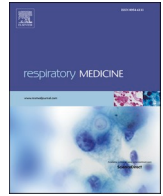




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Short communication

## Symptoms in patients with asthma infected by SARS-CoV-2

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### ABSTRACT

**Introduction:** Organ tropism of SARS-CoV-2 to the respiratory tract could potentially aggravate asthma. The susceptibility of patients with asthma to develop an exacerbation when they are infected with SARS-CoV-2 is unknown. We aimed to investigate the symptoms presented in patients with asthma who became infected with SARS-CoV-2.

**Methods and results:** All patients over 14 years of age who tested positive for SARS-CoV-2 (by RT-PCR) were included (n = 2995). In patients with asthma (n = 77, 2.6%; 44 females), symptoms, therapy and phenotype were recorded. Seventeen (22%) patients had mild asthma, 55 (71%) moderate and five severe (6%). Twenty-six patients with asthma (34%) were asymptomatic, 34 (44%) developed symptoms but did not require hospital admission, and 17 (22%) were hospitalised. One patient was admitted because of asthma exacerbation without pneumonia or other symptoms. Ten patients (13%) had wheezes (six with pneumonia). Comparison of wheezing between patients with non-T2 asthma and the rest of the patients was statistically significant, (p < 0.001).

**Conclusions:** SARS-CoV-2 infection is not a significant cause of asthma exacerbation, although some patients may present wheezing, especially in cases of pneumonia. The severity of asthma does not seem to be associated with symptoms of the disease.

### 1. Introduction

Current data indicate that asthma is not associated with an increased risk of developing or being hospitalised for COVID-19 after adjusting for confounding variables [1,2]. However, the organ tropism of SARS-CoV-2 to the respiratory tract could potentially aggravate asthma. In fact, although respiratory viruses are common triggers of asthma exacerbation, it has not yet been established whether this also applies to SARS-CoV-2 infection [3]. The susceptibility of patients with asthma to develop an exacerbation when they are infected with SARS-CoV-2 is unknown.

Consequently, we aimed to investigate the symptoms presented in patients with asthma who became infected with SARS-CoV-2 and to elucidate whether this infection was associated with exacerbation of the disease.

### 2. Patients and methods

This was an observational, retrospective study that included all consecutive patients over 14 years of age who tested positive for SARS-

CoV-2 (determined by RT-PCR technique) in our hospital. The recruitment period was from March 3 to December 11, 2020. The study was approved by the local institutional ethics board. The electronic medical record for each case was reviewed and patients with a diagnosis of asthma established by a physician (regardless of method) and with prescribed asthma therapy where recorded. Data on the treatment and phenotype were collected. Severity of asthma was determined at baseline status prior to infection according to the prescribed therapy following international GINA recommendations (<https://ginasthma.org/>): mild (step 1 and 2 of GINA), moderate (step 3 and 4) or severe (step 5). Phenotypes were established as allergic, eosinophilic and non-T2. The allergic group included patients with elevated IgE, a positive prick test to pneumo-allergens or seasonal asthma associated with rhinitis. Eosinophilic patients included those who were non-allergic with a blood eosinophil count of more than 300 per millilitre [4]. Patients who did not meet these criteria were classified as non-T2 phenotype.

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### 3. Results

In the study period, 2995 patients tested positive for SARS-CoV-2, 77 with asthma (2.6%). This included 44 females (57%). The median age of patients with asthma was 49 years (interquartile range 34–61). According to the medications prescribed to control the disease, 17 (22%) patients had mild asthma, 55 (71%) moderate and five severe (6%) (four receiving omalizumab and one benralizumab). No patient was receiving oral corticosteroids prior to SARS-CoV-2 infection.

Twenty-six patients with asthma (34%) were asymptomatic during SARS-CoV-2 infection, 34 (44%) developed symptoms but did not require hospital admission (two of them self-reported wheezing), and 17 (22%) were hospitalised (Table 1). Two patients were admitted to the ICU and required mechanical ventilation. Of the admitted patients, 14 had bilateral pneumonia (six with mild wheezing in pulmonary auscultation), one patient was admitted because of asthma exacerbation (dyspnoea and wheezing without pneumonia or other symptoms), one patient was admitted due to dyspnoea and general malaise, and one with fever, dyspnoea, wheezing, headache and myalgia. Forty-seven patients were classified as having allergic asthma, eight as eosinophilic asthma, and 22 as non-T2 asthma. Admitted patients were five allergic, four eosinophilic and eight non-T2 phenotypes. Ten patients (13%) had wheezes, of which six were classified as non-T2 phenotype, three as allergic and one as eosinophilic phenotype (comparison of wheezing between patients with non-T2 asthma and the rest of the patients was statistically significant,  $p < 0.001$ , Chi-squared test).

### 4. Discussion

In our series, 2.6% of patients with SARS-CoV-2 infection had asthma, in agreement with our previous experience and other studies that concluded that asthma patients are not over-represented among

COVID-19 patients [1,2,5,6]. Interestingly, we found that a few patients with asthma infected with SARS-CoV-2 developed wheezing (13%) but very rarely suffered an exacerbation of the disease. Only one of our 77 patients was admitted due to exacerbation of asthma without other symptoms of viral disease. There was also reported mild wheezing (self-reported or found on physical examination) in nine other patients. Only two of the 34 non-hospitalised symptomatic patients had mild dyspnoea and wheezing. This confirms the low risk of exacerbation of asthma associated with SARS-CoV-2 infection.

There is scarce information on the outcome of patients with asthma infected by SARS-CoV-2. In a study of COVID-19 hospitalised patients [7], 4.8% had a history of asthma and the authors concluded that none of them presented with an asthma exacerbation. However, the same study described wheezing, mostly mild, in 16% of cases [7]. Asthma exacerbations have rarely been documented in patients with COVID-19. Ono et al. [8] reported on a case of exacerbation of previously well-controlled eosinophilic asthma associated with COVID-19 pneumonia. Codispoti et al. [9] described four patients with asthma exacerbation also associated with COVID-19 infection. However, it can be stated that SARS-CoV-2 infection is not a frequent cause of asthma exacerbation. In 2020, there were no positive SARS-CoV-2 samples in children admitted with attacks of viral wheeze or asthma during the start of the school year [10], and a significant reduction in all-cause related asthma admissions during the pandemic has been reported [11].

Recent data suggests differing susceptibility to COVID-19 among asthma patients based on their phenotype, with a lower susceptibility in patients with underlying type 2 airway inflammation [3]. In our series, wheezing was significantly more frequent in the non-T2 phenotype.

Although there are some differences among studies, the use of asthma medication (inhaled or systemic corticosteroids and biologics), and asthma severity were not independent factors for poor clinical outcomes of COVID-19 [1,2,12]. In our experience there was no relationship between disease severity (established according to the treatment prescribed) and symptoms. Some of our patients taking biologics required admission for COVID-19, but others were asymptomatic.

Our study has several limitations. The phenotypic classification was established using retrospective and non-systematically recorded data and should therefore be interpreted with caution. In addition, we have not data on the relative frequency of these phenotypes in the asthmatic patients in our area. Although symptoms were reported via a questionnaire, it was not specifically designed to detect asthma exacerbations or asthma symptoms.

In conclusion, our results show that SARS-CoV-2 infection is not a significant cause of asthma exacerbation, although some patients may present wheezing, especially in cases of pneumonia. The severity of asthma as determined by its treatment does not seem to be associated with symptoms of the disease.

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**Eduardo Garcia-Pachon:** Conceptualization, Methodology, Writing - Original Draft

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**Table 1**  
Symptoms and clinical findings according to severity of asthma.

	Asymptomatic	Non-hospitalised, symptoms and clinical findings	Hospitalised, symptoms and clinical findings
Number	26	34	17
Age, years	46 (25–56)	44 (36–61)	61 (52–82)
Female, number and percentage	14 (54%)	20 (59%)	10 (59%)
<b>Mild asthma</b>	N = 8	N = 6	N = 3
N, 17		Fever, 4	Fever, 2
Female, 11		Cough, 1	Cough, 2
		Dyspnoea, 1	Dyspnoea, 2
		Anosmia/ageusia, 3	Wheezing, 1
		Wheezing, 1	Pneumonia, 3
<b>Moderate asthma</b>	N = 15	N = 28	N = 12
N, 55		Fever, 16	Fever, 7
Female, 31		Cough, 14	Cough, 6
		Dyspnoea, 5	Dyspnoea, 8
		Diarrhoea, 7	Diarrhoea, 3
		Headache, 6	Headache, 1
		Muscle pain, 10	Muscle pain, 2
		Anosmia/ageusia, 3	Anosmia/ageusia, 1
		Sore throat, 2	Wheezing, 6
		Wheezing, 1	Pneumonia, 9
<b>Severe asthma</b>	N = 3	N = 0	N = 2
N, 5			Fever, 1
Female, 2			Dyspnoea, 1
			Diarrhoea, 1
			Muscle pain, 1
			Sore throat, 1
			Wheezing, 1
			Pneumonia, 2

Age as a median and interquartile range. N = number. Clinical characteristics as a number of patients presenting each.

## Editing

**Justo Grau- Delgado:** Investigation, Validation, Writing - Review & Editing

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## References

- [1] K.D. Chhiba, G.B. Patel, T.H.T. Vu, et al., Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19, *J. Allergy Clin. Immunol.* 146 (2) (2020) 307–314, <https://doi.org/10.1016/j.jaci.2020.06.010>, e4.
- [2] J.L. Izquierdo, C. Almonacid, Y. González, et al., The impact of COVID-19 on patients with asthma, *Eur. Respir. J.* (2020) 2003142, <https://doi.org/10.1183/13993003.03142-2020>.
- [3] S.M. Assaf, S.P. Tarasevych, Z. Diamant, N.A. Hania, Asthma and severe acute respiratory syndrome coronavirus 2019: current evidence and knowledge gaps, *Curr. Opin. Pulm. Med.* 27 (1) (2021) 45–53, <https://doi.org/10.1097/MCP.0000000000000744>.
- [4] X. Muñoz, F. Pilia, I. Ojanguren, C. Romero-Mesones, M.J. Cruz, Is asthma a risk factor for COVID-19? Are phenotypes important? *ERJ Open Res* 7 (1) (2021), 00216 <https://doi.org/10.1183/23120541.00216-2020>, 2020.
- [5] E. Garcia-Pachon, L. Zamora-Molina, M.J. Soler-Sempere, et al., Asthma prevalence in patients with SARS-CoV-2 infection detected by RT-PCR not requiring hospitalization, *Respir. Med.* 171 (2020) 106084, <https://doi.org/10.1016/j.rmed.2020.106084>.
- [6] E. Garcia-Pachon, L. Zamora-Molina, M.J. Soler-Sempere, et al., Asthma and COPD in hospitalized COVID-19 patients, *Arch. Bronconeumol.* 56 (9) (2020) 604–606, <https://doi.org/10.1016/j.arbres.2020.05.007>.
- [7] A. Beurnier, E.M. Jutant, M. Jevnikar, et al., Characteristics and outcomes of asthmatic patients with COVID-19 pneumonia who require hospitalisation, *Eur. Respir. J.* 56 (5) (2020) 2001875, <https://doi.org/10.1183/13993003.01875-2020>.
- [8] Y. Ono, S. Obayashi, Y. Horio, et al., Asthma exacerbation associated with COVID-19 pneumonia, *Allergol. Int.* 70 (1) (2021 Jan) 129–130, <https://doi.org/10.1016/j.alit.2020.07.002>.
- [9] C.D. Codispoti, S. Bandi, P. Patel, M. Mahdavinia, Clinical course of asthma in 4 cases of coronavirus disease 2019 infection, *Ann. Allergy Asthma Immunol.* 125 (2) (2020) 208–210, <https://doi.org/10.1016/j.anai.2020.05.009>.
- [10] D. Roland, K.W. Teo, S. Bandi, D. Lo, E.A. Gaillard, COVID-19 is not a driver of clinically significant viral wheeze and asthma, *Arch. Dis. Child.* (2020), <https://doi.org/10.1136/archdischild-2020-320776>.
- [11] D.L. Sykes, S. Faruqi, L. Holdsworth, M.G. Crooks, Impact of COVID-19 on COPD and Asthma admissions and the pandemic from a patient's perspective, *ERJ Open Res* (2020), <https://doi.org/10.1183/23120541.00822-2020>.
- [12] Y.J. Choi, J.Y. Park, H.S. Lee, et al., Effect of asthma and asthma medication on the prognosis of patients with COVID-19, *Eur. Respir. J.* (2020) 2002226, <https://doi.org/10.1183/13993003.02226-2020>.