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## Differentiating characteristics of patients with asthma in the severe acute respiratory syndrome coronavirus 2 infection



The pandemic due to the infection by the betacoronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which began in Wuhan, People's Republic of China, in December 2019, causing the infectious coronavirus disease 2019 (COVID-19),<sup>1</sup> surpassed 21 million infections and more than 700,000 deaths globally,<sup>2</sup> with numbers that continue to rise. The prognosis of SARS-CoV-2 infection worsens when comorbidities such as high blood pressure (HBP), chronic obstructive pulmonary disease, diabetes mellitus (DM), cardiovascular disease, and obesity are associated.<sup>3,4</sup> There are communications that suggest that asthma may be a factor that determines the severity of COVID-19, compared with others, indicating it does not imply an increased risk.<sup>5</sup> The prevalence of asthma in Spain is estimated at 6.3% of the population<sup>6</sup> and in a cohort of hospitalized patients in Spain with SARS-CoV-2 infection was 8.4%.<sup>7</sup> The main objective of our study was to analyze how the SARS-CoV-2 infection has affected patients with asthma in terms of prevalence, morbidity, hospitalization, and mortality.

For the analysis of information contained in electronic health records, we used Savana, an artificial intelligence-enabled system based on natural language processing and neural networks, which combines computational skills with natural language processing by joining Big Data and artificial intelligence approaches, capable of reusing information expressed in natural language in clinical reports. It performs an immediate statistical analysis of patients found on the platform and provides relevant results for the input variables provided by the user.<sup>8</sup> To ensure the privacy of all patients, Savana anonymized the data. Savana carried out the search in the entire population of Castilla la Mancha community, extracting data from primary care, specialized care, hospitals, and emergency departments until July 2020, detecting COVID-19 diagnoses, and in this group, patients diagnosed as having asthma either by a pneumologist or an allergist with functional respiratory tests (spirometry with bronchodilation, methacholine test) or by a compatible clinic by the primary care physician. For this study, we included only patients who tested positive for SARS-CoV-2 with reverse transcriptase polymerase chain reaction and analyzed demographic characteristics, hospitalization data, comorbidities (HBP, dyslipidemia, DM, smoking), and mortality. For statistical analysis, Student t test was used for mean differences of independent variables and  $\chi^2$  for dichotomous variables with a 95% confidence interval.

A total of 6310 patients were diagnosed as having SARS-CoV-2 infection, confirming their positivity by reverse transcriptase polymerase chain reaction. From these, a total of 577 were diagnosed as having asthma, resulting in a prevalence of 9.14%. The mean age of the patients with SARS-CoV-2 (SC2) was  $59 \pm 19$  years, and that of the patients with asthma with SARS-CoV-2 (SC2-A) was  $55 \pm 20$  years. Among SC2, 2983 (41%) were men, whereas 3327 (59%) were women. Among SC2-A, 198 (31%) were men, whereas 379 (69%) were women. In the analysis of comorbidities, we found the following data when analyzing SC2 and SC2-A: HBP 3239 (51%) and

296 (51%), dyslipidemia 2283 (36%) and 216 (37%), DM 1641 (26%) and 142 (25%), smoking 873(14%) and 103(18%). Hospitalization was required for 2164 (34.2%) SC2 and 131 (22.7%) SC2-A, with a prevalence of 6.05% for the hospitalized patients with asthma. Deaths in the SC2 population were 250 (3.96%), and in the SC2-A population, there were 21 (3.64%) deaths (Table 1).

To our knowledge, this cohort is one of the first studies in Spain to describe the prevalence of infection, hospitalization, and morbidity/mortality of patients with asthma with SARS-CoV-2 infection.

The prevalence of infections in our population with asthma was 9.14%, similar to that obtained in a review of patients hospitalized with COVID-19 in Spain.<sup>7</sup> In the study by Chhiba et al,<sup>3</sup> the prevalence of SARS-CoV-2 infection in patients with asthma in the Chicago Illinois area, requiring hospitalization or not was 14.4%. These data suggest that the prevalence may vary by geographic area. In both groups (SC2/SC2-A), the average age was in the range of 50 to 60 years. In addition, there was a higher percentage of women among the infected patients with asthma, in those requiring hospitalization, and in deaths. In SC2, hospitalization and death occurred more frequently in men. Of the analyzed comorbidities, HBP was the most common in both groups, dyslipidemia and DM were similar in proportion, and smoking was more common in patients with asthma.

There is no consensus in the literature as to whether asthma is a comorbidity that increases the risk of a more severe form of SARS-CoV-2 infection.<sup>5</sup> The data from our study reveal that there is lower mortality in the population with asthma. A possible explanation is based on the fact that one of the targeted mechanisms of the entry of the virus into the host cell is through the angiotensin-converting enzyme 2 receptor, a process dependent on the TMPRSS2 protease, allowing the adhesion of the spike protein and performing fusion between the virus and the membrane cells.<sup>9</sup> The use of inhaled corticotherapy in asthma, which is very widespread in our environment, could have a protective effect by decreasing the expression of the angiotensin-converting enzyme 2 receptor and the TMPRSS2 protein, although more studies are needed to prove this.<sup>10</sup> To date, the recommendations for patients with asthma are to maintain their treatment, trying to achieve the best therapeutic adherence.

We consider the following limitations of our study: its retrospective nature and no consideration given to other variables that could influence the results. In addition, the basic treatment of each patient with asthma had not been assessed. The laboratory data that determine, to some extent, the evolution and severity of the SARS-CoV-2 infection had not been measured either. It is possible that there is a selection bias, as there is more surveillance of patients with asthma compared with the general population.

Our study reveals that the prevalence of asthma was 9.14% and the hospitalization rate was 6.05% in the total number of SARS-CoV-2 infections in the community of Castilla la Mancha. In addition, HBP was the most associated comorbidity analyzed in both groups (SC2 and SC2-A). We also found a difference in mortality, being lower in patients with asthma, although owing to the small number of patients in this group, it did not reach statistical significance.

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Table 1	
Characteristics of Patients	With SARS-CoV-2

Characteristics	SARS-CoV-2	SARS-CoV-2 and asthma	
Total patients, n (%)	6310 (100)	577 (9.14)	
Mean age, y	$59\pm19$	$55\pm20$	MD: $4 \pm 19$ (CI: 2.3-5.6), $P < .001^{a}$
Sex (woman), n (%)	3327 (59)	379 (66)	OR: 1.72 (CI: 1.4-2.0), P < .001 <sup>b</sup>
Hospitalization, n (%)	2164 (34.2)	131 (22.7)	OR: 0.56 (CI: 0.46-0.59), P < .001 <sup>b</sup>
Mortality, n (%)	250 (3.96)	21 (3.64)	OR: 1.00 (CI: 0.6-1.7), $P = .03^{b}$
HBP, n (%)	3239 (51)	296 (51)	OR: 1.00 (CI: 0.8-1.1), $P = .98^{b}$
Dyslipidemia, n (%)	2283 (36)	216 (37)	OR: 1.00 (CI: 0.8-1.2), $P = .54^{b}$
DM, n (%)	1641 (26)	142 (25)	OR: 1.10 (CI: 0.7-1.3), $P = .46^{b}$
Smoking, n (%)	873 (14)	103 (18)	OR: 1.35 (CI: 1.1-1.6), P = .008 <sup>b</sup>

Abbreviations: CI, confidence interval; DM, diabetes mellitus; HBP, high blood pressure, MD, mean difference; OR: odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

 ${}^{b}\chi^{2}$  test.

Table 1

More studies are, therefore, needed to conclude whether asthma is a factor that increases the severity of the SARS-CoV-2 infection.

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## Asthma is associated with increased risk of intubation but not hospitalization or death in coronavirus disease 2019

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused considerable morbidity and mortality. COVID-19 often presents with respiratory symptoms; however, the role of asthma in COVID-19 has not been well established. Although studies from China suggested that asthma was not a risk factor for severe COVID-19, other studies have revealed higher rates of asthma among hospitalized patients.<sup>1,2</sup> Therefore, the primary aim of this study was to assess the associations between asthma and hospitalization, intensive care unit (ICU) admission, or death among patients with COVID-19. Secondary objectives were to assess the associations

between asthma and intubation, duration of intubation and hospitalization, and inflammatory markers in COVID-19.

This retrospective study was conducted at the George Washington University School of Medicine and Health Sciences in Washington, DC, and approved by its institutional review board. Patients were identified by an electronic medical record search of positive SARS-CoV-2 polymerase chain reaction test results between March and May 2020. Patients with underlying lung disease other than asthma were excluded. Demographics, clinical history, and laboratory markers (trough white blood cell, platelet, and lymphocyte counts; peak D-dimer, ferritin, C-reactive protein [CRP], lactate dehydrogenase [LDH], and interleukin-6 [IL-6] levels) were collected. Diagnosis of asthma was based on the *International Classification of Diseases, Tenth Revision* codes and verified by clinical history by a board-certified allergist.

A total of 787 patients with confirmed SARS-CoV-2 were identified. A total of 60 patients were excluded owing to unknown medical history or pulmonary disease other than asthma,

<sup>&</sup>lt;sup>a</sup>Student's t test.

Drs Keswani and Ein share senior authorship.

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