Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Asthma may not be a risk factor for severe COVID-19 in children

Flore Amat, MD, PhD[a,b], Bertrand Delaisi, MD[c], Jean-Philippe Labbé, MD[d], Jacques Leonardi, MD[c], and Véronique Houdouin, MD, PhD[b,e]

Clinical Implications

- Asthma may not be a risk factor for contracting a severe form of COVID-19 in children, and COVID-19 does not appear to worsen short-term asthma control.

To the best of our knowledge, no studies to date have identified any risk factors for developing a severe form of COVID-19 in children, except young age.[1] However, worries remain regarding children with asthma, for whom more severe forms of COVID-19 are expected. However, data about whether asthma could be a risk factor for a severe form of COVID-19, or whether COVID-19 could worsen control of asthma, remain scarce.[2]

We performed a retrospective study in a residential pneumopediatric rehabilitation center for children with chronic lung diseases (La Guisane, Briançon, France). A cluster of COVID-19 cases were identified in September 2020. At this time, only asthmatic children attended the center. All the children were tested after the first case, using quantitative real-time PCR tests for SARS-CoV-2 (PCR-COVID19), according to French Health Authority recommendations.

Collected data included symptoms and results of PCR-COVID19 in nasopharyngeal secretions over time, sex, age, body mass index (BMI), sensitization to aeroallergens (defined by at least 1 IgE specific to an aeroallergen >0.35 kU/L), allergic asthma (defined by association with documented allergic rhinitis), daily dose of inhaled corticosteroids (expressed as fluticasone propionate equivalent for corticosteroids), any other add-on therapy for asthma, treatment step of asthma and level of asthma control according to Global Initiative for Asthma (GINA) recommendations,[3] and results of pulmonary function tests (forced expiratory volume in 1 second [FEV_1]) carried out before and 1 month after the infection with COVID-19.

All the statistical analyses were performed using Stata 13 software (StataCorp. 2013, Stata Statistical Software: Release 13; StataCorp LP, College Station, Tex). Distributions were presented as counts and percentages for categorical variables and mean and standard deviation or median and percentiles 25 to 75 for continuous variables. A comparison between FEV_1 before and after the infection was performed using the Kruskal-Wallis test. As a retrospective study, formal approval from an ethics committee was not mandatory according to the French law. However, the principles outlined in the Declaration of Helsinki were followed,[4] and all the families received written information and provided consent for data collection. Data were anonymized according to good clinical practice, and the study was registered with the French Commission Nationale Informatique et Libertés (number 2220513V0, December 21, 2020).

During the study period, the center managed 51 asthmatic children aged 14.14 ± 2.38 years. Most were boys (64.7%); 56.9% were allergic (40.8% to house dust mites, 28.6% to grass pollens, 23.6% to pet fur, 10.2% to birch tree pollen, and 8.2% to molds). The mean BMI was 21.7 ± 5 kg/m^2. The mean FEV_1 at baseline was 97 ± 13%; the mean equivalent of inhaled fluticasone propionate was 250 ± 332 μg/d; and 31.4% received a 4- to 5-step treatment according to GINA (associated with long-acting β_2-agonists for 51%, and/or montelukast for 23.5%). Two children (3.9%) received omalizumab as a long-term add-on therapy. All of the children had controlled asthma during the 4 weeks preceding the cluster.

On day 0, a 13-year-old boy presented with the following symptoms: abdominal pain, vomiting, headache, and conjunctivitis. On day 1, the nasopharyngeal swab returned positive for SARS-CoV-2. No contact case was found, but the child had been back at school for 2 weeks. Measures undertaken to protect the other patients are detailed in Table I. Thirty-eight children (74.5%) tested positive on days 2 to 3, and 43 (84. 3%) on day 9. On days 16 and 23, 6 children (11.8%) remained positive (11.8%). Finally, of the 46 of 51 children (90.2%) who were positive for SARS-CoV-2 at least once, 29 (56.9%) remained asymptomatic. Twenty-two (43.1%) presented with mild and transient symptoms: mainly headaches (14 of 22, 63.6%), vomiting (11 of 22, 50%), diarrhea (4 of 22, 18.2%), a subjective feeling of chest oppression (3 of 22, 13.6%), abdominal pain (3 of 22, 13.6%), asthenia (3 of 22, 13.6%), fever <38.5°C (2 of 22, 9%), conjunctivitis (1 of 22, 4.5%), cough (1 of 22, 4.5%), or dysphagia (1 of 22, 4.5%). None of the children presented with severe symptoms. No difference was found in terms of test positivity or symptomatology between allergic and nonallergic children. Asthma remained controlled in all patients, and mean FEV_1 measured 1 month later showed no significant difference from baseline.

These favorable outcomes suggest that asthma may not be a risk factor for contracting a severe form of COVID-19 in children and that COVID-19 does not worsen short-term asthma control. Our findings support evidence already available in asthmatic adults.[5] Several hypotheses could explain this specific reaction to SARS-CoV-2, in contrast to other respiratory viruses.

SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as its cellular receptor, as do some other coronaviruses. Higher ACE2 expression is thought to increase susceptibility to SARS-CoV-2.[6] Conversely, a reduced expression of ACE2 has been shown in allergic asthma.[7] Good adherence to daily treatment, due to the close follow-up in the center, may also be an explanation. Results from an online survey of physicians from different parts of the world concluded that children with asthma do not seem disproportionately affected by COVID-19 if their asthma is well treated.[8] Finally, an *in vitro* study showed that long-acting β_2-agonists and inhaled corticosteroids may inhibit the coronavirus 229E replication and the secretion of cytokines from human nasal and tracheal epithelial cells. A similar mechanism of action of antiasthmatic drugs could be expected in the case of SARS-CoV-2.[9]

Our results show that children with asthma may not experience a severe form of COVID-19.

TABLE I. Reinforced infection prevention measures implemented in the center

Center description	Infection control measures in place since day 1
Semiclosed residential pneumopediatric rehabilitation center	Isolation of the index case and confirmed cases in a specific area
	Isolation of the contact children in a separate specific area
All children attend school during daytime	Adult staff PCR testing and exclusion from work for 14 days if positive
30 bedrooms (2 individual and 28 double bedrooms)	Surgical masks mandatory for all children and all staff, FFP2 masks for medical and paramedical staff
40 members of staff including: 2 medical doctors, 6 nurses, 6 administrative staff, 11 educators	Single-use cutlery and plates for confirmed cases, disposed of after use in a garbage can for contaminated waste
	Laundry placed in water-soluble bags and washed at 60°C
Common living, dining, and play areas	No respiratory functional testing
	Drug distribution directly in the bedrooms through pillboxes, disinfected immediately afterward
	All the children were kept out of school for at least 7 days and group activities were stopped
	PCR-negative children were allowed to attend school after 3 weeks

Moreover, in contrast to other viral respiratory infections, COVID-19 did not appear to induce asthma exacerbation. Larger studies are needed to confirm our single-center experience and understand the mechanisms explaining such outcomes. Follow-up is now ongoing in these patients to detect any long-term sequelae.

[a]Faculté de Médecine Saint-Antoine, Institut Pierre Louis d'Epidémiologie et de Santé Publique, UMR_S1136, INSERM, Paris, France
[b]Pediatric Pulmonology and Allergology Department, Hôpital Robert Debré, AP-HP, Paris, France
[c]SSR Pneumopédiatrique La Guisane, Villard Saint Pancrace, Briançon, France
[d]Cardiologic Intensive Care Unit, Hôpital Saint Camille, Bry-sur-Marne, France
[e]Faculté Paris Diderot, UMR_S976, INSERM, Paris, France
No funding was received for this work.
Conflicts of interest: The authors declare that they have no relevant conflicts of interest.
Received for publication January 30, 2021; revised March 25, 2021; accepted for publication March 25, 2021.
Available online April 20, 2021.
Corresponding author: Flore Amat, MD, PhD, Pediatric Pulmonology and Allergology Department, Hôpital Robert Debré, 48 Boulevard Sérurier, 75019 Paris, France. E-mail: flore.amat@aphp.fr.
2213-2198

https://doi.org/10.1016/j.jaip.2021.03.046

REFERENCES

1. Castro-Rodriguez JA, Forno E. Asthma and COVID-19 in children—a systematic review and a call for data. Ped Pulmonol 2020;55:2412-8.
2. Hartmann-Boyce J, Gunnell J, Drake J, Otunla A, Suklan J, Schofield E, et al. Asthma and COVID-19: review of evidence on risks and management considerations [published online ahead of print September 3, 2020]. BMJ Evid Based Med. https://doi.org/10.1136/bmjebm-2020-111506.
3. Global Initiative for Asthma. GINA main report; 2020. Available from: https://ginasthma.org/gina-reports/. Accessed November 20, 2020.
4. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310:2191-4.
5. Grandbastien M, Piotin A, Godet J, Abessolo-Amougou I, Ederlé C, Enache I, et al. SARS-CoV-2 pneumonia in hospitalized asthmatic patients did not induce severe exacerbation. J Allergy Clin Immunol Pract 2020;8:2600-7.
6. Brake SJ, Barnsley K, Lu W, McAlinden KD, Eapen MS, Sohal SS. Smoking upregulates angiotensin-converting enzyme-2 receptor: a potential adhesion site for novel coronavirus SARS-CoV-2 (Covid-19). J Clin Med 2020;9:841.
7. Jackson DJ, Busse WW, Bacharier LB, Kattan M, O'Connor GT, Wood RA, et al. Association of respiratory allergy, asthma, and expression of the SARS-CoV-2 receptor ACE2. J Allergy Clin Immunol 2020;146:203-6.
8. Papadopoulos NG, Custovic A, Deschildre A, Mathioudakis AG, Phipatanakul W, Wong G, et al. Impact of COVID-19 on pediatric asthma: practice adjustments and disease burden. J Allergy Clin Immunol Pract 2020;8:2592-9.
9. Yamaya M, Nishimura H, Deng X, Sugawara M, Watanabe O, Nomura K, et al. Inhibitory effects of glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells. Respir Investig 2020;58:155-68.