


STATE OF THE ART

Pediatric asthma and COVID-19: The known, the unknown, and the controversial

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Abstract

The novel coronavirus disease-2019 (COVID-19), caused by the pathogen severe acute respiratory syndrome-CoV-2, is causing a global pandemic, with over 26.9 million cases and 880,000 deaths as of September 6, 2020. While there has been speculation and observational research about the impact of COVID-19 on asthma, much remains unknown. The goal of this article is to provide a scoping review on pediatric asthma and COVID-19 and summarize what we do and do not know from the first wave of the pandemic.

KEYWORDS

asthma, COVID-19, pediatrics, social determinants of health

1 | CORONAVIRUS DISEASE-2019 IN CHILDREN WITH ASTHMA

In general,¹ children are less commonly symptomatic with coronavirus disease-2019 (COVID-19) than adults. Those who are symptomatic less commonly require hospitalization.² Data from the Centers for Disease Control (CDC) of COVID-19 cases (last updated August 31, 2020) shows that among the 96% of cases where age was known, only 8.1% was among children less than 18 years of age.³ Children comprised less than 0.1% of all COVID-19 mortality. Similar findings were noted in a retrospective review of 72,314 COVID-19 cases in Wuhan, China, in which less than 1% were in children younger than 16 years of age.⁴ In addition, a retrospective review of 651 children and young people aged less than 19 admitted to hospitals within the UK with COVID-19, 6 (1%) died, in hospital, all of whom had profound

comorbidity.⁵ A report of 12,055 COVID-19 patients in Italy also supports a lower risk in children, although noting that COVID-19 can affect children of any age, including infants.⁶

However, among those children hospitalized with COVID-19, morbidity can be high. An analysis of pediatric COVID-19 hospitalization data from 14 states in the US this week (August 8, 2020) by the CDC found that while the cumulative rate of COVID-19 hospitalization was low in children compared to adults (8.0/100,000 population compared to 164.5), one in three hospitalized children required an intensive care admission.⁷ In addition, there were racial and ethnic disparities in morbidity with Hispanic and non-Hispanic black children having higher cumulative rates of COVID-19 associated hospitalizations than white children (16.4 and 10.5 per 100,000, respectively, compared to 2.1).

Multiple international organizations including the CDC list asthma as a prognostic factor for COVID-19 outcomes such as morbidity

and mortality.⁸ However, it has been noted that this classification is “based more on common sense rather than mounting evidence.”²² In a systematic review of whether asthma is associated with higher COVID-19 risk or severity in children, only two reports described asthma or recurrent wheeze as a COVID-19 risk factor.⁹ The conclusion of the systematic review was that “there is scarcely any data on whether childhood asthma...constitute risk factors for SARS-CoV-2 infection or COVID-19 severity.”⁹ There is also a theoretical risk that COVID-19 could trigger viral-induced asthma exacerbations.¹⁰ There are no data to support or refute this to date. There are data on the risk of asthma exacerbations from other coronavirus infections—severe acute respiratory syndrome, due to human coronaviruses HCoV-229E and HCoV-OC43 was not associated with an increased risk of asthma exacerbations and in fact during that time asthma exacerbations decreased (possibly due to increased hygiene measures).^{10,11} In contrast, seasonal coronavirus infection is associated with asthma exacerbations annually, albeit less than other viruses such as influenzae.^{12–14}

Paradoxically, asthma may also be protective as the angiotensin-converting enzyme 2 (ACE2) receptor, required for coronavirus recognition and infection, maybe underexpressed in the lungs of atopic children.^{15,16} A retrospective review of COVID-19 cases in children with asthma in Spain noted no demographic differences between children with asthma with probable COVID-19 and those without, including lung function, need for oral steroids, other measures of asthma control, or comorbidities.¹⁷ A retrospective review of pediatric asthma admissions in Slovenia from March to April noted a 71%–78% decrease in hospital asthma admissions compared to the same time period over the last 3 years as well as a 51%–68% decrease in admissions for acute respiratory tract infections.¹⁸ A retrospective review of asthma visits to a Children's Emergency Department (ED) in the Northeastern United States in the spring of 2020 also noted a 76% lower than pre-COVID ED utilization.¹⁹ The reasons for this are unknown, and require further validation, but are hypothesized to be related to reduced outdoor aeroallergen exposure, reduced traffic/industrial pollution, reduction in viral triggers, and improved air quality during the lockdown. Other possible contributors include reductions in physical activity, higher thresholds for ED use, and higher tolerance of risk during the pandemic.

As a result at this time, it remains unknown whether asthma confers a risk of COVID-19 morbidity or whether COVID-19 infection increases the risk of asthma exacerbations.¹⁰ Further larger scale data are required in pediatric populations.¹⁰ However, it is well established that an asthma exacerbation, if it occurred, “could require [children with asthma] to enter the healthcare system, which would put them at increased risk of being exposed to SARS-CoV-2 during the current pandemic.”²⁰

2 | COVID AND ASTHMA DIAGNOSIS/MONITORING

Diagnosis of pediatric asthma during COVID-19 may be complicated by a similarity in symptoms between COVID-19 (dry cough, shortness of breath) and worsening asthma.²¹ As a result, even if cough

history is consistent with asthma, screening protocols for COVID-19 should be applied to all children who have worsening cough or shortness of breath, and appropriate personal protective equipment worn.^{20,21}

There are barriers to proper asthma diagnosis and monitoring that are specific to the COVID-19 pandemic. These include suspension of spirometry (as it is a possible aerosol-generating procedure).^{20,22} It has been noted “in pandemic time, it is essential to avoid unnecessary risks with maneuvers such as the measure of lung function that can contribute to the spread of the virus to all healthcare workers and other patients.”²² The North American guidance on phased resumption of allergy care during COVID-19 notes that for Phase 2 rollout (community infection risk declining/stable) “spirometry is still contraindicated in most scenarios because of the aerosolization risk, except in highly individualized situations in which it would be essential for immediate treatment decision that could not otherwise be made without such information and where it can be performed with appropriate precautions and room/equipment disinfection.”²⁰ The European Respiratory Society notes that “lung function tests pose a considerable risk for the spread of infection to individuals and surrounding surfaces within and around the test areas even in asymptomatic patients” and recommends that “full operation of lung function services may only resume when viral prevalence is low and reliable testing based on a combination of symptom screening and testing is readily available.”²³

3 | IMPACT OF SOCIAL DETERMINANTS OF HEALTH

The association of adverse social determinants of health and COVID-19 morbidity and mortality is well established.²⁴ Crowded living spaces increase COVID-19 viral transmission, and lack of access to care reduces the ability to have COVID-19 screening/testing.^{25,26} There are racial and ethnic discrepancies in COVID-19 infection, with a three-fold higher rate of COVID-19 infection in predominantly non-Hispanic black counties in the US, and a six-fold higher mortality rate.²⁷ Unintended consequences of public health policies related to COVID-19—such as school closures—are likely to affect children living in poverty the most.²⁸ Malnutrition has been linked with effects on a child's physical and mental health, including a lower immune response which could potentially increase the risk of viral transmission.²⁹

The impact of adverse social determinants and COVID-19 outcomes are likely amplified in children with asthma.²⁴ Food insecurity has increased by up to 35% during COVID-19, which can have persistent effects on childhood asthma outcomes.²⁸ There is an interplay between race/ethnicity and asthma outcomes that may be further compounded during COVID-19.²⁴ It has been recommended that COVID-19 recovery policies ensure that no child goes hungry and that measures to directly address childhood poverty and food insecurity be implemented.²⁸ Moving forward, COVID-19 research and policy priorities must include the impact of social determinants of health.

4 | IMPLICATIONS FOR ASTHMA MANAGEMENT

4.1 | Medical management

4.1.1 | Maintenance care

Multiple international guidelines support children with asthma remaining on their maintenance asthma medications, such as inhaled corticosteroids (ICS) or antileukotrienes, during COVID-19 if they are well controlled.^{10,20,30,31} Reducing or suspending the use of controller asthma medications can worsen asthma control and increase the risk of a severe exacerbation.²²

It is not known whether inhaled corticosteroid use alters the susceptibility to COVID-19 or the morbidity associated with it.² A meta-analysis of 39 trials ($N = 11,615$ children with asthma) on ICS does not support an increased risk of respiratory infection in general.³² A cohort study of adults with asthma and COPD did not support a role of ICS therapy in protecting against COVID-19 related deaths; there was an increased risk of COVID-19 death in those with asthma on high dose ICS compared to SABA only (adjusted hazard ratio = 1.52; 95% confidence interval: 1.08–1.75) although this increased observed risk was thought to be “plausibly explained by unmeasured confounding due to disease severity.”³³ Inhaled ciclesonide has been shown *in vitro* to suppress severe acute respiratory syndrome-CoV-2 replication in cultured cells potentially due to antiviral in addition to anti-inflammatory activity, although to date no clinical trials have examined the use of ICS in COVID-19.³⁴ A statement from the European Academy of Allergy Asthma and Clinical Immunology (EAACI) notes that “since asthma itself may be a risk factor for the severity of COVID-19 disease and since the use of ICS does not pose an increased risk for pulmonary or systemic infections in children with asthma, their regular use is unlikely to increase the risk of acquiring the infection or increasing the severity of the present infection.”²

It is recommended that whatever the controller medication, it not be reduced or discontinued during COVID-19 unless “this is clearly favorable from an individual standpoint, with careful consideration of the balance between benefit and harm/burden.”²⁰ Other recommendations for good asthma control include an updated asthma action plan, regular review of asthma medication compliance, review of asthma medication technique, and aeroallergen avoidance measures.

Nebulization is an aerosol-generating medical procedure that can increase the risk of COVID-19 aerosolization and infection transmission by stimulating a cough reflex as well as generating a high volume of aerosolization that can be propelled over significant distances, increasing the possibility of infection transmission.³⁵ Anecdotally, some centers are actually seeing an overuse of aerosol medications in particular in patients with COVID-19.³⁶ However, a metered-dose inhaler (MDI) with valved holding chamber or dry powder inhaler is strongly preferred over nebulizers, and nebulization should only be considered for a child who is unable to follow directions for MDI use or in the rare case of medication shortages.^{10,20,31,35}

Current recommendations are to remain on biologic medications as well (with the possible exception of suspension of biologic medications during an acute phase of a COVID-19 infection).^{2,22} The American Academy of Allergy, Asthma and Immunology notes no evidence that immune response to COVID-19 will be impaired in patients with asthma on biologic therapies and that it would be “reasonable” to continue administration of biologics in patients with asthma,^{37,38} a recommendation supported by several international allergy/pulmonology organizations including the British Thoracic Society, and the Italian Society of Allergy, Asthma and Clinical Immunology.^{39,40} These organizations also support home-based administration of biologics when possible, an approach that improves access and is cost-effective.^{38,41,42}

In general, excessive shielding beyond public health recommendations is not at present recommended based on expert opinion—it is anticipated that children with asthma can go to school and partake in regular activities, in keeping with public health guidance, during COVID-19. However, in some countries, shielding (at home for up to 12 weeks) may be recommended in patients with severe asthma but “cannot be universally applied and each case should be approached on an individual basis.”² Schools need to be prepared to follow asthma school-based management to optimize the involvement of children with asthma in regular activities such as sports and to ensure ongoing optimal asthma management.

Aeroallergen immunotherapy (AIT) is often an adjunct for atopic asthma and can be effective as an adjunct in the maintenance of asthma control. With the transition to virtual visits and areas in lockdown, access to AIT may decrease at times throughout the pandemic.³⁰ Home immunotherapy administration has been proposed as a safe and cost-effective option that may be considered throughout the pandemic.⁴³ A statement by ARIA-EAACI advises against discontinuing either subcutaneous or sublingual immunotherapy (SLIT), and notes that SLIT can be taken at home.⁴⁴

4.1.2 | Exacerbations

While oral steroids are not currently recommended to treat COVID-19 lung disease,^{45,46} they are recommended for use in moderate to severe asthma exacerbations that are poorly responsive to bronchodilators.^{20,21,31} Systemic steroids (dexamethasone) have reduced mortality in COVID-19 patients.⁴⁷

Access to medical care and medications

During the pandemic, there have been medication shortages, such as the albuterol shortage in North America.⁴⁸ As a result of this shortage, the US Food and Drug Administration approved the first generic albuterol inhaler.⁴⁹ Guidance exists regarding options for asthma care in the case of shortages, such as the albuterol shortage.^{31,48,50} These recommendations include ensuring well-controlled asthma (thereby reducing albuterol requirements), ensuring at least a 1-month supply of asthma medications at home, only refilling prescriptions if you need them, and not discarding recently expired inhalers until a replacement is available.⁵⁰ Later in 2020, the UK will almost certainly

leave the European Union, and there is uncertainty around the impact this may have on certain drug supplies.

Virtual visits have been recommended during COVID-19, especially for lower acuity children with asthma (well controlled over the past 6 months—no record of ED visits, had ≤ 1 oral steroid burst or hospitalization in the immediate 6 months or ≤ 2 in the past year).³⁰ For children with recent asthma exacerbations, an in-person visit may be beneficial, assuming access to personal protective equipment.²⁰ At present, a shared decision-making approach with effective risk communication may provide opportunities for improved delivery of care, allowing care providers to re-examine how we deliver care and enhance the effectiveness of our management strategies.⁴²

Back to school care

A focus on “prevention efforts” to reduce the spread of COVID-19 has been noted to be “essential” by the CDC in congregate settings such as schools.⁷ While returning to school is an important measure for the educational and social development of children, ensuring a safe return for children with asthma will require monitoring and diligence.⁵¹ There is, at present, very little in the way of guidance for transition back to school for children at higher risk, such as those with asthma. A seasonal spike in asthma attacks is common in September (the “September epidemic”)⁵² and asthma symptoms may be confused with COVID-19 symptoms, both of which may lead to school absences.²¹ Measures to mitigate this risk include a focus on asthma control, access to influenza vaccination, ongoing asthma monitoring, and an appreciation of the impact of social determinants of health—including housing quality, access to transportation and care, and health literacy.^{28,51,53} There are a few specific recommendations that may be preventive in children with asthma. These include the use of cleaning products that are free of organic compounds, irritants, or fragrances (as various household cleaning products have been associated with wheeze),⁵⁴ improving classroom ventilation but taking care to reduce aeroallergen exposure,⁵¹ and monitoring of indoor air quality which may all play a role to improve asthma control.

Management of comorbidities

The importance of rhinitis control to optimize asthma management, in keeping with the united airway hypothesis, is especially poignant during COVID-19.⁵⁵ It has also been noted that rhinitis control is especially salient to prevent mimicking viral infection, and as uncontrolled rhinitis may increase the risk of viral transmission in those infected with COVID-19.⁵⁶ Optimizing other comorbidities that may worsen asthma control, or perception of dyspnea, such as obesity may be especially prudent at this time.

Public health measures

There is broad public health support for wearing facemasks (often homemade nonmedical face masks) in the community when physical distancing is not possible (or not consistently possible). In children with asthma, this recommendation would apply as well. While

wearing a mask may create a subjective sensation of breathlessness, there is no evidence that wearing a face mask exacerbates any underlying lung condition including asthma.⁵⁷ The CDC recommends for everyone, but in particular children/adolescents with chronic diseases, measures of disease prevention including regular hand washing (with soap and water or alcohol-based sanitizer), avoidance of people who are sick, physical distancing, avoidance of travel, and regular cleaning/disinfection of high-touch surfaces.⁶

Protracted stay-at-home recommendations are associated with environmental factors that could worsen asthma control including prolonged exposure to indoor aeroallergens, reduced physical activity, and exposure to second-hand smoke.^{6,51} Cigarette smoking, and smoke exposure, can increase the expression of the ACE2 receptors in the lower respiratory tract, which is the coronavirus receptor. As noted in the consensus statement of the Italian society of pediatric allergy on the management of pediatric allergic disease during COVID-19, “an increased expression of ACE2, induced by smoking, means increased susceptibility to contract the COVID19 infection and potentially to develop a more severe form.”²²

5 | CONCLUSION

The initial concerns about children and young people with asthma being particularly affected by COVID-19 have not been realized. It remains unclear if this is because of a reduction in other causes of asthma exacerbations (improved air quality, reduced other viral infections), or not. With the return to school, the balance of these risk factors will change, and continued vigilance is required. However, optimizing asthma management remains central to keeping these children and young people healthy.

CONFLICT OF INTERESTS

Elissa M. Abrams is a collaborator with the Institute for Health Metrics and Evaluation, is on the National Advisory Board for Food Allergy Canada, and has received honoraria from GSK and AstraZeneca. The other authors declare that there are no conflict of interests.

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