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Acute bronchiolitis - before and after the SARS-CoV-2 pandemic

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ABSTRACT

Aim. This study aimed to assess the changes in the number of patients diagnosed with acute bronchiolitis, the forms of severity of the disease, and the management after the COVID-19 pandemic.

Material and method. We included in the study children diagnosed with acute bronchiolitis between October 2019 and March 2020 and October 2022 and March 2023. It was a retrospective, descriptive, observational study. We collected the clinical data, investigations, and medication used from the medical records.

Results. A total of 233 patients were included in the study: 98 patients in the pre-pandemic group and 135 patients in the post-pandemic group. There was a higher number of patients diagnosed in November and December in the post-COVID-19 group. There was a significant increase in the number of chest radiographs that were performed ($p<0.0001$). In the pre-COVID-19 group, a chest X-ray was performed in 23/98 (23.4%) children, and in the post-COVID-19 group, 105/135 (77.7%) children had a chest X-ray. Eight/98 patients (8.2%) associated pneumonia in the first group and 31/135 (22.9%) in the second group. Antibiotics were administered in the pre-pandemic group in 36/98 (36.7%) children, while in the post-pandemic group 66/135 (48.9%).

Conclusions. There was a significant increase in X-rays performed after the COVID-19 pandemic in children with acute bronchiolitis. Overuse of investigations and medication in children with acute bronchiolitis, although not a new problem, might have been influenced by the measures taken during the COVID-19 pandemic in patients with respiratory symptoms.

Keywords: acute bronchiolitis, children, COVID-19

INTRODUCTION

Acute bronchiolitis is a disorder of the lower respiratory tract characterized by inflammation, edema, mucus production, and necrosis of the epithelial cells lining the small respiratory airways caused by a virus [1,2]. Acute bronchiolitis remains a clinical diagnosis with signs and symptoms of a lower respiratory tract infection (cough, wheezing, coarse crackles, prolonged expiration), preceded by signs of upper viral respiratory tract infection (rhinorrhea, nasal obstruction, low-grade fever) [1-6].

The leading causes of acute bronchiolitis in children are respiratory syncytial virus (RSV), followed by rhinovirus (RV) and Human bocavirus [7]. SARS-CoV-2 was rarely a cause of acute bronchiolitis [8]. RSV affects mostly small infants, while RV is detected more frequently in children over 12 months of age [9] and those with personal and family history of allergy and asthma [10].

Acute viral bronchiolitis has a variable course in children. A severe disease course had not been linked to a particular type of viral infection [11]. Vi-

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ral co-infections (mostly with RSV and RV) were found in 10-40% of the severe cases [12].

The transmission of all viruses during the COVID-19 outbreak has been influenced by the mandatory measures taken worldwide: social distancing, wearing masks, and more rigorous hand hygiene [6,13]. Several studies showed a decrease in the number of respiratory infections in children [14], including bronchiolitis [15-17], decreased number of hospitalizations, and duration of admittance during the social distancing and lockdown periods [18]. Cohen et al. [19] raise a concern that owing to the lack of immune stimulation during the COVID-19 pandemic, there will be negative consequences due to an "immunity debt," including more severe outbreaks of RSV [20,21].

Chest radiographs are not routinely recommended in children with acute bronchiolitis [1-6,11]. Indications for performing this investigation are severe disease, imminent respiratory failure, suspected foreign body aspiration, comorbidity (heart and lung disease), symptom progression, or no resolution as expected [11]. The main potential benefit is the identification of lobar consolidation [22]. No medication has been demonstrated to improve the outcome in children with acute bronchiolitis, and the effective treatment remains oxygen therapy and hydration [1-6,23]. Although there is no evidence of the benefit of medication, salbutamol, epinephrine, corticosteroids, and antibiotics are still largely used with significant variations in management between hospitals [23].

AIM

This study aims to assess the number of patients, age, clinical presentation, investigations performed, duration of hospitalization, severity, and medication used to treat bronchiolitis in children admitted to our Pediatrics ward before and after the COVID-19 pandemic.

MATERIAL AND METHOD

We conducted a retrospective, observational, descriptive study comparing the data collected from the medical records of patients with acute bronchiolitis admitted to our 3rd Pediatric Clinic, Emergency Hospital for Children, Cluj-Napoca, Romania between October 2019 and March 2020 and October 2022 and March 2023. Before the COVID-19 pandemic, children were admitted to our unit through the Emergency Department and the on-call room of our clinic. They were only admitted through the Emergency Department during and after the pandemic.

Patients

Children included in the study were children between 0 and 2 years of age diagnosed with acute bronchiolitis and admitted to our medical unit. Acute bronchiolitis was defined as the first episode of wheezing caused by a viral infection. The severity of bronchiolitis was classified into mild, moderate, or severe based on the assessment of feeding, respiratory distress, hypoxemia, and apnea [24]. Premature birth was considered birth before 37 weeks of gestation.

We diagnosed patients with respiratory failure type I if oxygen saturation was ≤92% and type II if the partial pressure of CO_2 (pCO_2) was higher than 45 mmHg.

Patients diagnosed with recurrent wheezing, immunodeficiencies, chronic respiratory, cardiovascular, or neuromuscular diseases were excluded from the study.

Data collected

The demographic and clinical data that we collected were: age at diagnosis, gender, gestational age, duration of symptoms before admittance, presenting symptoms and signs (signs of viral prodroma, fever, cough, apnea, feeding, signs of respiratory effort, respiratory rate, wheezing, prolonged expiration, crackles, heart rate, oxygen saturation, signs of dehydration) and their evolution.

We also collected data regarding the investigations that were performed (complete blood count, blood gases, acid-base balance, C-reactive protein (CRP), chest radiographs, chest ultrasound) and treatment received (oxygen therapy, salbutamol, epinephrine, corticosteroids, antibiotics).

Statistical analysis

Results were summarized as frequencies and percentages. The t-test was used for comparison between groups, with a p value of less than 0.05 being considered statistically significant. We used MedCalcSoftware to calculate the statistical parameters.

The study protocol was approved by the Ethics committee of the "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca (AVZ76/26.04.2024).

RESULTS

Our study included a total of 233 children diagnosed with acute bronchiolitis.

Epidemiology

Before the COVID-19 pandemic, between October 2019 and March 2020, 98 children were diagnosed with acute bronchiolitis out of 2513 children admitted to our clinic (3.9%). After the pandemic, between

October 2022 and March 2023, 135 children were diagnosed with acute bronchiolitis out of 2342 children admitted to our unit (5.76%). There was a statisticaly significant difference between the two studied periods in the number of patients admited with acute bronchiolitis (p=0.002).

The number of children diagnosed each month of the study period is depicted in Figure 1.

Clinical characteristics

The demographic and clinical characteristics of the patients are detailed in Tables 1 and 2.

There were no statistically significant differences in the age, gender distribution, and number of premature children in the two study groups (p>0.05). There was an increase in the number hospitalization days in patients with acute bronchiolitis in the October 2022-March 2023 group. The number of patients with each severity form is shown in Table 3.

There were no patients in the first group diagnosed with otitis media with an antibiotic treatment indication; in the second group, there were two such patients.

Investigations

Oxygen saturation measured by pulse oximeter was <92% in 16/98 (16.3%) patients in the first group and 20/135 (14.8%) in the second group (p=0.75). The

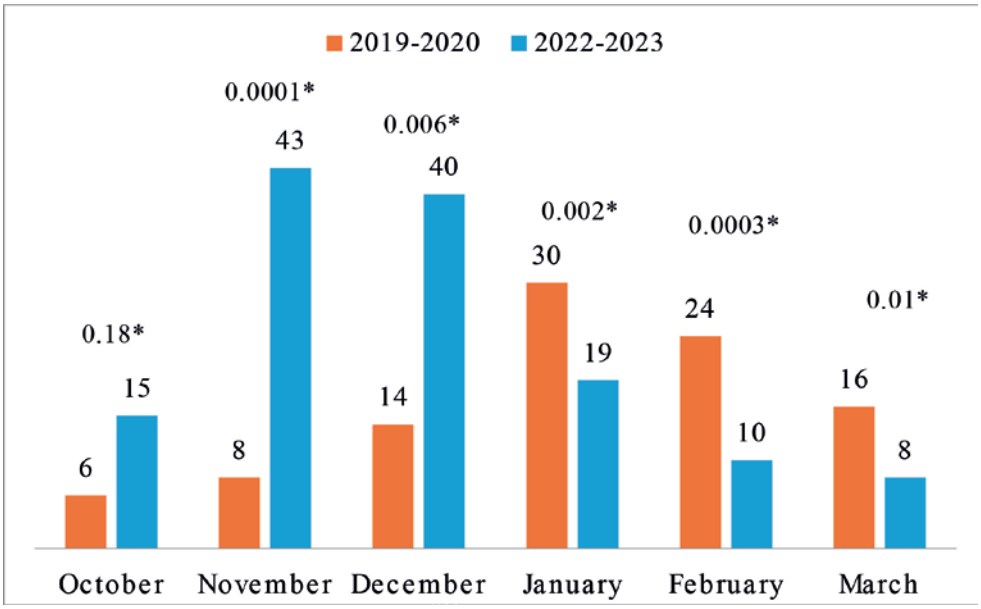

FIGURE 1. Number of cases of acute bronchiolitis in the two study groups per month
*p value showing the statistical significance of the differences between the number of cases for each month

TABLE 1. Demographic and clinical characteristics of the patients included in the study

	October 2019-March 2020		October 2022-March 2023		p value
Number of patients	98		135		
Gender	59 boys (60.2%)		80 boys (59.3%)		0.89
Mean age±SD (months)	6.27±5.17		6.06±4.88		0.75
Gestational age <37 weeks (number/%)	10/98 (10.2%)		17/135 (12.6%)		0.57
Hospitalization days (mean±SD)	5.05±2.02		5.73±2.25		0.01
Dehydration	12/98 (12.2%)		9/135 (6.6%)		0.14
Number of children/% Form	Mild	Moderate	Mild	Moderate	
Number of children	10	2	8	1	

TABLE 2. Number of patients (%) in each age group in the two study periods

	<3 months	3-6 months	6-12 months	>12 months
October 2019-March 2020	32 (32.7)	30 (36.2)	21 (21.4)	15 (15.3)
October 2022-March 2023	49 (36.2)	31 (22.9)	38 (28.1)	17 (12.6)
p value	0.58	0.02	0.24	0.55

TABLE 3. Number of patients (%) with each disease severity form

	Mild	Moderate	Severe
October 2019-March 2020	16 (16.3)	74 (75.5)	8 (8.2)
October 2022-March 2023	37 (27.4)	86 (63.7%)	12 (8.9)
p value	0.04	0.06	0.85

pCO2 was >45 mmHg in 7 out of 61 patients from the pre-pandemic group in which it was measured and 13/123 patients from the post-pandemic group.

Values of the CRP were measured in 84/98 patients from the pre-pandemic group and almost all patients from the post-pandemic group (134/135). Fifteen/84 patients (17.8%) of the first group had values above 1 mg/dl (11 patients had values between 1-5 mg/dl, two between 5-10 mg/dl, and two patients had values above 10 mg/dl). In the second group, 30/134 patients (22.3%) had values of the CRP above 1 mg/dl (28 patients with values between 1-5 mg/dl, two patients with values between 5-10 mg/dl, and no patients with values above 10 mg/dl).

In the pre-COVID-19 group, a chest X-ray was performed in 23/98 (23.4%) children with bronchiolitis. In the post-COVID-19 group, 105/135 (77.7%) children had a chest X-ray (p <0.0001). In the first group, X-ray consolidations were described on 8/23 (34.7%), and 8/98 patients (8.2%) were interpreted as associating pneumonia. In the second group, consolidation was described in 31/105 (29.5%) X-rays that were performed, and hence 31/135 (22.9%) children associated pneumonia, according to the interpretation of the chest radiographs (p <0.003).

Treatment

Oxygen therapy was needed in 16/98 (16.3%) of the patients before the pandemic, 2 (2%) which required nasal high-flow respiratory support throughout the disease. After the pandemic, 29/135 (21.4%) patients (p=0.33) with acute bronchiolitis required oxygen therapy, 5 (3.7%) of them also with nasal high-flow respiratory support.

The number of children in different age goups who received Salbutamol between October 2019-March 2020 and October 2022-March 2023, were, respectively: 6/32 (18.7%) and 6/49 (12.4) under 3 months of age (p=0.44), 9/30 (30%) and 14/31 (45.1%) aged between 3 and 6 months (p=0.23), 9/21 (42.8%) and 29/38 (76.3%) aged between 6 and 12 months (p=0.01), 12/15 (80%) and 15/17 (88.2%) aged over 12 months (p=0.53).

The number of children with different forms of disease who received nebulized Epinephrine between October 2019-March 2020 and October 2022-March 2023, were, respectively: 14/16 (87.5%) and 23/37 (62.7%) with mild form (p=0.07), 53/74 (71.6%) and 48/86 (55.8%) with moderate form (p=0.04), 6/8 (75%) and 8/12 (66.7%) with severe forms (p=0.69).

The number of patients who received corticosteroids, NaCl 3%, and NaCl 0.9% during the disease is summarised in Table 4.

Antibiotics were administered in the pre-pandemic group in 36/98 (36.7%) children, while in the post-pandemic group 66/135 (48.9%) (p=0.06). In most children, 3rd generation cephalosporins were used. Azithromycin was administered to 12/36 children in the first group and 14/66 in the second group.

DISCUSSION

The number of patients diagnosed with acute bronchiolitis increased in our medical unit 3 years after the COVID-19 pandemic outbreak as compared with the prepandemic period. The number of hospitalization days of our patients also increased. Curatola et al. also found an increase in the hospitalization rate in children with bronchiolitis in the post-COVID period (32.9%) compared to the pre-COVID period (25.9%) [8]. Similar to the Curatola et al. study [8], we did not notice a difference in the average age of the patients admitted in the two studied periods. The authors consider this increase in the hospitalization rate reported by some studies to be due to a greater virulence of the RSV and to the

TABLE 4. Number of patients (%) who received corticosteroids, and nebulization with NaCl3% or 0.9%

	Corticosteroids Number of patients who received corticosteroids on that route (%)		NaCl 3% (nebulization)	NaCl 0.9% (nebulization)
	Systemic	Inhalation		
October 2019-March 2020	55/98 (56.1)	43/98 (43.8)	10/98 (10.2%)	16/98 (16.3%)
October 2022-March 2023	103/135 (76.3)	56/135 (41.5)	4/135 (2.9%)	38/135 (28.1%)
p value	0.001	0.72	0.02	0.03

"immunity debt" of children born during the COVID-19 pandemic, a hypothesis also supported by Cohen et al. [19]. Grobben et al. also report a decrease in passive humoral immunity provided by the breast milk, but not in serum, during the COVID-19 pandemic because of reduced maternal exposure [25]. Although not statistically significant, after the pandemic, there was an increase in our patients aged less than three months, perhaps also due to the decreased level of maternal antibodies and passive immunity in those who were breastfed.

Curatola et al. found in a recent study that in the post-COVID-19 period (September 2021-March 2022), the bronchiolitis season started earlier, reaching a peak in November 2021 [8]. An earlier peak of the cases is also reported by Camporesi et al. [26]. The same research group finds that the 2022/2023 season on acute bronchiolitis was mostly similar with the 2021/2022 one [27]. We noticed the same trend for October 2022-March 2023, with most cases of bronchiolitis being diagnosed in November and December compared to the situation before the COVID-19 pandemic when most cases were diagnosed in January and February.

The course of COVID-19 was unknown at the beginning of the pandemic, and extra measures were taken to prevent serious illness, including more investigations such as chest radiographs and blood analysis. Curatola et al. report higher priority triage codes assigned by nurses, even unnecessary, in children with acute bronchiolitis, so children were kept under observation for longer [8]. During the COVID-19 pandemic, performing chest radiographs became a rule in most patients who presented with respiratory symptoms. Despite recommendations in the guidelines for acute bronchiolitis, in our study, in the season following the lifting of restrictions imposed during the COVID-19 pandemic, the use of chest radiographs and medication increased significantly. There was also an increase in the number of patients with mild forms admitted to the hospital post-pandemic season.

Several studies have shown that the utility of chest radiographs in children with bronchiolitis is limited; it leads to unnecessary radiation and increases antibiotic prescriptions, as well as costs [22,28]. There was a significant difference in the number of chest radiographs performed in the first study group, where almost one-third of the patients had this investigation indicated, to more than two-thirds of the patients having a chest X-ray in the post-pandemic group. This increase in the number of X-rays was not justified by the severity form of acute bronchiolitis or worsening of the symptoms in most cases.

Overuse of investigations and medication in children with acute bronchiolitis is an issue debated all over the world [29-31]. Studies have shown that many patients receive at least one medication despite the lack of evidence for medication use in acute bronchiolitis. According to Haskell et al., the factors influencing this practice are a need for more experienced doctors, turnover of medical staff, and time pressure in the Emergency Department [29]. Biagi et al. also mention the high turnover of medical staff as a factor influencing the management of acute bronchiolitis, adding personal and parental pressure [31]. De Brasi et al. also looked into the reasons why pediatricians prescribe so many drugs in children with bronchiolitis [28]. There was no correlation between the clinical severity of the disease and drug prescription [28]. Pediatricians felt pressured to "do something" by parents or, from personal experience, saw some effect of certain medications [30]. Wolf et al. reported differences in prescribing medication and investigations in acute bronchiolitis between family and emergency medicine providers and pediatricians, commercially or publicly insured patients, rural hospitals and urban centers, and inpatient and outpatient settings [32]. In their study, overuse was associated with rural locations and outpatient and emergency settings [32]. In our study, we noted all the measures taken in a patient, regardless of the stage of evolution of the disease and the specialty of the doctor who recommended that measure, including the medication prescribed by a doctor at home, before hospitalization. Guidelines have been developed and implemented to prevent unjustified medication use, and investigation and quality improvement initiatives have shown improvements in compliance with guideline recommendations, especially in hospitals where compliance was initially low (under 80%) [1-6,33].

Nebulized epinephrine reduces mucosal swelling in patients with acute bronchiolitis, but there is insufficient evidence to recommend it in the guidelines [6]. Some studies showed some benefits of nebulized epinephrine in reducing the need for supportive treatment and a shorter length of hospitalization. Still, it is recommended on demand rather than with a fixed schedule [34,35]. Administration of nebulized epinephrine decreased in both our study groups, but it was still high in patients with mild forms of acute bronchiolitis.

Rodriguez-Martinez et al. and Dumas O. et al. consider that a cause for the disagreements between research and clinical practice is the lack of consideration for different phenotypes of bronchiolitis and the specific response to various therapeutic options [36,37]. Several arguments exist against using salbutamol in treating bronchiolitis: infants seem to have inadequate β2-agonist receptor sites and immature bronchiolar smooth muscles [2]. Harford et

al. describe an impairment of the β2-agonist receptor function induced by the RSV, which might explain the ineffectiveness of the β2-agonist treatment [38]. Bronchodilators do not improve oxygen saturation or reduce admission rates or duration of hospitalization, but they showed minor improvements in clinical scores [2,39]. On the other hand, some authors argue that if bronchiolitis is considered a syndrome with more phenotypes and endotypes, children with personal or family history of allergies might benefit from using bronchodilators. This is why some guidelines recommend using a therapeutic trial with salbutamol. Still, in both our study groups, 25% of the infants under six months of age were treated with salbutamol. We did not assess the frequency of administration, so in some patients, it might have been a single dose as a therapeutic trial.

Beigelman et al. found a positive effect of azithromycin in children with RSV bronchiolitis: it reduced the IL-8 levels, prolonged the time to a third episode of wheezing, and reduced the respiratory symptoms in the subsequent year [40]. A recent meta-analysis by Ukkonen et al. showed that azithromycin therapy in patients with wheezing did not reduce the subsequent wheezing episodes or adverse events, but the hospital stay was shorter [41]. The authors conclude that further studies are needed to assess the antiviral and anti-inflammatory effects of azithromycin administered at the onset of symptoms [41].

Florin et al., in a review of viral bronchiolitis, note that antibiotic overuse is influenced by fever, young age, difficulty differentiating atelectasis from bacterial consolidation on X-rays, and concern for undetected secondary bacterial infection [6]. Almost half of our patients admitted with acute bronchiolitis in the post-COVID-19 season were administered antibiotics despite no consistent evidence of a bacterial infection. Although bacterial co-infection is not negligible in patients with bronchiolitis [42], there is a discrepancy between the number of our patients in which bacterial infection was proven or suspected and the use of antibiotics.

Our study has some limitations. It is a retrospective study with data collected from a single medical unit, part of a hospital. Etiology was not determined in most patients diagnosed with acute bronchiolitis. Patients diagnosed between October 2022 and March 2023 had negative rapid tests for SARS-CoV-2 and A and B influenza virus antigens from nasal swabs.

This study is meant to draw attention to current practice regarding the management of acute bronchiolitis in children, how guidelines and protocols are applied in our medical units, and that the increase in investigations during the COVID-19 pandemic in patients with respiratory symptoms might have caused a setback in following proper management in children with acute bronchiolitis. We recommend careful consideration of chest X-ray and antibiotic indications. Identifying the problems in diagnosing and treating patients with acute bronchiolitis could help increase awareness of some particular issues and improve protocols and management quality.

CONCLUSIONS

The number of patients with acute bronchiolitis admited to our unit increased after the COVID-19 pandemic. There was a significant increase in X-rays performed after the COVID-19 pandemic in children with acute bronchiolitis. Epinephrine is still administered in more than half of the patients with mild forms of bronchiolitis. Salbutamol was overused in infants under six months of age, even in mild forms of acute bronchiolitis. Antibiotics were administered in more patients without evidence of a bacterial infection. Overuse of investigations and medication in children with acute bronchiolitis, although not a new problem, might have been influenced by the measures taken during the COVID-19 pandemic in patients with respiratory symptoms.

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