Severe asthma during the COVID-19 pandemic: Clinical observations

Elisa Haroun-Díaz, MD, PhD*,
María Vázquez de la Torre, MD, PhD*,
Francisco Javier Ruano, MD, PhD,
Maria Luisa Somoza Álvarez, MD, Diana Pérez Alzate, MD,
Paula López González, MD, Ana Prieto-Moreno, MD,
Isabel Torres Rojas, MD,
María Desamparados Cervera García, MD,
Natalia Blanca-López, MD, PhD, and
Gabriela Canto Díez, MD, PhD

Clinical Implications

- This study describing the effects of the coronavirus disease 2019 pandemic in a selected group of patients with severe asthma suggests that coronavirus disease 2019 may not be severe or cause severe asthma exacerbations in such patients.

During the coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Spain has been one of the most severely affected countries in Europe. As of the time of writing, the country has reported 213,435 confirmed cases of the disease, approximately 10% of which have required intensive care, and 24,543 people have died as a result of infection. Within Spain, the region of Madrid has seen the highest number of cases (61,171) and fatalities (8,176).[1] The Infanta Leonor University Hospital, an institution serving a population of 300,000, is located in southeast Madrid, one of the hardest-hit areas in the entire region. Therefore, our hospital has experienced one of the highest rates of SARS-CoV-2 cases in the country, many of which have required hospitalization. Between March and April, the institution provided emergency care to 2968 patients with COVID-19, of whom 1211 were hospitalized.

SARS-CoV-2 is a respiratory virus that, when severe, is associated with pneumonia, possibly leading to acute respiratory distress syndrome (ARDS) and, in many cases, a fatal outcome.[2] In the early stages of the pandemic, patients with chronic pulmonary diseases were considered to be at risk. However, recent studies have identified advanced age, obesity, and arterial hypertension as the primary risk factors for severe disease. The prevalence of asthma among patients infected with the COVID-19 virus in Wuhan seems to be lower than that in the general population, although asthma has not been clearly defined.[3]

In Spain, 2% of public health expenditure is devoted to asthma-related care.[4] It is estimated that the global economic burden of asthma is between €1.5 billion and €3 billion annually, and higher costs are associated with greater disease severity.[5]

Severe asthma affects 3.9% of patients with asthma.[5] It is defined as an inflammatory chronic respiratory disease that remains uncontrolled despite optimal therapy and treatment of contributing factors, or which worsens when high-dose treatment is decreased.[6] Around 50% of patients with severe asthma experience uncontrolled or partially controlled symptoms despite maximal treatment.[5] These patients pose a special challenge for care providers because of the extensive diagnostic testing and care resources they require.

The aim of this study was to determine the prevalence and characterization of COVID-19 among patients with severe asthma according to European Respiratory Society/American Thoracic Society criteria who presented to our allergy department during the COVID-19 pandemic.

A total of 80 patients with severe asthma under follow-up in our Allergy Unit were included; all were treated with high-dose inhaled corticosteroids and additional controllers. Demographic data, clinical characteristics (ie, comorbidities including cardiovascular risk factors, asthma phenotype, and asthma treatment during the pandemic), and presence or absence of COVID-19 (signs and symptoms, X-ray results, laboratory findings, and CURB65 pneumonia severity score) were obtained by 2 allergists in April 2020 using face-to-face (23.6%) or telephone interview (76.4%) and by consulting the electronic medical record system.

The median age of patients was 49.7 years (range, 22-72 years; interquartile range, 41.25-56.75 years) and 71% were females. Severe allergic asthma was the most frequent phenotype, affecting 70% of the total sample, followed by eosinophilic nonallergic asthma in the remaining 30%. All cases were treated with high doses of inhaled corticosteroids combined with long-acting β-agonists; 80% of patients required additional medication to control the asthma disease, mainly montelukast (78.7%), tiotropium bromide (33.7%), and oral corticosteroids (2.5%). The remaining 23.7% were treated with 1 of the following biological agents: omalizumab (11.2%), mepolizumab (11.2%), and benralizumab (1.2%).

COVID-19 was confirmed by PCR testing in 3 patients with severe controlled asthma (3.75%). The others had controlled asthma and presented no SARS-CoV-2 symptoms. Controlled asthma was determined by Asthma Control Test questionnaire.

The patients with severe asthma with COVID-19 were aged 55, 56, and 62 years, with no cardiovascular risk factors. Two presented an eosinophilic phenotype and 1 was allergic. All were under chronic treatment consisting of daily fluticasone propionate (1000 μg) combined with 50 μg of salmeterol and 10 mg of montelukast. Two patients also required tiotropium bromide at 5 μg/d, and 1 patient was administered 100 mg of mepolizumab every 4 weeks.

Upon presentation to the emergency department, all patients reported fever and cough, 2 patients complained of myalgia, and 1 reported dyspnea. Results of X-ray imaging showed bilateral pneumonia in 2 cases. During the acute phase, only 1 patient received methylprednisolone during inpatient care due to an associated bronchospasm with respiratory failure.

No patients developed cytokine storm and thus did not require high-dose bolus of methylprednisolone, tocilizumab, or anakinra. Moreover, none of them developed ARDS and did not require intensive care or in-home oxygen therapy upon discharge. Data are presented in Table I.

TABLE I. Clinical characteristics of patients with severe asthma with SARS-CoV-2 infection

	Demographic characteristics			Severe asthma characteristics			COVID-19 data										
Patient	Age (y)	Sex	CV risk factors	Asthma phenotype	Asthma comorbidities	Asthma treatment	Symptoms/ signs	Respiratory function	SARS-CoV-2 PCR	Chest X-ray	Lymphocytes (u/µL)	CRP	LDH	D-dimer	CURB65	Hospitalization	Treatment
1	56	F	No	Eosinophilic	Nasal polyposis NSAIDs—cross-intolerance	Fluticasone propionate 1000 µg/d + salmeterol 50 µg/d; tiotropium bromide 5 µg/d; montelukast 10 mg/d	Fever Dyspnea Cough Myalgia Diarrhea	RF: 14 bpm O Sat: 97%	+	Bilateral lung infiltrates	800	43.5	277	490	0	10 d	Hydroxychloroquine Azithromycin Corticosteroids Oxygen therapy 4 LPM
2	55	M	No	Eosinophilic	Obesity BMI: 30 Bronchiectasis	Fluticasone propionate 1000 µg/d + salmeterol 50 µg/d; montelukast 10 mg/d; mepolizumab 100 mg/4 wk	Fever Cough Myalgia	RF: 16 bpm O Sat: 94%	+	Normal	1200	16.1	339	500	NA	No	Hydroxychloroquine Azithromycin
3	62	M	No	Allergic	None	Fluticasone propionate 1000 µg/d + salmeterol 50 µg/d; tiotropium bromide 5 µg/d; montelukast 10 mg/d	Fever Cough	RF: 15 bpm O Sat: 94%	+	Bilateral lung infiltrates	550	136	253	344	0	6 d	Hydroxychloroquine Lopinavir/Ritonavir

BMI, Body mass index; *CRP*, C-reactive protein; *CV*, cardiovacular; *F*, female; *LDH*, lactate dehydrogenase; *LPM*, liters per minute; *M*, male; *NA*, nonapplicable; *NSAID*, nonsteroidal anti-inflammatory drug; *O Sat*, (oxygen saturation) on admission; *RF*, respiratory frequency on admission (*rpm*, respiration per minute).

To our knowledge, this is the first published study describing the effects of the COVID-19 pandemic in a select group of patients with severe asthma.

We observed no increase in exacerbations of severe asthma due to SARS-CoV-2 infection. Contrary to expectations, these patients with severe asthma did not develop an aggressive form of COVID-19 (ARDS) and did not require intensive care. This may be caused by the fact that drugs used to control asthma can contribute to the inhibition of viral replication as described in recent *in vitro* studies.[7] Alternatively, this effect may be linked to the reduction in proinflammatory lipids observed when using montelukast as pretreatment in a mouse model of ARDS.[8]

Many patients with more severe disease had high levels of inflammatory mediators in blood such as INF-γ, IL-1β, IL-6, IL-8, IL-12, and TNF-α,[9] which are cytokines related to the T_H1 response. T cells are highly involved in asthma physiopathology, specifically the T2 pathway in allergic asthma.

Our patient with severe asthma with COVID-19 under mepolizumab (anti–IL-5) treatment since January 2018 did not develop pneumonia. The role played by biological asthma therapies in patients with COVID-19 should be further studied. However, further research based on larger samples is needed to establish whether severe asthma should be considered a risk factor for patients with COVID-19, and whether asthma treatment could protect patients from developing a severe form of COVID-19.

Finally, because patients with severe asthma residing in our area also received care in other hospitals, we cannot provide real incidence data of SARS-CoV-2 infection in these patients.

Allergy Service, Infanta Leonor University Hospital, Madrid, Spain
*These authors contributed equally to this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

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Corresponding author: Elisa Haroun-Díaz, MD, PhD, Allergy Service, Infanta Leonor University Hospital, Av. Gran Vía del Este, 80, 28031 Madrid, Spain. E-mail: elisaharoun@hotmail.com.

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