



COMMENT

COVID-19 and asthma: To have or not to have T2 inflammation makes a difference?



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During this pandemic, there has been some data discrepancy about whether patients with asthma have a lower risk of becoming infected or seriously ill from coronavirus disease 2019 (COVID-19)¹ but there is no information about the real impact of SARS-CoronaVirus-2 (SARS-CoV-2) on asthma control. Recent reports from the United States of America suggest that asthma is more common in children and adults with mild to severe COVID-19 than was previously reported in Asia and in Europe, but the prevalence is no higher than that described in the same population.²

SARS-CoV-2 binds mainly to angiotensin converting enzyme 2 (ACE2) receptors in host cells which are abundant in the lungs, heart, blood vessels and intestine and, after more than a decade of research, there are still no specific treatments or effective vaccines for coronavirus.³

COVID-19 mainly presents with respiratory symptoms, from mild to severe and a significant percentage of patients develop acute respiratory disease syndrome (ARDS); these severe symptoms are associated with a true cytokine storm, in particular IL-6, and death can occur.⁴

Old age and underlying morbidities, such as cardiovascular diseases (in particular hypertension), metabolic disorders (obesity and diabetes), and respiratory system diseases were identified as significant risk factors for COVID-19 morbidity and mortality.⁵

Even though respiratory viruses are one of the most common triggers for asthma exacerbations, not all of these viruses affect patients equally. In asthma exacerbations the human rhinovirus was identified as the main individual contributor and coronavirus does not seem to frequently induce asthma exacerbations.⁶ In a literature review concerning virus detection during asthma exacerbations, Zheng et al. confirmed that exacerbations were mainly associated with rhinovirus infection.⁷

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In previous SARS outbreaks, patients with asthma, in particular children, appeared to be less susceptible to the coronavirus: the rate of asthma exacerbations described is low and prognosis good.^{1,8} In contrast, during influenza epidemics, asthma is involved in more severe cases, some needing mechanical ventilation, including patients of paediatric age.⁹ The exact reasons for this remain unknown, but it has been confirmed during the current coronavirus pandemic with children having a better prognosis, although as likely as adults are to get infected with SARS-CoV-2.¹⁰ Different ACE2 expression or maturation, innate immunity memory and a constitutional high lymphocyte count in children may be part of the explanation.¹⁰

From the recent COVID-19 literature, no information can be extrapolated about asthma phenotypes, specifically about whether asthma was allergic or not. In a recent study that included paediatric and adult patients with asthma from three different cohorts, it was found that ACE2 expression was lowest in those with high levels of allergic sensitization, but non-atopic asthma was not associated with this reduced expression.¹¹ Given that ACE2 serves as the receptor for SARS-CoV-2, these data suggest that this expression may be a potential contributor, among several other factors, to reduced COVID-19 severity in patients with T2 inflammation,¹¹ namely in patients with allergic asthma but also with other allergic diseases, such as allergic rhinitis, which are more prevalent in all age groups.

Additionally, considering that the virus cell entry also depends on S protein priming by host cell proteases, including transmembrane protease serine 2 (TMPRSS2), there is some early evidence coming from the Severe Asthma Research Programme-3 (SARP), that inhaled corticosteroid therapy is also associated with reduction in ACE2 and TMPRSS2 gene expression from sputum.¹² Although gene expression for ACE2 and TMPRSS2 did not differ in healthy people and in asthmatics, the author's report that males, African Americans, and patients with diabetes mellitus have increased expression of ACE2 and TMPRSS2 in their sputum cells that can be associated with a poor prognosis when infected with the SARS-CoV-2.¹²

Dong et al.,¹³ described eleven selected cases of patients with COVID-19, children and adults, demonstrating the profile complexity and different clinical presentations, from asymptomatic cases to patients with mild to severe symptoms. Patients with common allergic diseases, such as rhinitis or atopic dermatitis, did not develop distinct symptoms and severe clinical courses, suggesting a role of type 2 immune regulation in COVID-19 pathogenesis.

During this outbreak it is more likely for a person with asthma to have an exacerbation caused by other triggers, including allergens or other virus exposures. New data are emerging daily, rapidly updating our understanding of this novel coronavirus, but it is crucial that patients with asthma and other allergic diseases maintain their controller medication, from inhaled steroids to biologics,^{14–16} including allergen immunotherapy.¹⁷ Self-dose adjustments or stopping medication may lead to higher risk of asthma exacerbations, increased OCS use and higher probability of recourse to emergency room and hospitalization which themselves represent risk factors for coronavirus exposure and spread.

Asthma may worsen the disease course of COVID-19, should infection occur, namely if rescue OCS are prescribed,¹⁸ as was suggested in previous coronavirus outbreaks when systemic steroids were associated with a higher viral load.^{19,20} Clinicians must be aware and recognize the differences between hypoxic respiratory failure and bronchospasm on physical examination to carefully judge the need for a course of OCS.¹⁴

Compliance with ethics

This study involves a comment on the literature and did not involve any studies with human or animal subjects performed by the authors.

Authorship

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Conflicts of interest

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