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Editorial

The evidence is in that asthma is not associated with severe coronavirus disease 2019

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In December 2019, a novel respiratory illness caused by severe acute respiratory syndrome coronavirus 2 was first noted in Wuhan, People's Republic of China, and was subsequently named coronavirus disease 2019 (COVID-19). COVID-19 presents with pneumonia and a severe respiratory illness similar to severe acute respiratory syndrome, another zoonotic illness caused by a coronavirus. COVID-19 was reported to have initial mortality rates as high as 15%.[1] In March 2020, the World Health Organization declared COVID-19 a global pandemic. With the rapid spread of a novel disease, health care providers faced a glaring lack of data and were required to use knowledge of previous coronaviruses and severe acute respiratory syndrome to make initial recommendations. Using this previous knowledge and early reports of chronic lung disease being a risk for poor outcomes, the Centers for Disease Control and Prevention declared asthma a high-risk condition for developing severe disease from COVID-19.[2]

Early on in the pandemic, there were reports noting that asthma was underrepresented in several case series, suggesting that asthma might not be a risk factor.[3] Nonetheless, there are reasons to be concerned regarding patients having asthma with a respiratory viral infection, and early on, reports of patients having asthma doing poorly with COVID-19 could be found in the literature.[4,5] We undertook our own study and found that asthma was not associated with increased odds of supplemental oxygen use, intensive care unit (ICU) admission, intubation, or mortality.[6] Multiple other groups performed similar small studies, and now large meta-analyses have analyzed these results.[7-10] In this issue of the *Annals*, Shi et al[7] evaluated studies that included more than 400,000 patients. Altogether, these meta-analyses have included patients from the first reports of COVID-19 through June 26, 2020,[8] August 18, 2020,[9] September 18, 2020,[7] and December 22, 2020.[10] More importantly, although each of these studies had slightly differing inclusion and exclusion criteria, they all yielded similar results and found that a diagnosis of asthma is not associated with increased risk of severe COVID-19.

All 4 studies looked at asthma prevalence among patients with COVID-19, revealing a pooled prevalence ranging from 7.56%[8] to 8.3%,[7] and when stratified by location, the asthma prevalence ranged from 2.2% to 11.1%—similar or slightly lower than the population prevalence of asthma in each location.[7,9,10] In fact, 2 of the meta-analyses suggested that asthma may be protective. Sunjaya et al[8] found a decreased relative risk (RR) of patients with asthma acquiring COVID-19 when compared with patients without asthma (RR, 0.86; 95% confidence interval [CI], 0.80-0.94; $P < .001$). In addition, Terry et al[10] found the prevalence ratio for a positive test of severe acute respiratory syndrome coronavirus 2 in people with asthma was 0.74 (95% CI, 0.68-0.81; this is the ratio of the proportion of those with asthma who tested positive over the proportion of those with exposure, with a value below 1 suggesting protection), suggesting asthma may protect from testing positive for COVID-19. Of note, 2 of the meta-analyses looked at the risk of hospitalization and found conflicting results, with Sunjaya et al[8] reporting a relative risk of 0.87 (95% CI, 0.77-0.99; $P = .03$), or a 13% reduction in risk, whereas the subsequent and larger meta-analyses from Liu et al[9] found no difference (RR, 1.15; 95% CI, 0.92-1.43). Overall, although it seems that asthma may confer slight protection from acquiring COVID-19 and clearly is not associated with worse disease, it also does not seem to associate with a change in risk for hospitalization from COVID-19.

Asthma was not associated with an increased risk of severe disease from COVID-19 among all investigated metrics and may even offer some minor level of protection against mortality. All 4 studies investigated severe disease and poor outcomes. The definitions of severe disease and poor outcomes varied, but, in general, included ICU admission, intubation, and mortality. Each meta-analysis found no increased risk for severe disease or poor outcomes among patients with asthma compared with patients without asthma.[7-10] Notably, 2 studies specifically looked at ICU admission and mechanical ventilation and found no increased risk for patients with asthma. In terms of mortality, all 4 studies revealed no increased risk in patients having asthma, but there were some notable differences. Shi et al[7] found no difference in effect size (ES) for mortality when looking at all studies; but by focusing on studies reporting an adjusted ES, they found decreased ES for mortality in patients having asthma (ES, 0.8; 95% CI, 0.74-0.86; $P = .13$). Liu et al[9] analyzed studies reporting death among patients having COVID-19 with and without asthma and found a lower mortality risk among patients with asthma (RR, 0.65; 95% CI, 0.43-0.98; $P = .04$). The other 2 studies found no difference in mortality but did note a trend toward decreased risk, with Terry et al[10] noting an RR of 0.85 (95% CI, 0.71-1.01; $P = .07$) and Sunjaya et al[8] finding a RR of death of 0.87 (95% CI, 0.72-1.04; $P = .13$) in patients with asthma. Although these studies are somewhat varying in terms of statistical significance, they all revealed that having asthma does not increase one's risk of a severe or lethal outcome from COVID-19.

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Why asthma continues to be listed as a potential risk factor for severe COVID-19 remains unclear. It may be that chronic obstructive pulmonary disease, which is a clearly defined risk factor for worse outcomes, is being confused with asthma. This was exhibited in our own investigation, in which chronic obstructive pulmonary disease was found to be a substantial confounding variable that required additional statistical analyses to address.[6] Regardless of the reason, the overwhelming evidence from these 4 meta-analyses illustrates that patients with asthma are at no increased risk for hospitalization, severe disease, or mortality from COVID-19, and should provide reassurance for our patients. It is important that we share these results with our patients with asthma to allay their fears, and to remind them that the most important thing they can do regarding asthma in this pandemic is to take their controller medications and keep their asthma under control.[3]

Dylan T. Timberlake, MD[*,†]
Mitchell H. Grayson, MD[*,‡]
[*]*Division of Allergy and Immunology*
Department of Pediatrics
Nationwide Children's Hospital
The Ohio State University College of Medicine
Columbus, Ohio
[†]*Division of Allergy and Immunology*
Department of Otolaryngology
The Ohio State University Wexner Medical Center
Columbus, Ohio
[‡]*Center for Clinical and Translational Research*
The Abigail Wexner Research Institute
Nationwide Children's Hospital
Columbus, Ohio
wheeze@allergist.com
Mitchell.Grayson@Nationwidechildrens.org

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