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LETTER



## Asthma endotypes and COVID-19

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To the Editor,

I read with great interest the article “Is asthma an exclusionary condition for SARS-CoV-2 infection in China?” by Ma et al. (1), about the incidence of coronavirus disease 2019 (COVID-19) in asthmatic patients.

This manuscript raises some interesting questions about the relationship between asthma and COVID-19, such as the different incidence of asthma in EUA and China, angiotensin-converting enzyme 2 (ACE2) receptor expression in asthmatic patients and the influence of corticosteroids treatment in asthma as a modulator of ACE receptor. Despite the interesting manuscript, I humbly want to state a few key points for further consideration.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the strain of coronavirus that causes COVID-19. SARS-CoV-2 uses the human ACE2 as an entry receptor (2).

Many factors can influence ACE2 expression such as age (3,4) and morbidities such as pulmonary hypertension, chronic obstructive pulmonary disease, and asthma (5,6).

Asthma is a complex and heterogeneous respiratory syndrome that affects over 300 million individuals worldwide (7). Asthma can be divided into different endotypes such as eosinophilic asthma with a hallmark increase in type 2 cytokines such as IL-4, IL-5, and IL-13 (8,9); and neutrophilic asthma with a hallmark increase in IL-17 cytokine (10,11). The asthma endotype may be crucial in ACE2 expression as IL-4 and IL-13 reduce ACE2 expression (12,13) and IL-17 increases ACE2 expression (12).

Another caveat is that viral infections can increase the expression of ACE2 in the lungs of asthmatic patients (14), therefore is not fully understood how SARS-CoV-2 influences ACE2 expression in asthmatic patients.

Ma et al. also highlight that usage of an anti-inflammatory drug for asthma treatment may also present an advantage in SARS-CoV-2 infection. But long-term usage of corticosteroid is also associated with the development of hypertension, diabetes, obesity (15) risk factors for COVID-19 (16).

Corticosteroids are effective controllers of asthma but may affect patients with eosinophilic asthma and neutrophilic asthma differently (17,18). Oral corticosteroid treatment is effective in moderate and severe eosinophilic asthma (19), but could increase airway neutrophil in eosinophilic patients (20). A common feature in neutrophilic asthma is poor response to oral and inhaled and corticosteroid (21), therefore may receive different anti-asthma treatments (22,23).

In conclusion, Ma et al. presented interesting points concerning asthma and COVID-19, nevertheless, further investigations are needed to better understand the impact of COVID-19 on different asthma phenotypes.

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