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Asthma phenotypes, comorbidities, and disease activity in COVID-19: The need of risk stratification. Reply to Morais-Almeida

To the Editor,

We appreciate Dr. Morais-Almeida's comments¹ about our Letter to the Editor, presenting additional literature about asthma prevalence in severe COVID-19-infected patients and highlighting data that contrast our hypothesis that asthma, particularly type 2 asthma, may be protective against severe disease.

The data that protection may be dependent on type 2 immunity are derived from the higher percentage of asthmatics being atopic,² also reflected in the series of ~2500 patients regularly followed up in our Allergy Unit. Yu et al³ provided preliminary evidence about this in a single-center retrospective study, where COVID-19 atopic patients had less severe infections, milder lung damage compared with age- and gender-matched COVID-19 controls.

As an additional hint, expression of ACE-2, which is one of SARS-CoV-2 receptors and is linked to type 1 and 2 interferon signatures and to low blood eosinophils in adults, was found to be increased in type 2-low asthmatics, while the cluster of lowest ACE-2 corresponds to type 2-high patients.⁴ Nevertheless, different outcomes still need to be addressed in COVID-19 studies, using available clinical and inflammatory biomarkers to distinguish between distinct asthma phenotypes.

Besides Italy and China, reports from Russia⁵ on ~1300 intensive care unit patients with SARS-CoV-2 infection confirm the observation of a low prevalence of chronic lung diseases (ie, asthma as well as COPD).

Although preliminary data on the first COVID-19 cases in the United States⁶ seem to contrast these observations, the higher prevalence of asthma in US COVID-19 hospitalized patients should be considered alongside a higher overall prevalence of asthmatics in these countries compared with Europe and China. Additionally, other comorbidities (ie, obesity) and host/socioeconomic factors (ie, race: 33% were non-Hispanic black patients in the study by Garg et al; unequal access to health system), possibly affecting asthma phenotype and control, may overall impact on COVID-19 outcomes. Another report from Sweden⁷ highlights the association between severe asthma and severe COVID-19.

The severe asthma phenotype is often characterized by mixed granulocytic populations (neutrophilic and eosinophilic), prevalent type 1 inflammation, increased IFN- γ levels in the airways, and ineffectiveness of ICS. This severe phenotype by itself, although accounting for less than 5% of asthmatic patients, would justify the CDC (and

other institutions) including asthma as a risk factor for COVID-19. Data from the UK,⁸ apart from confirming the role of additional comorbidities, draw attention to the recent use of oral steroids, which, indeed, may be a clue for uncontrolled and/or severe asthma.

Uncontrolled asthma is a risk factor for viral exacerbations and hospitalizations, and we embrace the opportunity to stress the importance of optimal adherence to asthma controlling medications, regular follow-up, and specialist-assessment of disease activity. Moreover, treatable comorbidities, which may impair asthma control, should always be managed. Promoting vaccination for preventable respiratory infections (ie, Influenza and Pneumococcal pneumonia) is also advisable. Future studies may help better distinguishing the impact of different asthma phenotypes and comorbidities on COVID-19 outcomes.

KEYWORDS

asthma, epidemiology, infections, virus

CONFLICTS OF INTEREST

Dr Carli, Dr Cecchi, Prof. Parronchi, and Dr Farsi have nothing to disclose. Prof. Stebbing's conflicts of interest can be found at <https://www.nature.com/ncj/editors>, and none are relevant here.

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