

Unexpected peak of bronchiolitis requiring oxygen therapy in February 2020: Could an undetected SARS-CoV2-RSV co-infection be the cause?

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January 29, 2021

Abstract

Respiratory syncytial virus (RSV) infection is the leading cause of bronchiolitis among infants <12 months old. It is widely known that coinfections between RSV and other viruses can worsen the clinical picture of affected patients. To evaluate the severity of clinical pictures of bronchiolitis in the 2019-2020 winter season, we performed a retrospective study of our third-level Pediatric Emergency Department (ED) admission charts. From February 2 to March 9, 2020 (start date of the Italian lockdown), we observed a peak of patients with a clinical picture of bronchiolitis requiring oxygen therapy of 55.1%, compared with 18% and 14.5% during the same period in 2017-2018 and 2018-2019, respectively ($p < 0.0001$), without other clinically significant differences between the groups. Several authors hypothesized that SARS-CoV2 was present in northern Italy some weeks before the first confirmed case. We suggest that one of the causes of this unexpected severe bronchiolitis peak may be a SARS-CoV2 - RSV coinfection in a period when SARS-CoV2 was already circulating in north-ern Italy. Given the lack of real-time polymerase chain reaction (RT-PCR) tests for SARS-CoV2 at that time, our suggestion remains a hypothesis.

Unexpected peak of bronchiolitis requiring oxygen therapy in February 2020: Could an undetected SARS-CoV2-RSV co-infection be the cause?

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ABSTRACT

Respiratory syncytial virus (RSV) infection is the leading cause of bronchiolitis among infants <12 months old. It is widely known that coinfections between RSV and other viruses can worsen the clinical picture of affected patients.

To evaluate the severity of clinical pictures of bronchiolitis in the 2019-2020 winter season, we performed a retrospective study of our third-level Pediatric Emergency Department (ED) admission charts.

From February 2 to March 9, 2020 (start date of the Italian lockdown), we observed a peak of patients with a clinical picture of bronchiolitis requiring oxygen therapy of 55.1%, compared with 18% and 14.5% during the same period in 2017-2018 and 2018-2019, respectively ($p < 0.0001$), without other clinically significant differences between the groups.

Several authors hypothesized that SARS-CoV2 was present in northern Italy some weeks before the first confirmed case.

We suggest that one of the causes of this unexpected severe bronchiolitis peak may be a SARS-CoV2 - RSV coinfection in a period when SARS-CoV2 was already circulating in northern Italy. Given the lack of real-time polymerase chain reaction (RT-PCR) tests for SARS-CoV2 at that time, our suggestion remains a hypothesis.

To the editor:

In the current winter season, children's hospitals may have to face the seasonal outbreak of bronchiolitis in a never seen context of COVID-19 pandemic. Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis among infants < 12 months, presenting with a seasonal pattern with greater prevalence in the winter and spring months(1). SARS-CoV2 officially appeared in Italy just as the RSV-bronchiolitis season was winding down. As a result, there was never a real overlap between SARS-CoV2 and RSV.

However, several authors hypothesized that SARS-CoV2 was present in northern Italy some weeks before the first Italian confirmed case on February 20, 2020 (2–5). As a result, we suspected that this virus, circulating as early as 2020, may have aggravated the course of some infants with bronchiolitis.

We performed a retrospective study to evaluate the frequency and severity of infants presenting with a clinical picture of bronchiolitis to the Pediatric Emergency Department (ED) of Giannina Gaslini Institute, the largest children hospital in northern Italy, in the period between, the first identification of COVID-19 in the polluted water of the city of Milan (2) and the start of Italian lockdown, (December 1st 2019-March 9th 2020).

Results were compared with the same time frame in 2017-18 and 2018-19 seasons.

The Kruskal-Wallis test was used to determine if there are statistically significant differences between groups. A p -value less than 0.05 was considered as statistically significant. All data analyses were done with Stata® version 13 software (StataCorp LLP, Texas, USA).

A total of 125, 244 and 211 patients with a clinical picture of bronchiolitis were observed in 2019-2020, 2018-2019 and 2017-2018 group, respectively.

No statistically significant differences in age, pre-existing medical conditions (including prematurity), triage severity score at ED presentation, hospitalization rate and length of stay were noted between groups (table 1).

Figure 1 report the proportion of severe bronchiolitis observed in the three time periods. From February 2nd to March 9th, 2020, (weeks 10 to 13), 55.1% of the patients admitted with a clinical picture of bronchiolitis required oxygen therapy (given when oxygen saturation < 92%) compared with the 18% and 14.5% observed in the same period in 2017-2018 and 2018-2019, respectively ($p < 0.0001$) (table 1).

We found no differences between groups in the type of ventilatory support. High flow nasal cannulae (HFNC) was used in 45.5%, 55%, and 39% of cases in groups 2019-20, 2018-19, and 2017-2018, respectively.

Neither in the week-10-13 period, no significant difference in HFNC was observed between the three groups (26.6%, 60%, and 40%, respectively).

Continuous positive airway pressure (CPAP) was used in only one case in each period.

Although not statistically significant we observed an increase in the length of oxygen therapy in the 2019-2020 (median: 96 hours; IQR: 72-144) and 2018-2019 (96 hours; IQR: 48-120) groups as compared with the

2017-2018 group (48 hours; IQR 24-108).

Multiplex PCR on specimen of nasal swab was performed in almost 60% of patients observed and an etiological diagnosis was obtained in 100%, 98% and 91% of tested patients in 2019-2020, 2018-2019 and 2017-2018 group, respectively.

RSV was the most common causative germ (Table 1).

At that time real-time polymerase chain reaction (RT-PCR) test for SARS-CoV-2 detection in the respiratory tract was not available.

RSV is the leading cause of bronchiolitis and has a seasonal epidemiology with a peak in the period December-March, when frequently co-circulate with coronaviruses(1).

Our data show the presence of an unexpected proportion of infants with a clinical picture of severe bronchiolitis requiring oxygen therapy in the season 2019-2020, just in the weeks preceding the declaration of COVID-19 pandemic in Italy. Co-infections of SARS-CoV-2 and other viruses has been described in children(6). However the description of cases of RSV bronchiolitis with severe respiratory distress who tested positive also for SARS-CoV2 is rare (7). Our data seem to suggest the possible co-circulation of these 2 viruses that lead to an increase in the proportion of severe cases of bronchiolitis in 2019-2020 compared with the 2 previous years. Unfortunately, because of the lack of RT-PCR test in that period this remains an epidemiology-driven hypothesis. Anyway, we want to stress the possibility of RSV and SARS-CoV-2 (or other “new” respiratory viruses in the future) co-infection as a cause of severe bronchiolitis during the winter season for its implications (therapy and isolation procedures) in infants’ management in ED and to stress the need of continuous epidemiological surveillance for the occurrence of new and unexpected clinical conditions.

Author contributions

GAR, Em.C developed study design and wrote the paper. GB, EP, El.C performed manuscript revision. GAR analyzed data. El.C supervised the work. All authors reviewed and approved the final version.

Funding sources

None reported.

Declaration of interests

The authors have no conflicts of interest to declare.

REFERENCES

1. Meissner HC. Viral Bronchiolitis in Children. *N Engl J Med.* 2016 Jan 7;374(1):62–72.
2. La Rosa G, Mancini P, Bonanno Ferraro G, Veneri C, Iaconelli M, Bonadonna L, et al. SARS-CoV-2 has been circulating in northern Italy since December 2019: Evidence from environmental monitoring. *Sci Total Environ.* 2021 Jan 1;750:141711.
3. Amendola A, Bianchi S, Gori M, Colzani D, Canuti M, Borghi E, et al. Evidence of SARS-CoV-2 RNA in an Oropharyngeal Swab Specimen, Milan, Italy, Early December 2019. *Emerg Infect Dis.* 2020 Dec 8;27(2).
4. Gianotti R, Barberis M, Fellegara G, Galván-Casas C, Gianotti E. COVID-19 related dermatosis in November 2019. Could this case be Italy’s patient zero? *Br J Dermatol.* 2021 Jan 7;
5. Apolone G, Montomoli E, Manenti A, Boeri M, Sabia F, Hyseni I, et al. Unexpected detection of SARS-CoV-2 antibodies in the pre-pandemic period in Italy. *Tumori.* 2020 Nov 11;300891620974755.
6. Di Nardo M, van Leeuwen G, Loreti A, Barbieri MA, Guner Y, Locatelli F, et al. A literature review of 2019 novel coronavirus (SARS-CoV2) infection in neonates and children. *Pediatr Res.* 2020 Jul 17;
7. André MC, Pätzug K, Bielicki J, Gualco G, Busi I, Hammer J. Can SARS-CoV-2 cause life-threatening bronchiolitis in infants? *Pediatr Pulmonol.* 2020 Sep 4;

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