


The effects of COVID-19 outbreak on pediatric emergency department admissions for acute wheezing

Lorenzo Di Sarno MD¹ | Antonietta Curatola MD¹  | Giorgio Conti MD² |
Marcello Covino MD³ | Chiara Bertolaso MD⁴ | Antonio Chiaretti MD¹ |
Antonio Gatto MD⁴

¹Department of Pediatrics, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy

²Pediatric Intensive Care Unit, Department of Anesthesia and Intensive Care, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy

³Department of Emergency, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy

⁴Department of Pediatrics, Fondazione Policlinico Universitario "Agostino Gemelli" IRCCS, Rome, Italy

Correspondence

Antonietta Curatola, MD, Department of Pediatrics, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy.
Email: c.anto91@libero.it

Abstract

Introduction: Acute wheezing is a common clinical presentation of viral respiratory infections in children, which can also be caused by exposure to allergens and, rarely, by foreign body inhalation. Since the beginning of the COVID-19 (coronavirus disease 2019) outbreak, several public health interventions have been adopted to reduce viral spread. The aim of this study was to analyze the impact of the COVID-19 pandemic and lockdown measures on Pediatric Emergency Department (ED) admission for acute wheezing.

Materials and Methods: We compared demographics and clinical data of patients admitted to the ED for acute wheezing during the COVID-19 outbreak and in the 5 previous years through a retrospective cross-sectional study.

Results: During the COVID-19 outbreak we observed an average drop of 83% in pediatric ED admission for acute wheezing, compared to the 5 previous years. In this period, 121 (80.7%) children presented with wheezing and 29 (19.3%) with bronchiolitis. The mean age of the sample was higher compared to the 5 previous years. We also noted an increased number of children presenting with higher acuity color codes during the COVID-19 period, while no differences emerged as for the hospitalizations. During the pandemic we recorded a decrease in the number of viral infections detected. Only two cases of wheezing associated with SARS-CoV-2 were identified.

Conclusion: The COVID-19 outbreak and the national lockdown led to a drop of the number of admission to the ED for wheezing in children. This could be due to a reduction in the circulation of common respiratory viruses and partially to a reduced exposure to aeroallergens during the COVID-19 period. Future epidemiological surveillance studies will be needed to support these preliminary findings.

KEYWORDS

children, COVID-19, emergency department, outbreak, wheezing

1 | INTRODUCTION

Acute respiratory infections (ARIs) in children represent the main cause of admission to Pediatric Emergency Departments (ED) during the autumn and winter months.¹ Wheezing is a common symptom of these respiratory infections and one in three children will have at least one acute wheezing illness before the age of 3 years.^{2,3} ARIs represent a major cause of morbidity and mortality worldwide and have a significant impact on antibiotic prescriptions and the rate of hospitalization.⁴ In addition to viral infections, the exposure to allergens in asthmatic children, anaphylaxis and, rarely, foreign body inhalation are other causes of acute wheezing in the paediatric population.⁵

Bronchiolitis is the most common ARI involving children under 2 years of age, and is usually due to respiratory syncytial virus infection (RSV).⁶ However, other viruses such as rhinovirus, metapneumovirus, human bocavirus, (para) influenza, adenovirus and seasonal coronavirus can be responsible for wheezing.⁶ Nowadays, seven Coronavirus (alpha, beta, gamma, and delta coronaviruses) are known to infect humans, causing respiratory and gastrointestinal symptoms. A new Coronavirus (2019-nCoV) was identified as the cause of pneumonia in China at the end of December 2019 and on March 2020, the World Health Organization declared the novel coronavirus (COVID-19) outbreak a global pandemic.⁷ Subsequently, several public health interventions have been put in place including border control, quarantine, massive reverse-transcription polymerase chain reaction testing for case detection, rapid contact tracing, hand hygiene, community-wide wearing of face masks and social distancing measures, to avoid the risk of community transmission.⁸ These measures not only contained the pandemic but also limited the transmission of other respiratory viruses.⁹ In contrast to adult patients, the current SARS-CoV-2 pandemic showed low morbidity and near-absent mortality in previously healthy children.^{10,11} However, although there were fewer pediatric ED admissions and hospitalizations due to the virus, there still was a potentially increased risk of acute respiratory diseases due to COVID-19 in asthmatic children.¹² The aim of this study was to analyze the impact of the COVID-19 pandemic and lockdown measures on ED visits for acute wheezing in children since the beginning of the pandemic, comparing these data with those of the 5 previous years.

2 | MATERIALS AND METHODS

A retrospective, analytical, cross-sectional study was carried out at the ED of a tertiary University Hospital in Rome (Italy), with annual attendance of about 15,000 patients from the ages of 1 month to 18 years of age. Pediatric patients presenting to the ED with wheezing, cough or respiratory distress were studied. We included children with a diagnosis of acute wheezing after a respiratory viral infection, bronchiolitis, acute respiratory failure and acute asthma exacerbations according to ICD-10 (International Classification of Diseases) guidelines, selected from the hospital's Electronic Medical Record

system used in the ED (Gipse®). We excluded children with upper airway infections, pneumonia and other respiratory infectious diseases not accompanied by wheezing on auscultation. Demographic, epidemiological and clinical data were collected, including age, gender, triage color code, prematurity and/or other comorbidities (bronchopulmonary dysplasia, asthma, atopy, genetic syndromes), modality of transport to the ED, duration and rate of hospitalization and therapy. The triage color codes, assigned to patients by the triage nurse based on the child's general conditions, symptoms, and vital signs, were: "red code" for maximum priority, "yellow code" for high priority, and "green code" for low priority care. In the group of hospitalized patients, we analyzed microbiological data as well, including nasopharyngeal swabs for all respiratory viruses. Thus, two patient groups were studied: patients admitted to the ED from March 2020 to March 2021 (COVID-19 period) and patients admitted in the same period in the 5 previous years. This study protocol was approved by the Institutional Review Board and Medical Ethics Committee of our institution.

3 | STATISTICAL ANALYSIS

Categorical variables are reported as counts and percentages. Normality of distribution of continuous variables was tested by means of Shapiro Wilk test. Continuous variables are expressed as means and standard deviations or as median and interquartile ranges, if not normally distributed. Statistical comparisons between groups was performed by Chi-squared tests or Fisher's exact test, as appropriate, for categorical variables. Differences in normally distributed continuous variables were tested by two-tailed unpaired Student's *t* test, while Mann-Whitney *U* test was used for not normally distributed continuous variables. The incidence rate was obtained by dividing the number of cases of wheezing by the number of visits to the ED during the COVID-19 outbreak and other years. A two sided *p* value <0.05 was considered as statistically significant. A bivariate logistic regression model was estimated to assess whether the period (COVID-19 period or previous 5 years) was associated with the diagnosis of infectious wheezing. All data analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 25.0, SPSS Inc.).

4 | RESULTS

During the COVID-19 period 7873 children were admitted to our pediatric ED compared to a mean of 13,488 per year in the previous 5 years, which represents a 42% decrease of total ED visits. During the COVID-19 pandemic period 150 (1.9%) patients suffered wheezing, compared to 4510 (33.4%) in the previous 5 years, corresponding to a mean of 902 children per year; this is equivalent to an average drop of 83% in pediatric ED visits for acute wheezing. Among total ED visits for wheezing, during the COVID-19 period we observed 121 children (80.7%) who presented with wheezing and 29

who presented with bronchiolitis (19.3%) compared to a mean of 619 cases per year (68.6%) presenting with wheezing and a mean of 282 presenting with bronchiolitis (31.3%) in the previous 5 years ($\chi^2(1, N = 4660) = 9.81, p < 0.01$). Therefore, we found a greater reduction in the rate of bronchiolitis (89.8%) than in wheezing (80.4%).

The demographic characteristics of the study population are detailed in Table 1. During the COVID-19 period, 98 (65.3%) children admitted to ED for wheezing were male, overall there were no statistically significant differences for gender in the two study periods. The mean age was 6.25 ± 4.93 years in the COVID-19 group compared to 5.33 ± 4.75 years in the previous 5 years ($t = -2.32$ (4658); $p = 0.020$). No major differences were found in the proportion of patients with a history of prematurity, while children with other comorbidities were more represented during the COVID-19 period (27.3% vs. 13.0% in the previous 5 years, $p < 0.01$). At admission to the ED, fever was present in 71 (47.3%) children during the

COVID-19 period and in 1772 (39.3%) in the 5 previous years ($p = 0.047$).

Focusing on the triage color code assigned to the patient on arrival to the ED, we detected a meaningful reduction of patients triaged as Low Priority during the COVID-19 period compared to the previous 5 years (67.3% vs. 86.1%, $p < 0.01$). Whereas the number of patients admitted as Emergency and High Priority increased during the COVID-19 period (0.7% vs. 0.5% for Emergency cases, 31.3% vs. 12.9% for High Priority cases, $p < 0.01$). Analyzing data concerning the modality of transport to the ED, we observed an increase in the number of patients transported by ambulance during the pandemic period (9.3% vs. 4.5% in the previous 5 years) and a decrease in the number of children who came to the ED by family (90.7% vs. 95.3% in the previous 5 years, $p = 0.020$).

The median time spent in the emergency room during the COVID-19 pandemic was 100 min [40.72–260.25] compared to

TABLE 1 Demographics, clinical features, triage codes and treatment of children with wheezing admitted to ED during the COVID-19 outbreak compared to the previous 5 years

	2015–19 Years no. (%)	Mean (\pm SD)	COVID-19 period no. (%)	Mean (\pm SD)	<i>p</i> value
Total number patients to ED	67440		7873		–
Total number of wheezing	4510 (33.4)		150 (1.9)		–
Gender (M)	2612 (57.9)		98 (65.3)		0.070
Age (years)		5.33 \pm 4.75		6.25 \pm 4.93	0.020
Prematurity	74 (1.6)		4 (2.7)		0.520
Other comorbidity	585 (13.0)		41 (27.3)		<0.01
Fever	1772 (39.3)		71 (47.3)		0.047
Infectious etiology	2933 (65.0)		81 (54.0)		<0.01
Urgency (triage code)					< 0.01
Emergency consultations (red code)	21 (0.5)		1 (0.7)		
High priority consultations (yellow code)	583 (12.5)		47 (31.3)		
Low priority consultations (green code)	3883 (86.1)		101 (67.3)		
Treatment					
Antihistamines	657 (34.5)		22 (34)		0.94
Corticosteroids	1136 (59.6)		34 (54)		0.37
Salbutamol	650 (34.1)		26 (41.3)		0.23
Ipratropium bromide	69 (3.6)		1 (1.6)		0.39
Respiratory support					
Without respiratory support	4390 (97.3)		143 (95.3)		<0.01
Low flow oxygen therapy	120 (2.7)		5 (3.3)		
High flow oxygen therapy	0 (0)		2 (1.3)		

Note: Bold values correspond to statistically significant *p* values.

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; SD, standard deviation.

73 min [32–152] in the previous 5 years ($p < 0.01$). In addition, the rate of Short Stay Observation (SSO) of children admitted to ED for wheezing, increased during the SARS-CoV-2 pandemic compared to the 5 previous years (14% vs. 3.6%, $\chi^2(1) = 40.89$, $p < 0.01$). On the other hand, no significant differences were observed as for the rate of hospitalizations for wheezing to the inpatient units and to the pediatric intensive care units (PICU). We also looked at therapies (including antihistamine, steroid, salbutamol, ipratropium bromide and oxygen therapy) administered to patients in the ED according to the severity of the disease. No statistically significant differences were found between the two study periods for the use of antihistamines, steroids, salbutamol and ipratropium bromide; instead, we saw an increase in Low Flow Oxygen therapy (3.3% vs. 2.7%) and High Flow Oxygen therapy use (1.3% vs. 0%) ($\chi^2(2, N = 4660) = 15.19$, $p = 0.001$) during the COVID-19 pandemic compared to the previous 5 years (Table 1).

Finally, regarding the etiology of acute wheezing, we recorded a decrease in viral infections during the COVID 19 period: 54% during the pandemic versus 65% in the previous 5 years ($p < 0.01$). A logistic regression model was used to assess whether the COVID-19 period influenced the probability of having infectious wheezing. The analysis showed that the risk of infectious wheezing decreased by a factor of 0.63 in the COVID-19 period compared to the previous 5 years ($\chi^2(1) = 7.47$, $p < 0.01$). In addition, among the 150 patients admitted to the ED for wheezing during the COVID-19 pandemic, 67 (44.7%) children had nasopharyngeal swabs for SARS-CoV-2 performed and only 2 (1.33%) of them were positive. These two children presented as High Priority codes on admission to the ED but both were discharged without complications.

5 | DISCUSSION

This retrospective study showed a significant drop in pediatric ED visits for acute wheezing since the spread of quarantine measures related to the COVID-19 pandemic, as shown in previous studies such as an American study by Kenyon et al, that reported an overall 76% drop in visits for asthma, both mild and severe,¹³ or a Spanish study, conducted after the first wave of COVID-19, which showed a 82% reduction in ED visits for asthma compared with the previous year.¹⁴ Gujon et al.,¹⁵ in a study on a large sample of children treated for asthma at The Children's Hospital of Orange County network stated a 90% reduction in ED visits during the first lockdown (April–June 2020) compared to the same period of the previous year.

In our ED, we usually see children from 1 month to 18 years of age, suffering not only from acute wheezing after a respiratory viral infection but also from acute bronchiolitis. During the COVID-19 period, we observed an increase in the average age of children admitted to the ED with wheezing as well as a reduction in the rate of bronchiolitis, affecting children younger than 2 years of age. This is consistent with other data in the literature that showed a marked reduction of acute bronchiolitis during the pandemic worldwide.^{16,17}

In regard to the severity of wheezing on admission to the ED, according to the triage color code, we found a decrease in patients triaged as Low Priority and an increase in children admitted as Emergency and High Priority during the pandemic compared to previous years. In addition, the number of cases brought into the ED by ambulance also increased compared to the previous 5 years of observation. On the one hand, this aspect may reflect the parents' fear of contracting the virus, which brought them to the ED only when their children presented with more severe symptoms.

On the other, at the beginning of COVID-19 pandemic nurses and physicians did not know the evolution of COVID-19 disease in children, consequently nurses assigned children with symptoms suspicious for COVID-19 a higher priority code to the triage and ambulances were required more often if only to avoid transporting suspected patients by other means.

Unlike a recent Spanish study, we showed an increase in median time spent in the emergency room during the COVID-19 outbreak, as well as an increase in the rate of SSO in children with wheezing.¹⁴ This could be due to several factors.

First, the prolonged time spent in the ED in our hospital could have been related to the waiting times for COVID testing, which required about 4 h. During the pandemic, institutional protocols required the result of a molecular swab for SARS-CoV-2 before a patient could be hospitalized, in order for the patient to be admitted to the correct unit; this certainly increased the rate and duration of SSO and often required for treatment to be initiated promptly in the ED. In addition, during the first wave pediatricians required longer observation times for children as they did not know the clinical evolution of COVID-19 disease.

Differently to other studies,^{15,18} in our sample no statistically significant differences were found as for the rate of hospitalization, both on the ward and in the PICU between the two periods. This suggests that the higher number of children admitted as higher priority codes was due to nurses' fear and lack of knowledge of COVID-19 disease. In the United States (US) an analysis, performed on 77 PICUs at the beginning of the pandemic, found a marked decrease in asthma-related hospitalizations.¹⁸

As for treatment, no differences emerged as for the use of antihistamine, steroids, salbutamol and ipratropium bromide between the two periods analyzed. Differently, Gujon et al.¹⁵ showed a 68% decrease in oral corticosteroid use. Furthermore, guidelines on the management of acute asthma exacerbations in the ED have changed since the beginning of the pandemic. The use of nebulization was discouraged because of the increased risk of exposure to the virus for caregivers and health care professionals.^{19,20} As our study was retrospective, we could not tell from our analysis whether during the COVID-19 outbreak inhaled medications were administered by nebulization or pressurized metered dose inhaler. In addition, during the COVID-19 period we observed an increase of Low Flow and High Flow Oxygen therapy in children with acute wheezing, which could be due to the higher acuity of wheezing cases admitted to the ED. However, because of the prolonged waiting times for COVID testing results, children started oxygen therapy in the ED, Short Stay

Observation had a longer duration, and patients were directly discharged after a few days. Analyzing the etiology of pediatric wheezing, our study highlighted a marked decrease in the infections detected (54% during the pandemic vs 65% in the previous 5 years). This agrees with previous reports, which showed a reduction in respiratory infectious diseases during the COVID-19 outbreak.²¹⁻²³ In this period, the use of facemasks, social distancing, and hand hygiene to prevent the spread of SARS-CoV-2, had a protective effect on children from respiratory viral infections, and younger children benefitted strongly from these public health measures.⁹ However, regardless of the reduction in infectious wheezing episodes, overall the average rate of ED admissions for wheezing was less frequent during the COVID-19 pandemic according to other studies.¹⁷ We hypothesized that, during the lockdown children were forced to stay home, and therefore experienced a reduction in exposure to seasonal allergens, such as pollens. A decrease in air pollution could also explain these findings. In support of this hypothesis, Gujon et al.¹⁵ in California confirmed a correlation between the reduction in ED visits for asthma exacerbation and the reduction in particulate matter as well as in viral infections.¹⁵ Differently, Sayed et al.²⁴ in Philadelphia did not observe changes in the rate of air pollution and in the environmental aeroallergens during the pandemic compared with previous seasonal data, while they highlighted a significant reduction of viral infections including RSV, Rhinovirus, Influenza A and B.

During the COVID-19 period in our sample only two children, admitted to ED, resulted positive to SARS-CoV-2 PCR test. From our data analysis, SARS-CoV-2 infection does not appear to be associated with an increased risk of wheezing and asthma exacerbations in children. Our previous study demonstrated that SARS-CoV-2 infection is not related to an increased risk of developing bronchiolitis in childhood.¹⁶ In a study conducted in the United States no positive SARS-CoV-2 samples were observed in children admitted with viral wheezing or asthma during the start of the school year.²⁵ Makrinioti et al.²⁶ hypothesized that the reduced rate of wheeze attacks triggered by SARS-CoV-2 could be due to the low expression of ACE2 receptor in children. A review analyzing the relationship between asthma and COVID-19 in childhood showed that asthma did not appear to be a risk factor for more severe SARS-CoV-2 infections, rather it was considered as a protective factor.²⁷ The explanation could be that some immunological mechanisms that cause high morbidity and mortality in respiratory infections triggered by other viruses in asthmatics, are the same responsible for protection during SARS-CoV-2 infection.²⁷

Our study shows several limitations. First of all, the retrospective and single-center design of the study limits some assessments, such as the use of nebulization or pressurized metered dose inhaler, and does not allow generalization of our findings to all the pediatric population. Secondly, we do not know the etiology of wheezing for all patients admitted to the ED, because in our Department the nasopharyngeal swab is performed only for children admitted to the pediatric ward or intensive care unit. Therefore, we cannot give a real assessment of the changes in viral circulation during the pandemic period. Finally, we have not included, in our analysis, any chronic

treatment carried out by asthmatic patients, which may have affected the actual exposure of these patients to the virus.

In conclusion, the ongoing COVID-19 outbreak and public health measures adopted to reduce the spread of coronavirus could also have reduced the circulation of other respiratory viruses. Future epidemiological surveillance studies will be needed to support these initial findings. In addition, the initial total lockdown worldwide led to a significant reduction in children's exposure to various aeroallergens, thus resulting in a drop of visits to the ED for wheezing. We therefore want to highlight the importance for children suffering from recurrent wheezing to respect hygienic measures, such as handwashing and use of face-masks, to reduce the risk of wheezing or asthma exacerbations during epidemic viral season.

AUTHOR CONTRIBUTIONS

Lorenzo Di Sarno: conceptualization-equal, data curation-equal, writing—original draft-equal. **Antonietta Curatola:** conceptualization-equal, data curation-equal, formal analysis-equal, writing—original draft-equal. **Gior-gio Conti:** conceptualization-equal, writing—review and editing-equal. **Marcello Covino:** data curation-equal, writing—review and editing-equal. **Chiara Bertolaso:** data curation-equal, writing—review and editing-equal. **Antonio Chiaretti:** Project administration-Equal, Writing—review and editing-Equal. **Antonio Gatto:** conceptualization-equal, writing—review and editing-equal.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Antonietta Curatola  <https://orcid.org/0000-0002-2430-9876>

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