause bronquiolitis aguda y no se asocia a una evolución clínica grave. Durante la pandemia de COVID-19 se produjo un descenso pronunciado de los casos de bronquiolitis.

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Palabras clave:

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◇ COVID-19 Study Group in Children is provided in Appendix A.

Introduction

Acute viral bronchiolitis is the main cause of hospitalisation in children under 1 year of age. Although all respiratory viruses can cause bronchiolitis, respiratory syncytial virus (RSV) is the primary agent in more than 70% of cases.¹

The coronavirus disease 2019 (COVID-19) pandemic has drastically changed the epidemiology of other viral respiratory infections in both children and adults. Worldwide, the autumn and winter RSV epidemics have virtually disappeared, and in some countries in the Southern Hemisphere like South Africa or Australia, the RSV season has moved to spring, marking an unprecedented phenomenon.² The incidence of symptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children is relatively low, and the disease causes lower symptom severity compared to adults. There is little information about the role of SARS-CoV-2 in bronchiolitis, although experimental studies performed in ferrets have shown lung lesions compatible with bronchiolitis.³ In addition, other human coronaviruses (HCoV) have been detected in up to 5% infants with bronchiolitis, with OC43 and 229E being associated with greater disease severity.⁴

We aimed to describe the epidemiology of bronchiolitis requiring hospitalisation during the fourth quarter of 2020 and characterise bronchiolitis associated with SARS-CoV-2 infection. Additionally, we compare the number of cases during the same period in 2019.

Methods

This is a prospective multicentre study carried out in 2 large university hospitals in Madrid (Hospital La Paz and Niño Jesús Children's Hospital) between 1 October and 31 December 2020. Inclusion criteria were infants under 1 year of age admitted with a diagnosis of acute bronchiolitis (first acute episode of wheezing with respiratory dyspnoea and catarrhal prodrome). Local research teams conducted structured interviews, reviewed medical records, and collected supplemental test results during hospitalisation. Within 24 h of admission, all children underwent testing with SARS-CoV-2 polymerase chain reaction (PCR) assay of nasopharyngeal swabs (Vircell; sensitivity 96%, specificity 100%) as well as a respiratory virus PCR panel that included RSV (FTD Respiratory Pathogens 21, Fast Track Diagnostics, Siemens). Patients with a severe underlying disease such as haematological cancer, immunodeficiency, or chronic pulmonary disease (e.g., cystic fibrosis, obliterative bronchiolitis, interstitial disease) and those undergoing chronic immunosuppressive treatment were excluded.

Additionally, we reviewed the number of cases and the proportion of RSV bronchiolitis recorded during the same period in 2019.

Qualitative data were expressed as absolute and relative frequencies and quantitative data as median and interquartile range (IQR). Categorical variables were compared using the chi-square and Fisher's exact test, and continuous variables were analysed with non-parametric tests as appropriate. A two-tailed *p* value <0.05 was considered statistically significant. All analyses were performed using the Statistical Package for the Social Sciences, version 21.0 (IBM Corp., CA, USA).

The study was approved by the ethics committee of both hospitals and parents signed informed consent.

Results

Out of 33 children hospitalised with bronchiolitis, 4 had SARS-CoV-2 infection and 28 had rhinovirus (RV) infection. One patient presented coinfection with both viruses and was excluded from

the analysis. No cases of RSV were identified. The median age at admission was 99 days (IQR 39–257) and 24 were male. Clinical characteristics of patients with RV and SARS-CoV-2 infection are shown in Table 1. SARS-CoV-2 bronchiolitis was associated with a shorter hospital stay: median 3 days (IQR 2.5–3) vs 4 days (IQR 2.2–6.7); *p*=0.003, likely related to the reduced need for oxygen therapy [median 1 day (IQR 1.0–1.5) vs 4 days (IQR 2.0–6); *p*=0.006]. In terms of clinical presentation, the groups had a similar course, although fewer patients with RV bronchiolitis developed fever (50.0% vs 10.7%, *p*=0.043) and diarrhoea (25.0% vs 0%, *p*=0.007). No patients with SARS-CoV-2 bronchiolitis required intensive care unit (ICU) admission or advanced life-support treatments such as nasogastric tube feeding or non-invasive mechanical ventilation, while 21% of patients in the RV group required such measures.

We found a dramatic decrease in the total number of paediatric admissions between 2019 and 2020 for the same seasonal period (833 vs 435 children) and in the number of admissions due to bronchiolitis (271 vs 33 children), a difference that was statistically significant (32.53% vs 7.59%, *p*<0.001). In 2019, most bronchiolitis cases were caused by RSV (241/271 bronchiolitis), while in 2020 there were no cases.

Discussion

Our results confirm the substantial change in the epidemiology of viral respiratory infections caused by the COVID-19 pandemic. The yearly wave of bronchiolitis admissions was virtually nonexistent, as in other countries.^{5–7} The annual RSV epidemic has not taken place yet, and it is unclear whether it will start during the next few months. In Australia, after the reduction of COVID-19 non-pharmacological interventions and the arrival of summer, an unusually delayed and steeper 'summer bronchiolitis and RSV peak' has been seen in certain regions, with an older median age and higher total numbers compared to the usual winter peaks.⁸ We might be pushing the 'RSV curve' forward and may not be able to stop this trend when we arrive at the exponential phase.

Due to the small number of patients included, we lack sufficient data to reach precise conclusions about SARS-CoV-2 bronchiolitis and how it differs from other viral infections. In our sample, infection with SARS-CoV-2 was not associated with increased disease severity. SARS-CoV-2 and RV bronchiolitis seem to have a similar clinical course although patients with SARS-CoV-2 bronchiolitis had shorter hospital stay and did not require advanced support treatment or ICU admission. This could be due, at least partially, to none of the COVID-19 patients having underlying diseases and only one being prescribed parenteral antibiotics because of suspected bacterial superinfection.

Regarding our case with coinfection due to SARS-CoV-2 and RV, it is known that coinfection is possible but might occur infrequently; not only the elderly or people with systemic diseases are at risk from this coinfection, but healthy children are also,⁹ which could impact the treatment and prognosis of the disease.

The number of bronchiolitis admissions in both centres for the current autumn-winter season has been much lower than predicted based on previous years.

More surprisingly, we have not detected any cases of RSV within the population areas served by the 2 hospitals, this despite rapid diagnostic tests performed in the emergency department in all symptomatic cases. Although some authors believe this to be the result of measures instituted to prevent SARS-CoV-2 transmission such as awareness-raising regarding handwashing, mask wearing, and isolation,² this does not seem to be the only plausible explanation. In our city, nurseries and primary schools have been fully open since the beginning of the academic year (autumn 2020). Although stricter hygiene measures have been implemented and the number

Table 1
Patient characteristics and respiratory pathogens in infants with bronchiolitis.

Variable	SARS-CoV-2 infection (n = 4)	Rhinovirus infection (n = 28)	p
Age, d, median (IQR)	133.5 (45.0– 248.5)	96.50 (39.25– 254.50)	0.381
Sex, n (%)			
Male	3 (75.00)	21 (75.00)	0.999
Female	1 (25.00)	7 (25.00)	
Prematurity (gestational age <37 wk), n (%)	2 (50.00)	6 (21.43)	0.217
Confirmed cohabitation with an individual positive for COVID-19, n (%)	3 (75.00)	0 (0)	<0.001
Underlying disease (heart disease, Down syndrome, chronic lung disease, immunodeficiency, others), n (%)	0 (0)	7 (25.00)	0.258
Clinical presentation, n (%)			
Onset of symptoms <24 h	1 (25.00)	5 (17.86)	0.732
Fever	2 (50.00)	3 (10.71)	0.043
Vomiting	0 (0)	7 (25.00)	0.258
Diarrhoea	1 (25.00)	0 (0)	0.007
Refusal to eat	2 (50.00)	9 (32.14)	0.482
Irritability	0 (0)	5 (17.86)	0.358
Wheezing	4 (100.00)	25 (89.29)	0.492
Apnoea	2 (50.00)	5 (17.86)	0.146
Exanthema, conjunctivitis	1 (25.00)	3 (10.71)	0.419
Vital signs on presentaion to the emergency department			
Tachycardia, n (%)	2 (50.00%)	7 (25.93)	0.322
Tachypnoea, n (%)	2 (50.00)	21 (75.00)	0.298
Baseline oxygen saturation (%); median (IQR)	95 (95– 96.5)	94 (92– 97)	0.718
Clinical course			
Length of hospital stay, d, median (IQR)	3.00 (2.5– 3.0)	4.00 (2.2– 6.7)	0.003
Oxygen therapy, d, median (IQR)	1.00 (1.0– 1.5)	4.00 (2.0– 6.0)	0.006
Tube feeding, n (%)	0 (0)	8 (28.57)	0.217
Mechanical ventilation, n (%)	0 (0)	12 (46.15)	0.124
Intensive care admission, n (%)	0 (0)	6 (21.43)	0.304
Radiological findings, n (%)			
Chest X-ray	2 (50.00)	16 (57.14)	0.788
Pneumonia	0 (0)	5 (31.18)	0.358
Pleural effusion	0 (0)	0 (0)	NA
Treatment, n (%)			
Oxygen therapy	3 (75.00)	26 (92.86)	0.252
Antibiotic	1 (25.00)	5 (17.86)	0.732
Salbutamol	1 (25.00)	9 (32.14)	0.773
Corticosteroids	0 (0)	5 (17.86)	0.358
Adrenaline	0 (0)	0 (0)	NA

n: number of cases; p: p-value; d: days; IQR: interquartile range; wk: weeks; h: hours; NA: not available.

of students per class has been limited, the use of masks is not mandatory until age 6 years. Even so, the circulation of respiratory viruses has diminished dramatically, except for SARS-CoV-2. Van Brusselen et al. suggest that this happens because infectious diseases such as bronchiolitis do not become real epidemics when transmission is inhibited by non-pharmaceutical interventions by adults and older children.⁶

Another hypothesis to explain this phenomenon is competition between respiratory viruses, in this case SARS-CoV-2 and RSV. Some viruses such as RV may interfere with and block infection by other respiratory viruses, either by competition of viral receptors in the mucosa of the respiratory tract or due to the production of interferon by infected respiratory-tract cells. Interactions between co-circulating, taxonomically different respiratory viruses can influence patterns of infection. RV interference may have produced a similar effect during the 2009 H1N1 influenza pandemic in Europe¹⁰ and, nowadays, has impaired SARS-CoV-2 replication and spread within the human respiratory epithelium. According to a forthcoming article by Dee et al., RV triggers an IFN response that makes most cells nonpermissive to SARS-CoV-2 infection.¹¹ The susceptibility of SARS-CoV-2 to the IFN response is illustrated by the number of genes present in its genome that are devoted to overcoming the innate immune response.¹² If accurate, these findings would support the theory that viral interference may alter the course of an epidemic and we must consider viral

interactions in the host as an influence in the observed population dynamics.

Our series of cases confirms that SARS-CoV-2 infection may cause acute bronchiolitis as has been previously published in other reports from around the world. Possibly due to various causes including public-health interventions aimed at preventing SARS-CoV-2 transmission and others factors such as the pandemic itself and interference between viruses, we have found an unexpected sharp decrease in admissions from acute respiratory illness and lower frequencies of RSV detection.

Conflict of interest

The authors declare that they have no conflict of interest.

Appendix A. COVID-19 Study Group in Children

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