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.

Does asthma affect outcomes of patients with COVID-19 infections?

To the Editor:

We have read with great interest the article entitled "Asthma prolongs intubation in COVID-19," recently published by Mahdavinia et al.[1]

This article has shown that asthma was independently associated with prolonged ventilation time in patients with COVID-19. In addition, asthma was associated with obesity, which, as the authors point out, "is another predictor of poor outcome in patients with COVID-19."

Allergic diseases, asthma, and chronic obstructive pulmonary disease were not found to be risk factors in a study conducted on 140 patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China. Asthma is a heterogeneous disease characterized by type 2 eosinophilic inflammation in more than 50% patients. Eosinophil count is decreased in the peripheral blood of patients infected with SARS-CoV-2. The increased eosinophil count in the airways of patients with asthma has been considered as a potential protective mechanism against the exaggerated inflammatory responses of severe COVID-19 phenotype.[2,3]

It is known that the level of angiotensin-converting enzyme 2 (ACE-2) in the lung tissues of patients with COVID-19 increases and is found to play an important role in the pulmonary involvement.[4] It is proposed that inhaled corticosteroids, as the essential component of asthma treatment, may have a positive impact on the prognosis of patients with COVID-19 by reducing the level of ACE-2 in lung tissues.[5]

We conclude that regularity and dosage of inhaled corticosteroid administration, as reported in the medical history of patients with asthma, may have an impact on the treatment outcomes. Although the analyses in the study of Mahdavinia et al[1] adjusted for albuterol and systemic steroids use, it would be important to know how many of the patients were being treated with inhaled corticosteroids and the outcomes in those patients. Moreover, although the authors state that "peripheral eosinophilia was assocaited with asthma" in their study, more information regarding the type of inflammation in the patients with asthma involved in this study would be enlightening with respect to asthma heterogeneity and COVID-19 outcomes.

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Reply to "Does asthma affect outcomes of patients with COVID-19 infections?"

To the Editor:

We would like to thank Kalemci et al[1] for highlighting our paper published in the August issue of the *Journal of Allergy and Clinical Immunology: In Practice*.[2] The impact of COVID-19 on patients with asthma and their COVID-19 outcome has been a matter of several investigations in the past few months. As the authors mentioned, asthma is a heterogenic disease with several endotypes, which may respond to infectious processes differently. Our results are in agreement with other papers that were published in the following month showing that asthma does not decrease or increase hospitalization rate and length for COVID-19.[3] Additional studies showed that atopy might play an important role in the response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Our follow-up large 2-center study has also shown that atopy is a potential protective factor and a positive prognostic factor for decreased severity of COVID-19.[4] Furthermore, we have found that, among different endotypes of asthma, only nonallergic asthma was associated with prolonged need for intubation,[4] which agrees with a recent comprehensive large study.[5] This study showed that nonallergic asthma was associated with a higher risk of severe COVID-19.[5] This is also consistent with translational studies. Although gene expressions of 2 key mediators for SARS-CoV-2 infection, angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2), have been shown to be different in allergic individuals, potentially protecting them from severe illness, in a large study in which all patients with asthma were combined together, the expression of both genes was similar between patients with asthma and healthy subjects.[6] This indicates that asthma in general is not a risk factor for more or less severe COVID-19 illness. However, as a chronic lung disease prone to viral-induced exacerbation, this might place those with severe COVID-19 at risk for a longer duration of pulmonary inflammation.[2,5] Furthermore, an allergic background and differential expression of ACE2 and TMPRSS2 may dampen the strong inflammatory response to SARS-CoV-2 in patients with allergic asthma, leading to the lack of increased severity reported in patients with nonallergic asthma.[2,4,5]

Another important factor that needs to be considered and further investigated is the impact of racial differences on COVID-19 outcome in patients with asthma. The studies that did not find any difference in terms of COVID-19 severity or intubation time in patients with asthma were performed in predominantly non–African American (AA) populations, such as from China, or study populations with only 21% to 26% AAs.[3] In our series from the city of Chicago, 59% of COVID-19 patients with asthma were AA.[2] Interestingly, Peters et al[6] have demonstrated that, among patients with asthma, AA race was associated with higher expression of ACE2 and TMPRSS2. Consistent with that study, our as yet unpublished follow-up study has shown that AAs with asthma and COVID-19 infection had a significantly higher rate of asthma exacerbation and longer duration of asthma symptoms after COVID-19 compared with their white counterparts. Specifically, 68% of AAs versus 35% of whites ($P = .032$) report symptoms suggestive of asthma exacerbation after COVID, and mean ± standard deviation durations of asthma exacerbation symptoms were 3.6 ± 2.1 weeks versus 1.5 ± 1.3 weeks in AAs and whites, respectively ($P = .045$). We have also demonstrated that, although asthma is not a risk factor for COVID-19 hospitalization in any age group, AA children are at a significantly higher risk for COVID-19 adverse outcomes.[7] Multiple interrelated variables, such as uncontrolled comorbidities, reduced access to health care, and other socioeconomic factors, and possibly a genetic predisposition can impact these important results and need to be further investigated.

Kalemci et al[1] also bring up another important concept about the use of inhaled corticosteroids (ICS) for asthma therapy and risk of COVID-19 severity. Based on the impact of ICS on decreasing the expression of ACE2 expression, it was hypothesized that the use of ICS in asthmatics might decrease COVID-19 severity.[6] However, in a large study, Chhiba et al[3] reported that ICS did not increase or decrease the risk of COVID-19 hospitalization in patients with asthma after adjusting for multiple potential confounding factors.

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Quality-of-life researchers in ocular allergy may benefit from the newer methods

To the Editor:

Mikhail et al[1] reviewed the patient-reported outcome measures (PROMs) used to evaluate quality-of-life (QOL) parameters in people with ocular allergy. It is important to note the usefulness of non–allergy-specific (ophthalmic and generic) PROMs depending on the research purpose and intended populations. For example, dry eye questionnaires such as the Ocular Surface Disease Index can be used to evaluate dry eye in ocular allergy.[2]

Also noteworthy is that all the PROMs reviewed[1] were developed using Classical Test Theory, which uses summary scoring. The scale scores in the summary scoring method are obtained by summing and averaging ordinal data obtained using Likert scales. Each item gets an equal weight for calculating an overall score, and an equal distance between adjacent response categories is assumed. For example, in the Quality of Life in Children with Vernal Keratoconjunctivitis questionnaire, "Problem practising sports" and "Problems meeting friends" items are given the same weights.[3] The scores to response options are allocated such that the response option "Sometimes (2)" is considered twice-frequent than "Never (1)" and 0.67 times less-frequent than "Always (3)."[3] Assuming the Likert-scale data as continuous data is erroneous. In 2010, Pesudovs[4] described such PROMs as the first-generation PROMs. Second-generation PROMs address the limitations of the first-generation PROMs by converting the categorical data to interval-level data by log-transformation using Item Response Theory models or Rasch analysis.[4]

In the last 2 decades, the popularity of second-generation PROMs, particularly those using Rasch analysis, has grown exponentially in ophthalmology.[5] Now QOL researchers in ophthalmology are developing third-generation PROMs, item-banking administered with a computer-adaptive testing (CAT) system.[4,6,7] An item bank is a pool of questions calibrated using Rasch analysis or other Item Response Theory models. A CAT system administers only the most informative, individually tailored items using an algorithm with predefined step size and stopping criteria. The CAT system uses automatic scoring and provides real-time feedback, and thus has the potential to be used as a clinical tool to promote value-based medicine.[4,7] Ocular allergy PROMs however are lagging behind.

Researchers interested in QOL outcomes in ocular allergy need to be aware of the advances in QOL research so that the field may benefit. Rasch analysis, in particular, is based on sound scientific principles of measurement and offers several advantages in addition to addressing the limitations of the first-generation