



Correspondence

Children and adolescents with allergy and/or asthma seem to be protected from coronavirus disease 2019



To the Editors: Akenroye et al¹ discussed the use of corticosteroids and biologics in asthma during coronavirus disease 2019 (COVID-19) pandemic. COVID-19 began in the People's Republic of China and rapidly spread worldwide.² Italy was the first European country involved in the pandemic and the first cluster occurring in South Lombardy. The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), penetrates the host cells binding to the angiotensin-converting enzyme 2 (ACE2) receptors.

Initially, asthma was considered a risk factor for severe COVID-19. However, a preliminary study reported that no hospitalized patient had asthma or allergies.³ Consistently, another Chinese study reported an asthma prevalence of 0.9% in inpatients with COVID-19, which is substantially lower than in the general population (6.4%).³ In contrast, eosinopenia has been associated with poor COVID-19 prognosis.⁴ Eosinophil responses to COVID-19 have been recently discussed.⁵ Eosinophils orchestrate the immune response to a respiratory virus, releasing cytotoxic proteins, increasing nitric oxide, producing type 1-associated cytokines, mainly interleukin 12 (IL-12) and interferon gamma, and recruiting CD8 T lymphocytes. Eosinophils clear viral load; thus, guaranteeing recovery from viral infections. Patients with allergy usually present with eosinophilia as a mechanism of protection against infections; however, it is well known that patients with allergy, such as those who have asthma, are more susceptible to viruses. Coronavirus is, however, scarcely associated with asthma exacerbations. Nevertheless, anti-IL-5 biologics, including mepolizumab, deplete eosinophils, and, theoretically, could promote viral infections.

Considering this background, we present our data concerning both COVID-19 in children and adolescents and mepolizumab treatment in patients with severe asthma. We considered the records of the following 2 hub hospitals: (1) South Lombardy, which started the first Italian cluster; and (2) Liguria, a neighboring region. Concerning eosinophil count, patients with allergy had higher values than inpatients with COVID-19 (median values 423 and 112 cells/ μ L, respectively). A total of 5 patients (mean age 22.4 years, 3 men) were treated with mepolizumab for at least 12 months and had levels of 319 eosinophils/ μ L (median value). Therefore, α -IL-5 biologic did not completely abolish eosinophilopoiesis. Patients with asthma were well-controlled and significantly reduced the rate of asthma exacerbations in the previous year. Notably, none of them suffered from COVID-19, at least to date.

Moreover, we considered the young people admitted to the 2 hub hospitals for COVID-19. Of the 52 patients hospitalized for

COVID-19 (24 boys, mean age 6.2 years), only 1 required high-level care. Interestingly, only 2 patients (4%) were allergic (atopic dermatitis and allergic rhinitis), and only 1 patient (2%) has asthma. The prevalence of allergy and asthma is 32% and 11%, respectively, in this geographic area (Fig 1). These outcomes are consistent with the literature data and pathophysiologic mechanisms. Young people are spared from SARS-CoV-2 infection probably because of the highly expressed thymic repertoire and activated innate and adaptive immunity.⁶ Patients with allergies are rare in the COVID-19 population, and these outcomes suggest that allergy could be a protective factor for coronavirus infections. To further support this hypothesis, a very recent study provided evidence that allergic sensitization was inversely related to ACE2 expression, and natural exposure to an allergen and subsequent challenge significantly reduced ACE2 expression.⁷ In conclusion, it seems that allergy and controlled asthma could be partially protected from COVID-19. Moreover, corticosteroids and biologics could be reasonably continued.

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Authors' response



We thank Ciprandi et al¹ for their salient points related to our recent article and description of their experiences with Italian patients.² As they pointed out, children and those with allergy and asthma seem to be at a lower risk of coronavirus disease 2019 (COVID-19) and have milder disease.^{3,4} Recently, however, a severe complication called multisystem inflammatory syndrome in children, which appears to be associated with COVID-19, has been described in pediatric patients.⁵ The incidence of this Kawasaki disease–like condition, its causes, and optimal management are still under investigation. Nonetheless, there is mounting evidence supporting a lower risk of COVID-19 among children in general.

Furthermore, there is now suggestive evidence that children and adults with allergic sensitization and asthma are protected from severe COVID-19 disease. It has been hypothesized that this may be related to the reduced nasal epithelial expression of angiotensin-converting enzyme 2, the receptor that severe acute respiratory syndrome coronavirus 2 uses for entry into host cells.⁶ In fact, a recent study using RNA sequencing found that angiotensin-converting enzyme 2 levels are lower in children with allergic sensitization and allergic asthma.⁷ However, it is important to note that although most studies in adults with COVID-19 have reported that asthma is uncommon, the Centers for Disease Control and Prevention reported that in children hospitalized and/or admitted to the intensive care unit for COVID-19, chronic lung disease (including asthma) was the most frequently documented comorbidity, which accounted for 40% of comorbidities.³ These studies have also not included details regarding asthma phenotypes, making it difficult to clarify the role that allergic disease plays in COVID-19 incidence and severity.

Ciprandi et al¹ also discussed the role that eosinophils play in COVID-19, given the increasing use of biologics, which may cause eosinopenia for asthma treatment. Eosinopenia is not uncommon in patients with severe or fatal COVID-19.^{8,9} Eosinopenia, however, seems to be a consequence of severe COVID-19 rather than a cause of severe disease. Acute inflammation suppresses eosinophil production and decreases eosinophil survival and activation.¹⁰ Type 1 interferons also lead to eosinophil apoptosis, and potent T_H1 responses antagonize T_H2 cytokines such as interleukin-5, a key mediator in eosinophil activation.¹⁰ Thus, we agree with the authors that asthma treatment, including biologics, should be continued in individuals who develop COVID-19, given that poor asthma control could increase the risk of adverse outcomes.

We agree that many questions remain unanswered, including whether an allergic disease is truly protective and how this protective effect is bolstered or dampened by asthma treatment, including biologics.

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