

CORRESPONDENCE

Asthmatic patients and COVID-19: Different disease course?

We read with great interest the article "Asthma and COVID-19: Is asthma a risk factor for severe outcomes?" by Johnston¹ about the possible implications of asthma treatment and coronavirus disease 2019 (COVID-19).

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the number of SARS-CoV-2-infected patients with asthma is consistent with the asthma incidence in the population despite the virus outbreak.² There are few reports of COVID-19 in asthmatic patients. Therefore we aimed to investigate the disease course of COVID-19 in asthmatic patients from hospitalization until COVID-19 resolution.

Patients were recruited at the Hospital das Clínicas—University of São Paulo (HCFMUSP). Asthma patients were selected based on the previous asthma diagnoses. COVID-19 was confirmed by the nasopharyngeal detection of SARS-CoV-2 by reverse transcriptase polymerase chain reaction. Patients were evaluated daily until SARS-CoV-2 clearance and hospital discharge. This study was approved by the Ethics Committee of HCFMUSP (No. 30 800 520.7.0000.0068-2020).

We recruited 215 COVID-19-infected patients. Among those 5 (2.32%) had asthma and systemic arterial hypertension (SAH) a common comorbidity associated with asthma.³ A total of 7

TABLE 1 Clinical characteristics and fate of COVID-19 patients included in the study

Group	Patient	Age (y)	Sex	SAH	Diabetes	Smoking	Secondary bacterial infection	Death	Hospitalization time (d)
Moderate	#1	63	Male	No	No	No	No	No	6
	#2	67	Male	No	No	No	No	No	13
	#3	51	Female	No	No	No	No	No	16
Severe	#1	50	Female	No	No	No	No	No	20
	#2	61	Male	No	No	No	No	No	20
	#3	43	Male	No	No	No	No	No	18
	#4	65	Male	No	No	No	No	No	18
Asthma + SAH	#1	43	Male	Yes	No	No	No	No	14
	#2	61	Female	Yes	No	No	No	No	8
	#3	64	Male	Yes	No	No	No	No	18
	#4	41	Male	Yes	No	No	No	No	5
	#5	61	Female	Yes	No	No	No	No	8
SAH	#1	74	Male	Yes	No	No	No	No	13
	#2	45	Female	Yes	No	No	No	No	15
	#3	47	Male	Yes	No	No	No	No	13
	#4	59	Male	Yes	No	No	No	No	44
	#5	67	Female	Yes	No	No	No	No	11
	#6	74	Male	Yes	No	No	No	No	19
	#7	52	Male	Yes	No	No	No	No	19
	#8	72	Female	Yes	No	No	No	No	18
	#9	69	Female	Yes	No	No	No	No	18
	#10	53	Male	Yes	No	No	No	No	41

Abbreviations: Moderate, nonasthmatic and non-SAH patients in the general ward with moderate COVID-19; Severe, nonasthmatic and non-SAH patients in the intensive care unit with severe COVID-19; SAH, SAH patients in the intensive care unit; asthma + SAH, asthmatic and SAH patients in the intensive care unit.

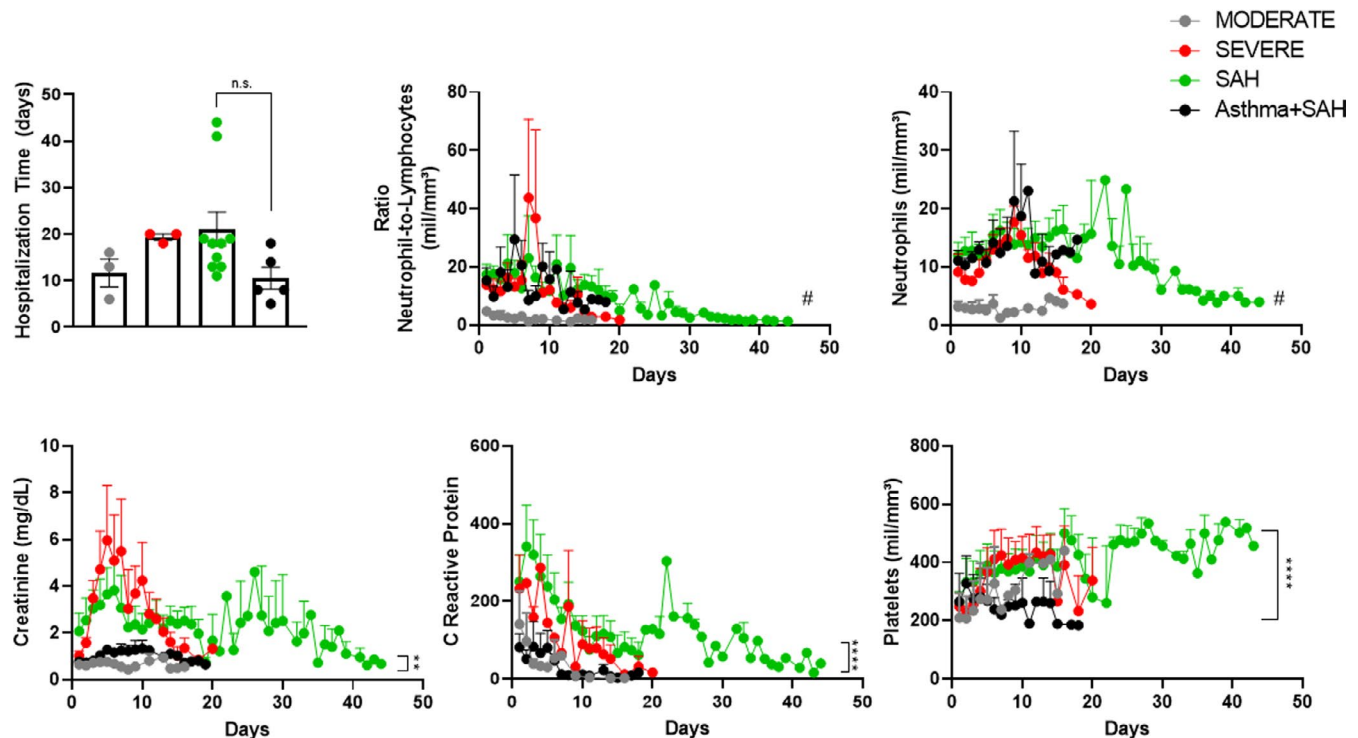


FIGURE 1 Daily clinical features of COVID-19 patients. (A) hospitalization time, (B) ratio of neutrophils to lymphocytes, (C) neutrophils, (D) creatinine, (E) C-reactive protein, and (F) platelets. MODERATE, nonasthmatic and non-SAH patients in the general ward with moderate COVID-19; SEVERE, nonasthmatic and non-SAH patients in the intensive care unit with severe COVID-19; SAH, SAH patients in the intensive care unit; asthma + SAH, asthmatic and SAH patients in the intensive care unit. # $P < .05$ difference from MODERATE in relation to all other groups. ** $P < .01$ for asthma + SAH in relation to SAH. **** $P < .001$ for asthma + SAH in relation to SAH. The Kruskal-Wallis test with Dunn's multiple comparison. Data collected between March 1, 2020, and July 24, 2020

patients without comorbidities were included in the study: 3 patients were in the general ward with moderate COVID-19 infection (MODERATE) and 4 were in the intensive care unit with severe COVID infection (SEVERE). Seventy-four patients had SAH (34.4%) as a comorbidity and only 10 (4.65%) were included in the study. The other 64 patients presented other comorbidities or secondary infections that could influence COVID-19 disease course.⁴ All patients with SAH underwent regular daily usage of losartan (50 mg). There was no sex difference between groups and patients were hospitalized between 3 and 4 days after COVID-19 symptom onset. All patients in this study survived (Table 1). Statistical analyses were performed using the Kruskal-Wallis test with Dunn's multiple comparison and the data are shown as the mean $\pm$ standard error of the mean. P -value of $< .05$ was considered to be statistically significant.

Viral infections are associated with asthma exacerbations and can modulate the expression of angiotensin-converting enzyme 2 (ACE2)⁵ the most described SARS-CoV-2 entry receptor. Nevertheless SARS-CoV-1 did not increase asthma exacerbations.⁶

Asthma is a complex respiratory syndrome that compresses different inflammatory profiles which could influence the immune response to SARS-CoV-2 and ACE2 expression differently. A caveat of this investigation is that all asthmatic patients were

previously diagnosed and we could not determine their asthma endotype.

Inhaled corticosteroid (IC) and anti-asthma (AA) drugs could act as possible modulators of SARS-CoV-2 infection which could reduce the incidence of COVID-19 in asthma patients but in our cohort asthma patients did not regularly use IC or AA drugs. Although the number of cases was low our asthma patients also presented SAH a risk factor for COVID-19 but no difference was verified in the hospitalization time between all groups (Figure 1A).

The MODERATE group presented a lower ratio of neutrophils to lymphocytes and neutrophils in the blood which are relevant COVID-19 severity markers in relation to the other groups (Figure 1B-C).

Asthma patients showed reduced levels of creatinine C-reactive protein and platelets in comparison with SAH patients (Figure 1D-F). Our data indicate that asthmatic patients did not present an increase in hospitalization time or COVID-19 severity; in contrast asthmatic patients exhibited a reduction in some of the COVID-19 severity-associated markers.

We hypothesize that type 2 cytokines produced in eosinophilic asthma may downregulate ACE2 expression or counteract type 1 cytokines released in COVID-19⁵ therefore presenting as a protective factor; however patients with asthma are not immune to COVID-19.

Our university hospital is a referral unit for moderate or severe cases of COVID-19; hence this profile may not be present in mild COVID-19 cases. Our study is the first asthma-related report in the Brazilian population but further investigation is needed to better understand the influence of asthma on COVID-19.

KEYWORDS

asthma, COVID-19, SARS-CoV-2, systemic arterial hypertension

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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REFERENCES

1. Johnston SL. Asthma and COVID-19: Is asthma a risk factor for severe outcomes? *Allergy*. 2020;75:1543-1545.
2. Caminati M, Lombardi C, Micheletto C, et al. Asthmatic patients in COVID-19 outbreak: Few cases despite many cases. *J Allergy Clin Immunol*. 2020;146(3):541-542.
3. Ferguson S, Teodorescu MC, Gangnon RE, et al. Factors Associated with Systemic Hypertension in Asthma. *Lung*. 2014;192(5):675-683.
4. Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. *J Infect*. 2020;81(2):266-275.
5. Castelo Branco ACC, Sato MN, Alberca RW. The possible dual role of the ACE2 receptor in asthma and SARS-COV2 infection. *Front Cell Infect Microbiol*. 2020;10:537.
6. Van Bever HP, Chng SY, Goh DY. Childhood severe acute respiratory syndrome, coronavirus infections and asthma. *Pediatr Allergy Immunol*. 2004;15:206-209.