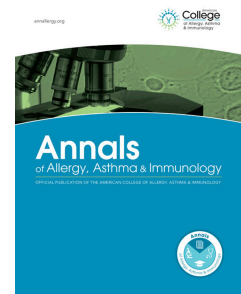


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Asthma in COVID-19 suspected and diagnosed patients

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L.W. conceived and coordinated this study. J.A.O., C.G., P.A.M., A.M.R. and R. P. coordinated and recruited patients. L.C. and L.W. performed data analysis. P.A.M. and D.R. performed cytokine studies. S.L., J.G.K. and L.W. wrote the manuscript. All authors provided critical comments on the manuscript and approved the manuscript.

Conflict of Interest

The authors declare no conflict of interests.

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Key Words: Asthma; clinical symptoms; COVID-19; cytokine; interleukin (IL)-8; respiratory viral infection; SARS-CoV-2; severe outcomes; St. Louis

Abbreviations Used

COVID-19: coronavirus disease 2019

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2

COPD: chronic obstructive pulmonary disease

ICU: intensive care unit

ACE2: angiotensin-converting enzyme 2

ICD-10: International Classification of Disease, Tenth Revision

IL: interleukin

OR: odds ratio

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Background: Asthma patients are comparatively susceptible to respiratory viral infections and more likely to develop severe symptoms than people without asthma. During the coronavirus disease 2019 (COVID-19) pandemic, it is necessary to adequately evaluate the characteristics and outcomes of the asthma population in the COVID-19 tested and diagnosed population.

Objective: We performed a study to assess the impact of asthma on COVID-19 diagnosis, presenting symptoms, disease severity, and cytokine profiles.

Methods: This was an analysis of a prospectively collected cohort of patients suspected of having COVID-19 who presented for COVID-19 testing at a tertiary medical center in Missouri, USA between March and September 2020. We classified and analyzed patients according to their preexisting asthma diagnosis and subsequent COVID-19 testing results.

Results: COVID-19 suspected patients (n=435) were enrolled in this study. The proportion of patients testing positive for COVID-19 was 69.2% and 81.9% in the asthma and non-asthma groups respectively. The frequency of relevant symptoms are similar between asthma groups with positive and negative COVID-19 test results. In the COVID-19 diagnosed population (n=343), asthma was not associated with several indicators of COVID-19 severity, including hospitalization, admission to an intensive care unit (ICU), mechanical ventilation, death due to COVID-19, and in-hospital mortality after multivariate adjustment. COVID-19 patients with asthma exhibited significantly lower levels of plasma interleukin (IL)-8 compared to patients without asthma (adjusted p=0.023).

Conclusion: The asthma population is facing a challenge in preliminary COVID-19 evaluation due to overlap in symptoms of COVID-19 and asthma. However, asthma does not increase the risk of COVID-19 severity if infected.

1 Introduction

2 Coronavirus disease 2019 (COVID-19) is caused by the novel severe acute respiratory syndrome
3 coronavirus 2 (SARS-CoV-2) and leads to multiple respiratory symptoms, amongst a myriad of
4 other symptoms.¹ COVID-19 has been characterized as a pandemic by the World Health
5 Organization (WHO), and has affected more than 73 million people worldwide at the time of this
6 writing according to COVID-19 dashboard at Johns Hopkins University. People with asthma are
7 generally more susceptible to respiratory viral infections compared to people without asthma due
8 to an abnormal airway epithelium and less effective or deficient anti-viral innate immune
9 responses.^{2 3} In the setting of respiratory viral infections, which include human rhinovirus,
10 respiratory syncytial virus, seasonal coronaviruses, and many others, asthma patients usually
11 exhibit more severe and longer durations of respiratory symptoms compared to healthy
12 individuals and may experience asthma exacerbations.⁴⁻⁶

13 Researchers have postulated that asthma patients may be both at high risk of being infected with
14 SARS-CoV-2 and experience more severe outcomes when infected.⁷ However, these
15 assumptions have not been clearly demonstrated in numerous studies to date.⁸⁻¹² Early findings
16 from Wuhan, China revealed that asthma was under-represented in COVID-19 infected patients,
17 with the prevalence of asthma only at 0.9% among 548 patients with COVID-19, whereas the
18 overall prevalence of asthma was 6.4% in the adult Wuhan population.¹³ Similarly, COVID-19
19 infection was noted to be comparatively low in patients in the Severe Asthma Network in Italy,
20 and asthma patients also had comparatively low mortality rates if infected.¹⁴ Even though the
21 prevalence of asthma among COVID-19 patients in Europe and the United States has been
22 substantially higher, ranging from about 8% to 17%, asthma was not observed to be associated
23 with an increased risk of adverse outcomes, such as hospitalization, intensive care unit (ICU)

transfer, intubation, hospital readmissions, and mortality, in patients with COVID-19.^{8 15-17} Several explanations for the surprisingly equivalent or favorable infection rates and outcomes of COVID-19 in asthma patients have been proposed including decreased epithelial angiotensin-converting enzyme 2 (ACE2) expression in asthma.^{18 19} However, interestingly, a large cohort study from England identified asthma patients with recent oral corticosteroid use as being at increased risk for death due to COVID-19, while other studies found that asthma prolonged endotracheal intubation times.²⁰⁻²³

While most COVID-19-related research in asthma to date has focused on associations with morbidity and mortality, less focus has been placed on assessing two other pressing issues. First, are there difficulties in differentiating between COVID-19 symptoms and other infections and asthma symptoms? The majority of patients who are diagnosed with COVID-19 report non-specific signs and symptoms including dyspnea, cough, wheezing, fever, fatigue, anosmia, and ageusia. Unfortunately, there is an overlap between the common symptoms of COVID-19 and other viral infections and asthma exacerbations.²⁴ These shared symptoms may cause considerable confusion among people with asthma and their providers regarding need for COVID-19 testing, isolation recommendations and disease management. Second, are there any differences in presenting signs and immune responses between COVID-19 patients with and without asthma? To date, no studies have described and compared the presenting characteristics between COVID-19 patients with and without preexisting asthma. Clues on presenting symptoms could help providers better understand the common presentation of COVID-19 infection in asthma patients and risk-stratify them.

To this end, we conducted an analysis using a prospectively collected cohort of patients who presented with COVID-19-like symptoms and received testing at a medical center. We evaluated

characteristics of patients with and without preexisting asthma in this suspected COVID-19 population and subsequently, within the COVID-19 diagnosed population. Furthermore, we compared the cytokine profiles between COVID-19 diagnosed patients with and without preexisting asthma, and assessed the associations between asthma and subsequent COVID-19 outcomes.

Methods

1. Patient recruitment

This study was approved by the institutional review board at Washington University in St. Louis (IRB number: 202003085). Patients who presented with symptoms consistent with COVID-19 to two urban medical centers within the BJC Healthcare system in St. Louis, Missouri AND for whom a healthcare provider requested SARS-CoV-2 testing were eligible for enrollment in this study from March through September 2020. Patients who were interested in the study provided written consent and were asked about their symptoms, which were collected through participant interviews, with additional medical data extracted from medical records. SARS-CoV-2 positivity was determined using PCR-based testing performed on nasopharyngeal specimens.

2. Definition of variables

Asthma and other comorbidities were identified based on the International Classification of Disease, Tenth Revision (ICD-10) codes noted in health records. Patients were defined as having a preexisting diagnosis of asthma if their health records contained an ICD-10 code beginning with J45. Obesity was defined by a body mass index (BMI) greater than or equal to 30 found in the electronic medical record. Race and presenting symptoms were self-reported by participants in the interview.

3. Cytokine quantification

Plasma samples from a subset of participants were analyzed using cytokine quantification as described before.²⁵ Plasma was analyzed using a human magnetic cytokine panel providing parallel measurement of 35 cytokines (ThermoFisher). Each sample was performed in duplicate and then analyzed on a Luminex FLEXMAP 3D instrument.

4. Statistical Analysis

Only adults older than 18 years old were included in this analysis. All statistical analysis, graphs, and figures were produced using RStudio. A p-value <0.05 was the standard used to determine if the statistical tests and models were significant. Demographics, major co-morbidities, symptoms, and clinical outcomes were compared using the non-parametric Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. Multivariable logistic regression models were used to evaluate whether asthma was a predictor of COVID-19 severe outcomes (including the individual outcomes of hospitalization, ICU admission, mechanical ventilation, death due to COVID-19, and in-hospital mortality) after adjustment for sex, age, race, chronic obstructive pulmonary disease (COPD), and obesity.

Results

1. Among the COVID-19 suspected population, asthma patients had lower rates of testing positive for COVID-19 compared to those without asthma.

There were 435 patients in this cohort who were suspected of having COVID-19 by a healthcare provider and subsequently tested. The algorithm for identifying patients into different categories is noted in Fig 1. Among the 435 patients, 104 patients (23.9%) had a preexisting diagnosis of asthma and 331 patients (76.1%) had no asthma diagnosis. Among participants with an asthma

diagnosis, 72 of the 104 patients (69.2%) subsequently tested positive for COVID-19, while among the non-asthma participants, 271 of the 331 patients (81.9%) subsequently tested positive for COVID-19. Patients with a diagnosis of asthma who were suspected of having COVID-19 had significantly lower rates of receiving positive test results as compared to non-asthma patients suspected of having COVID-19 ($p=0.0059$, chi-square test).

We compared different characteristics between COVID-19 positive and negative patients stratified by asthma (Table 1). Regardless of asthma status, the COVID-19 group was older ($p=0.0014$ in the asthma group and $p<0.0001$ in the non-asthma group) and had a higher percentage of underlying comorbidities [hypertension ($p=0.0012$ in the asthma group and $p<0.0001$ in the non-asthma group) and diabetes ($p=0.017$ in the asthma group and $p<0.0001$ in the non-asthma group)]. More males were in the COVID-19 group, but this was only significant for the non-asthma patients. Participants who were diagnosed with COVID-19 were more likely to report their race as Black in the non-asthma group ($p<0.0001$), but this did not reach statistical significance in the asthma group ($p=0.053$). In addition, participants diagnosed with COVID-19 had a substantially higher BMI ($p=0.00096$) and percentage of obesity ($p=0.0055$) than non-COVID-19 patients, but statistical significance was only observed in the asthma population.

2. Asthma patients exhibited similar symptoms regardless of COVID-19 test results.

To examine whether people with positive and negative COVID-19 tests exhibited different symptoms at enrollment, we compared the frequencies of major symptoms stratified by asthma diagnosis. Among patients with asthma, no significant differences regarding the frequency for any of the presenting symptoms were observed between those who eventually tested positive for COVID-19 and those who did not (Fig 2 and eTable 1 in the Supplement), suggesting that asthma patients suspected of having COVID-19 have very similar symptoms regardless of

subsequently testing positive for SARS-CoV-2 infection or not. However, interestingly, in people without an asthma diagnosis, we identified significant differences between eventual COVID-19 diagnosis: patients who tested negative for COVID-19 experienced more frequent sore throat, sputum production, nasal congestion, fatigue, and headache than those who tested positive (Fig 2 and eTable 2 in the Supplement).

3. Among the COVID-19 diagnosed population, asthma was not associated with increased risks for severe outcomes.

We next focused specifically on patients who tested positive for COVID-19 (n=343) to evaluate whether those with asthma have distinct symptoms and cytokine profiling as compared to those without asthma. Basic characteristics of these participants are shown in Table 2. COVID-19 patients with asthma (n=72) were older compared to those without asthma (n=271, $p=0.00066$). Males were more prevalent in the non-asthma group (62.6%) than females, but this was not the case in the asthma group (31.9%). BMI was higher in the asthma group compared to the non-asthma group ($p=0.00038$). The presence of obesity ($p=0.0040$) and COPD ($p<0.0001$) was higher among patients with asthma, but no significant differences in the prevalence of hypertension and diabetes existed between the two groups. There were also no significant differences with known COVID-19 exposure prior to illness.

When comparing symptoms, COVID-19 patients with asthma have higher percentage of respiratory symptoms, including shortness of breath ($p=0.034$), sputum production ($p=0.036$), and nasal congestion ($p=0.012$) compared with COVID-19 patients without an asthma diagnosis (eFig 1 in the Supplement). However, there were no significant differences in systemic and gastrointestinal symptoms (eFig 1 in the Supplement).

To evaluate associations between preexisting asthma and COVID-19 severity, multivariable logistic regression models were used and included age, sex, race (Black, not Black), COPD, and obesity as covariates. We did not find statistically significant relationships between an asthma diagnosis and several indicators of COVID-19 severity, including hospitalization, ICU admission, mechanical ventilation, death due to COVID-19, and in-hospital mortality (eTable 3).

4. COVID-19 patients with asthma exhibited lower levels of plasma interleukin (IL)-8 than those without asthma.

In order to assess differences in the underlying immune responses between COVID-19 patients with and without asthma, we measured 35 plasma cytokine levels from 42 patients including 21 asthma-control pairs matched with age (within 5-year interval) and sex. We found that for 23 out of 35 cytokines, asthma patients had lower median cytokine levels than non-asthma patients and for 11 out of 35 cytokines, asthma patients had higher median cytokine levels (Fig 3A). A direct comparison further revealed that COVID-19 patients with asthma exhibited significantly reduced levels of IL-8 than those without asthma (Bonferroni adjusted $p=0.023$, Fig 3B), but no other measured cytokines demonstrated statistical differences between these two groups. Comparison of selective cytokines (VEGF, IL-15, MIP1 α , IL-2, IL-4, IL-5, IL-13, TNF- α , and IFN- γ) are displayed in the eFig 2 in the Supplement.

Discussion

We performed an analysis on a prospectively collected cohort of patients suspected of having COVID-19 and presenting to two BJC Healthcare hospitals in St. Louis, Missouri. Our results showed that among COVID-19 suspected patients, those with asthma were more likely to test negative for COVID-19 than those without asthma, which is consistent with results from a large retrospective cohort study in Israel.²⁶ Furthermore, we found that the presenting symptoms were

similar regardless of subsequent COVID-19 diagnosis among patients with and without asthma, and this confirms the sometimes-vague nature of COVID-19 and similarities in symptoms with other respiratory infections. Since people with asthma are generally more susceptible to various respiratory viral infections or environmental allergens and subsequently develop asthma symptoms, they are at increased risk for exhibiting symptoms that are similar to COVID-19 symptoms, but they may not necessarily have COVID-19. Therefore, asthma patients may be confused about their symptoms and their healthcare providers face a great challenge in risk-stratifying them for COVID-19 testing – a problem which may be only worsened as the winter season begins. The proclivity for respiratory symptoms in asthma patients may explain their lower rate for eventual positive COVID-19 tests, because they are more likely to present with concerning symptoms, but they may not necessarily have COVID-19. Unfortunately, asthma patients may nevertheless be at increased risk of being exposed to COVID-19 just by presenting to the hospital due to confusion about their symptoms.⁸ Thus, there urgently needs to be more research on how to find better and quicker ways to differentiate an asthma exacerbation from a COVID-19 infection and perform testing safely in outpatient or home settings.

Among the COVID-19 suspected population without asthma, we found that patients who tested positive for COVID-19 showed fewer prominent upper airway signs, such as sore throat and nasal congestion, as well as other symptoms, including sputum production, headache and fatigue than people who tested negative for COVID-19. This finding is consistent with previous reports and suggests that SARS-CoV-2 may have distinct infection mechanisms compared to previous common respiratory viruses.^{1 27 28} Interestingly, this unique symptom pattern related with COVID-19 was not observed in patients with asthma, reflecting a possibly different modulation of respiratory infections, including SARS-CoV-2, in asthma patients and greater difficulties for

asthma patients to differentiate other infections with a SARS-CoV-2 infection solely based on their symptoms.

In our study, asthma was not a risk factor for severe COVID-19 outcomes, which strengthens the belief that asthma may not be a relevant risk factor for COVID-19 severity, as found in other studies.^{15 16 29} A novel aspect of our study was the comparison of symptoms and cytokine profiles in COVID-19 patients with and without asthma. While more COVID-19 patients with asthma reported respiratory symptoms (shortness of breath, sputum production, and nasal congestion) than patients without asthma, the frequency of systemic symptoms (fever, myalgia, fatigue, and headache) remained the same regardless of preexisting asthma. Furthermore, the plasma cytokine patterns were similar between COVID-19 diagnosed patients with and without asthma at enrollment, except for IL-8. COVID-19 patients with asthma expressed reduced levels of IL-8 compared to patients without asthma. As a pro-inflammation chemokine, IL-8 upregulation is robustly associated with COVID-19 infection and critical outcomes.³⁰⁻³² IL-8 is well known to trigger the activation and migration of neutrophils and is a key mediator in innate immune responses and systemic inflammation.³³ The reduced levels of IL-8 in the asthma population upon SARS-CoV-2 infection might be a mechanism underlying favorable COVID-19 outcomes. It is worth noting that a previous study found that COVID-19 patients with comorbid COPD had a higher risk of developing severe outcomes and had a significantly higher serum IL-8 than COVID-19 patients with asthma.³⁴

Some limitations of this study need to be considered. First, the self-reported symptoms might introduce under- and over-estimation of symptom association with COVID-19 or asthma. Second, a preexisting asthma diagnosis was determined solely based on patients' health records without diagnostic testing. Therefore, possibility exists that asthma may be either systemically over- or

underestimated in this study. Third, a sudden loss of smell or taste has been remarkably prevalent among people who test positive for COVID-19.^{35 36} However, these two symptoms were not listed in our data because our study started in March when loss of smell or taste was less recognized as a prominent symptom of COVID-19 infection. Therefore, our comparison of symptoms could be improved if loss of smell or taste is included in future studies.

In conclusion, this study examined the characteristics and outcomes of COVID-19 suspected and diagnosed patients stratified by an asthma diagnosis. This study raised a particular area of concern for asthmatics during the COVID-19 pandemic: asthma patients are facing a great challenge in differentiating between symptoms of COVID-19 with other respiratory infections and routine asthma exacerbations. As some asthma-related testing and care has been disrupted during the pandemic, this difficulty with differentiating symptoms could pose a great risk for asthma management and COVID-19 prevention among the asthma population. It is critical to continue investigations on the relationship between asthma and COVID-19, better characterize unique features of COVID-19 in the asthma population, and identify safe and reliable testing mechanisms.

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Table 1. Characteristics of COVID-19 suspected patients with and without asthma

	Asthma (N=104)			Non-asthma (N=331)		
	SARS-CoV-2 positive (N=72)	SARS-CoV-2 negative (N=32)	p-value	SARS-CoV-2 positive (N=271)	SARS-CoV-2 negative (N=60)	p-value
Age (years), mean	55.42 (15.66)	44.72 (15.36)	0.0014	62.07 (15.71)	49.71 (17.98)	<0.0001
Sex: Male [†] , n (%)	23 (31.9%)	10 (31.2%)	0.94	169 (62.6%)	23 (38.3%)	0.00057
Race: Black [†] , n (%)	56 (77.8%)	19 (59.4%)	0.053	186 (68.9%)	22 (36.7%)	<0.0001
BMI, mean (SD)	36.20 (12.12)	28.86 (7.48)	0.00096	31.03 (8.58)	30.39 (8.18)	0.63
Obesity, n (%)	48 (66.7%)	12 (37.5%)	0.0055	129 (47.6%)	26 (45.6%)	0.78
COPD, n (%)	27 (37.5%)	8 (25.0%)	0.21	43 (15.9%)	6 (10%)	0.25
Hypertension, n (%)	60 (83.3%)	17 (53.1%)	0.0012	202 (74.5%)	29 (48.3%)	<0.0001
Diabetes, n (%)	43 (59.7%)	11 (34.4%)	0.017	137 (50.6%)	12 (20%)	<0.0001

[†]having missing data; SD: standard deviation. BMI: body mass index. Obesity was defined as

BMI $\geq$ 30. COPD: chronic obstructive pulmonary disease. Significance was evaluated based

on Mann-Whitney *U* test or chi-square test. Bolded numbers are p-values < 0.05 .

Table 2. Characteristics of COVID-19 patients with and without asthma

	Asthma (N=72)	Non-asthma (N=271)	p-value
Age (years), mean (SD)	55.42 (15.66)	62.07 (15.71)	0.00066
Sex: Male [†] , n (%)	23 (31.9%)	169 (62.6%)	<0.0001
Race: Black [†] , n (%)	56 (77.8%)	186 (68.9%)	0.14
BMI, mean (SD)	36.2 (12.12)	31.03 (8.58)	0.00038
Obesity, n (%)	48 (66.7%)	129 (47.6%)	0.0040
COPD, n (%)	27 (37.5%)	43 (15.9%)	<0.0001
Hypertension, n (%)	60 (83.3%)	202 (74.5%)	0.12
Diabetes, n (%)	43 (59.7%)	137 (50.6%)	0.17
Known COVID-19 exposure [†] , n (%)	40 (56.3%)	130 (48.5%)	0.24
Current smoker, n (%)	9 (12.5%)	33 (12.2%)	0.94

[†]having missing data. SD: standard deviation. BMI: body mass index. Obesity was defined as

BMI $\geq$ 30. COPD: chronic obstructive pulmonary disease. Significance was evaluated based on

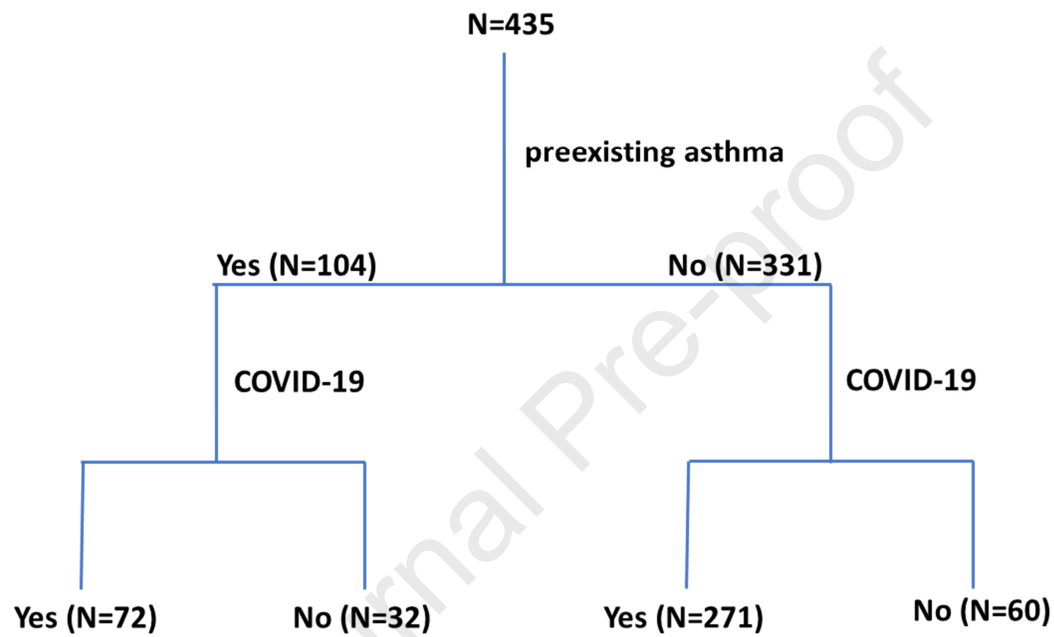
Mann-Whitney *U* test or chi-square test. Bolded numbers are p-values $\leq$ 0.05.

Table 3. Multivariable logistic regression models of asthma and COVID-19 severe outcomes

	OR (95% CI)	p-value
Hospitalization	1 (0.34,3.28)	1
ICU admission	0.59 (0.31,1.08)	0.094
Mechanical ventilation	1.10 (0.56, 2.12)	0.77
Death due to COVID-19	0.73 (0.30,1.64)	0.46
In-hospital mortality	0.72 (0.31,1.57)	0.42

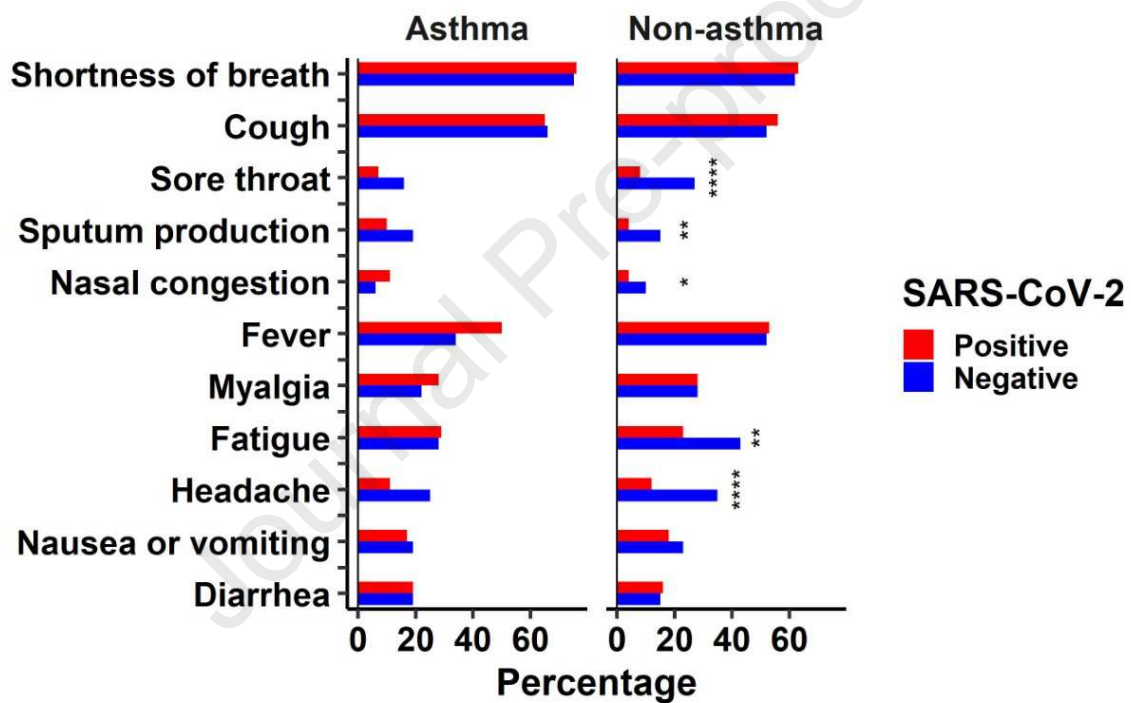
Multivariable regression models adjusted for age, race (black or not black), sex, chronic obstructive pulmonary disease, and obesity. OR: odds ratio; CI: confidence interval.

Fig 1. Algorithm for identifying patients with asthma and COVID-19



Patients with preexisting asthma were identified by the International Classification of Disease, Tenth Revision (ICD-10) codes and confirmed by chart review. Patients with COVID-19 were identified using PCR-based testing on nasopharyngeal specimens.

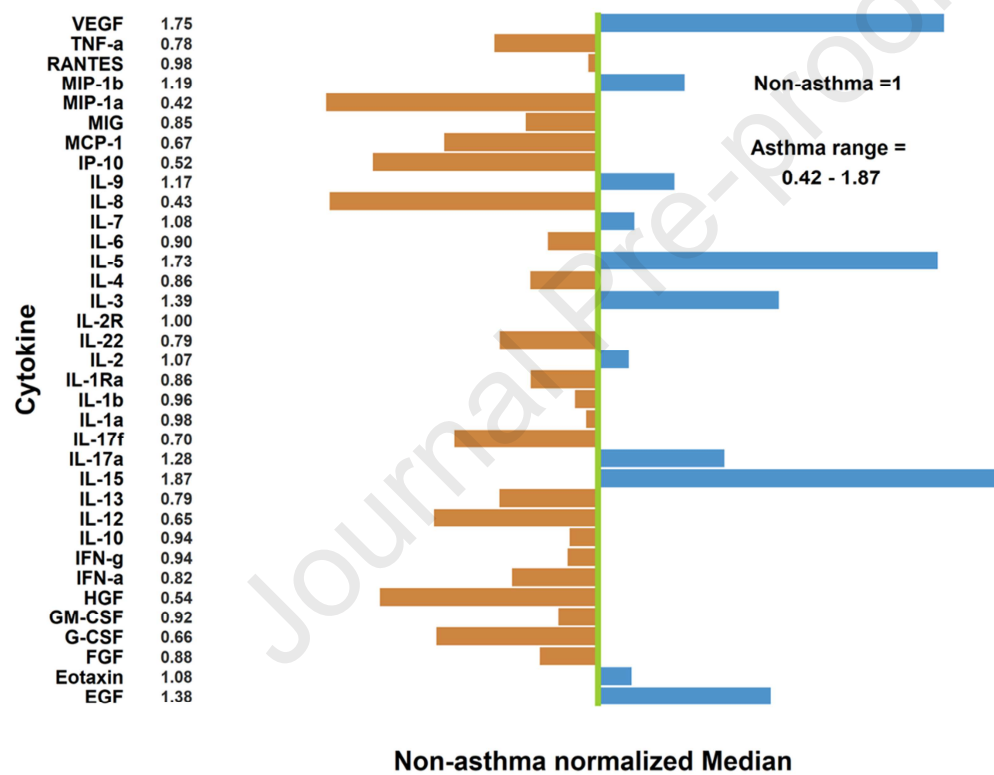
Fig 2. Differences in symptoms between patients who tested positive and negative for COVID-19 stratified by asthma

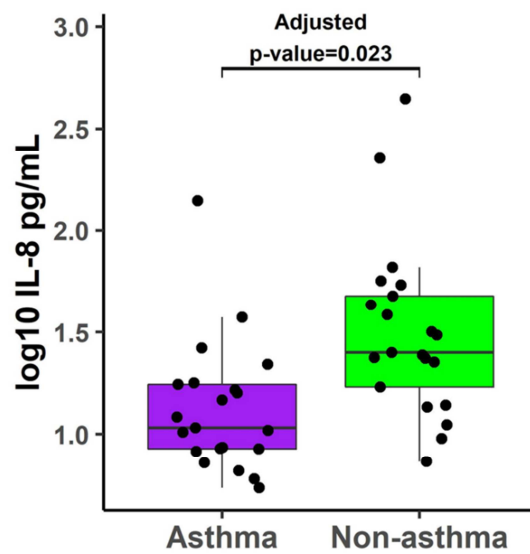


Symptoms were self-reported by patients at enrollment. Significance was evaluated based on chi-square tests. *, p -value < 0.05; **, p -value < 0.005, ****, p -value < 0.0001.

Fig 3. Cytokine concentrations in COVID-19 patients with and without asthma

A





399 **B**

400 (A) Cytokine relative abundance. Green line: normalized median cytokine level in non-asthma
 401 patients. Each bar: median cytokine level in asthma patients relative to the green line. (B)
 402 Interleukin (IL)-8 values plotted on log₁₀ scale. P-values from Mann-Whitney *U* test
 403 (Bonferroni adjusted).

Acknowledgement

We appreciate the critical scientific advice from Dr. Gregory Storch (Washington University in St. Louis School of Medicine) and the cytokine data from Dr. Ali Ellebedy (Washington University in St. Louis School of Medicine).

E-Supplement

Asthma in COVID-19 suspected and diagnosed patients

eTable 1. Symptoms reported at enrollment by asthma patients stratified by SARS-CoV-2 test results

Symptom	SARS-CoV-2 positive (N=72)	SARS-CoV-2 negative (N=32)	p-value
Shortness of breath	55 (76.4%)	24 (75.0%)	0.88
Cough	47 (65.3%)	21 (65.6%)	0.97
Sore throat	5 (6.9%)	5 (15.6%)	0.17
Sputum production	7 (9.7%)	6 (18.8%)	0.20
Nasal congestion	8 (11.1%)	2 (6.2%)	0.44
Fever	36 (50.0%)	11 (34.4%)	0.14
Myalgia	20 (27.8%)	7 (21.9%)	0.53
Fatigue	21 (29.2%)	9 (28.1%)	0.91
Headache	8 (11.1%)	8 (25.0%)	0.070
Nausea or vomiting	12 (16.7%)	6 (18.8%)	0.80
Diarrhea	14 (19.4%)	6 (18.8%)	0.93

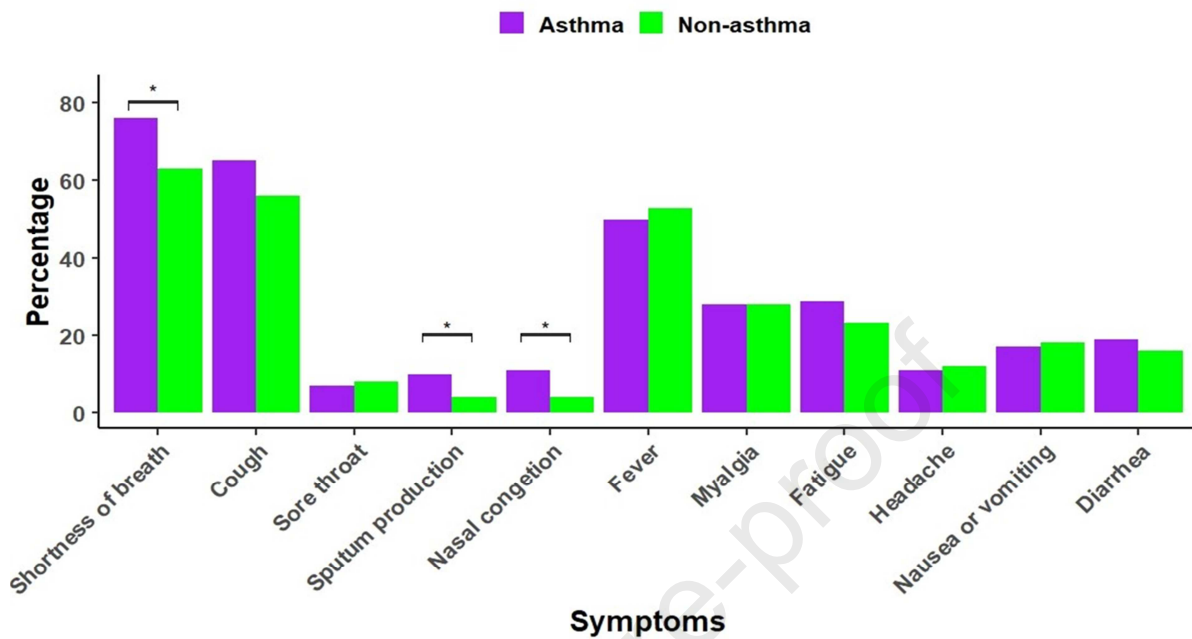
Value format is n (%). Symptoms were self-reported at enrollment. Significance was evaluated based on chi-square tests.

eTable 2. Symptoms reported at enrollment by non-asthma patients stratified by SARS-CoV-2 test results

Symptom	SARS-CoV-2 positive (N=271)	SARS-CoV-2 negative (N=60)	p-value
Shortness of breath	171 (63.1%)	37 (61.7%)	0.84
Cough	152 (56.1%)	31 (51.7%)	0.53
Sore throat	22 (8.1%)	16 (26.7%)	<0.0001
Sputum production	10 (3.7%)	9 (15.0%)	0.00065
Nasal congestion	10 (3.7%)	6 (10.0%)	0.039
Fever	144 (53.1%)	31 (51.7%)	0.84
Myalgia	77 (28.4%)	17 (28.3%)	0.99
Fatigue	61 (22.5%)	26 (43.3%)	0.00091
Headaches	32 (11.8%)	21 (35.0%)	<0.0001
Nausea or vomiting	50 (18.5%)	14 (23.3%)	0.39
Diarrhea	43 (15.9%)	9 (15%)	0.87

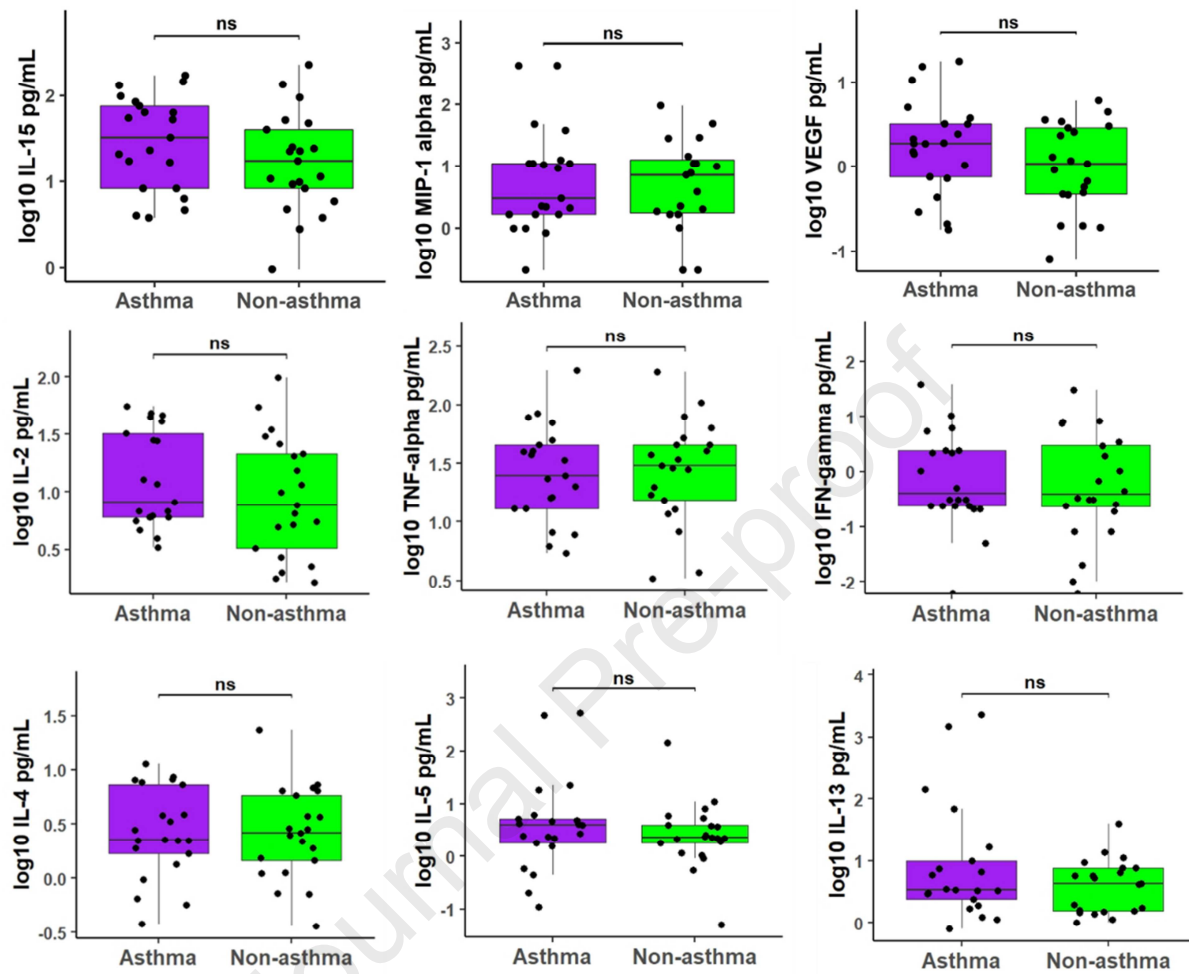
Value format is n (%). Symptoms were self-reported at enrollment. Significance was evaluated based on chi-square tests. Bolded numbers are p-values < 0.05.

eFig 1.



Comparison of symptom frequencies reported at enrollment between COVID-19 patients with and without asthma. Significance was evaluated based on chi-square tests. *, p-value < 0.05.

eFig 2.



Selective cytokine raw values plotted on a log₁₀ scale. P-values were calculated using Mann-Whitney *U* test and were adjusted for multiple comparison using Bonferroni method. ns: not significant.