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Asthma prolongs intubation in COVID-19

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Clinical Implications

- Asthma was independently associated with prolonged duration of intubation for coronavirus disease 2019. The co-occurrence of asthma with obesity, another predictor of poor outcome in these patients, places obese patients with asthma at markedly higher risk for a worsened disease course from coronavirus disease 2019.

The pandemic of coronavirus disease 2019 (COVID-19) has been rapidly taking over the vast majority of countries, overwhelming health care systems across the world.[1] The recent data from the Centers for Disease Control and Prevention (CDC) indicate that asthma is present in about 17% of all admitted COVID-19 patients in the United States, and in as high as 27% of patients in the age group of 20 to 49 years, which marks asthma as the second most common comorbidity in this age group, following obesity.[2] However the effect of asthma on the disease course has not been reported yet. Considering that more than 19 million adults in the United States have asthma,[3] it is crucial to understand the impact of preexisting asthma on the course and outcome of COVID-19. Here, we report the result of our study on the role of asthma in the outcome of COVID-19 in a large cohort of COVID-19–positive patients.

The study was approved by the Institutional Review Board of Rush University Medical Center. An electronic medical records (EMRs) database search was performed by the Information Technology Department to identify patients who were evaluated by an EMR algorithm for COVID-19 and had a positive COVID-19 test result between March 12 and April 3, 2020.

All encounters of these patients were carefully reviewed. Demographic factors, and clinical factors including asthma, asthma-related variables, and variables related to COVID-19, were retrieved from their EMRs and entered into our database. To identify and confirm these diagnoses and clinical variables, all charts were reviewed by 2 independent trained researchers and 20% of the charts were randomly checked by the principal investigator, who is a board-certified practicing allergist immunologist, to confirm the asthma diagnosis based on Global Initiative for Asthma (GINA) guidelines.[4]

The terminology and categories used for race are based on the National Institutes of Health recommendation of reporting 5 racial categories and 2 ethnic categories (Latino and Not Latino) (National Institutes of Health policy notice no. NOT-OD-01-053). Age was divided into 3 different age groups on the basis of CDC-reported grouping for CVOID-19 patients[2] (Table I).

Initial comparisons between groups were performed applying either the χ^2 test or ANOVA. Logistic and linear regressions were used to test whether demographic factors as well as comorbid conditions influenced categorical and numeric outcomes, respectively.

We used SPSS (IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY) for statistical analysis. Differences were considered statistically significant at $P \leq .05$. Analyses of COVID-19 outcomes in association with asthma were adjusted for demographic variables and body mass index (BMI).

The initial series included 1003 patients who were tested by the on-demand COVID telemedicine clinic or the emergency room through an algorithm for COVID-19, and had positive COVID-19 test results. Complete data on demographic variables, asthma, and COVID-19 management were available in 935 (93.2%) patients who were used for our analysis. Overall, 241 (25.8%) were found to have an established diagnosis of asthma. The rate of asthma was similar in all age groups (Table I). Asthma was significantly associated with female sex and higher BMI (Table I). Analysis of COVID-19 outcomes in association with asthma were carried out according to the CDC age groups and adjusted for demographic variables and BMI.

Overall, among the whole series, asthma was significantly associated with longer intubation time: mean ± SD of 10.17 ± 6.9 and 5.28 ± 5.9 days in patients with and without asthma, respectively ($P = .002$; Table I). The longer intubation time was present in both age groups of 18 to 49 years and 50 to 64 years, but not in the age group of 65 years and above. Duration of the hospitalization showed a trend to be longer among patients with a history of asthma compared with those without this history in those aged 50 to 64 years (mean, 10.64 ± 7.38 vs 8.11 ± 5.26 in patients with asthma vs patients without asthma; $P = .07$), but not in the younger or older age groups (Table I). Asthma was not associated with a higher rate of death (1.1% vs 3% in patients with asthma vs patients without asthma; $P = .22$) nor with acute respiratory distress syndrome (8.9% vs 9.5% in patients with asthma vs patients without asthma; $P = .92$) among COVID-19 patients. Peripheral eosinophilia was associated with asthma. No other laboratory finding was different between patients with and without asthma.

This is the first report, to our knowledge, to study the role of asthma in the outcome of COVID-19 patients. The published cohorts of COVID-19 from China did not include patients with asthma.[5,6] This could be partially due to markedly lower rates of asthma in China (2%-4%) compared with Western countries (8%-11% in the United States).[3,7] The effect of asthma on other virulent species of coronavirus that are associated with severe acute respiratory syndrome has not been studied either. However, members of the Coronaviridae family that are associated with common cold have been linked to asthma exacerbations.[8]

In our series, history of asthma was neither associated with increased rate of acute respiratory distress syndrome nor with hospitalization. However, among the patients who developed severe respiratory symptoms requiring intubation, asthma was associated with a significantly longer intubation time. Asthma particularly prolonged the intubation time in younger

TABLE I. Characteristics and outcomes of COVID-19 patients in association with asthma in different age groups

	Age groups (y)											
	Overall			18-49			50-64			Above 65		
Characteristics and outcomes	With asthma	Without asthma	*P* value*	With asthma	Without asthma	*P* value*	With asthma	Without asthma	*P* value*	With asthma	Without asthma	*P* value*
Characteristic												
Number	241	694		138	364		65	213		38	117	
Sex: female												
n (%)	161 (66.8)	357 (51.4)		90 (65.2)	215 (59.1)		44 (67.6)	88 (41.3)		27 (71.1)	54 (46.1)	
Odds ratio (95% CI)	1.83 (1.34-2.49)	Reference	.0001	1.27 (0.84-1.92)	Reference	.25	2.95 (1.63-5.36)	Reference	.001	2.58 (1.14-5.82)	Reference	.02
BMI												
Mean ± SD	33.59 ± 9.24	31.63 ± 7.5	.0001†	33.22 ± 10.08	31.84 ± 7.9	.18†	35.95 ± 7.54	32.97 ± 7.0	.01†	31.11 ± 8.30	28.48 ± 6.1	.04†
Race												
African American												
n (%)	150 (59.7)	355 (49.1)	.38	83 (60.1)	159 (43.7)	.10	42 (64.6)	126 (59.2)	.71	25 (65.8)	70 (59.8)	.38
Odds ratio (95% CI)	1.34 (0.70-2.58)	Reference		2.10 (0.88-5.01)	Reference		0.79 (0.23-2.71)	Reference		0.43 (0.06-2.89)	Reference	
Asian												
n (%)	22 (8.7)	117 (16.2)	.27	14 (10.1)	70 (19.2)	.69	7 (10.8)	29 (13.6)	.67	1 (2.6)	18 (15.4)	.09
Odds ratio (95% CI)	0.64 (0.30-1.40)	Reference		0.82 (0.30-2.24)	Reference		0.73 (0.17-3.10)	Reference		0.09 (0.01-1.45)	Reference	
White non-Latino												
n (%)	56 (11.3)	180 (24.9)	.9	34 (24.6)	107 (29.4)	.60	12 (18.5)	47 (22.1)	.54	10 (26.3)	26 (22.2)	.51
Odds ratio (95% CI)	1.0 (0.50-2.01)	Reference		1.28 (0.51-3.18)	Reference		0.66 (0.17-2.53)	Reference		0.51 (0.07-3.71)	Reference	
White Latino												
n (%)	13 (5.1)	42 (5.8)	.34	7 (5.1)	28 (7.7)	.37	4 (6.2)	11 (5.2)	.84	2 (5.3)	3 (2.6)	.40
Odds ratio (95% CI)	1.22 (0.42-2.14)	Reference		1.12 (0.46-2.47)	Reference		1.19 (0.37-2.67)	Reference		0.45 (0.82-2.58)	Reference	
Outcomes												
Hospitalized												
n (%)	73 (30.7)	224 (32.8)		30 (22.2)	75 (20.9)		22 (33.8)	80 (33.3)		21 (55.3)	69 (59.5)	
Odds ratio (95% CI)	1.08 (0.77-1.53)	Reference	.65	0.98 (0.58-1.66)	Reference	.93	1.17 (0.62-2.19)	Reference	.63	1.37 (0.63-3.01)	Reference	.43
Duration of hospitalization												
Mean ± SD	8.36 ± 6.02	7.81 ± 5.19	.25†	7.48 ± 5.81	6.64 ± 4.11	.18†	10.64 ± 7.38	8.11 ± 5.26	.07†	7.05 ± 3.70	8.71 ± 5.92	.30†
Intubated												
n (%)	23 (9.7)	56 (8.3)		6 (4.4)	14 (3.9)		11 (17.2)	22 (10.7)		6 (15.8)	20 (17.7)	
Odds ratio (95% CI)	1.18 (0.45-1.32)	Reference	.35	1.04 (0.34-2.62)	Reference	.91	1.24 (1.00-1.50)	Reference	.09	1.14 (0.40-3.25)	Reference	.81
Duration of intubation												
Mean ± SD	10.17 ± 6.91	5.29 ± 5.98	.01†	12.00 ± 5.55	3.53 ± 4.70	.01†	10.73 ± 7.84	5.23 ± 6.49	.03†	7.33 ± 6.50	7.25 ± 6.08	.72†
ARDS												
n (%)	21 (8.9)	65 (9.5)		6 (4.5)	18 (5.0)		9 (14.1)	27 (13.0)		6 (15.8)	20 (17.2)	

(continued)

TABLE I. *(Continued)*

Characteristics and outcomes	Overall			18-49			50-64			Above 65		
	With asthma	Without asthma	*P* value*	With asthma	Without asthma	*P* value*	With asthma	Without asthma	*P* value*	With asthma	Without asthma	*P* value*
Odds ratio (95% CI)	0.97 (0.57-1.67)	Reference	.92	1.13 (0.42-3.03)	Reference	.81	0.71 (0.30-1.71)	Reference	.45	1.27 (0.45-3.63)	Reference	.65
Deaths												
n (%)	2 (1.1)	16 (3.0)		0 (0.0)	3 (1.1)		2 (3.7)	7 (4.1)		0 (0.0)	6 (6.5)	
Odds ratio (95% CI)	2.56 (0.57-11.5)	Reference	.22	NA	Reference	NA	1.19 (0.21-6.67)	Reference	0.85	NA	Reference	NA

Age groups (y)

ARDS, Acute respiratory distress syndrome; *NA*, not applicable/available.

*All reported *P* values for categorical variable are calculated by logistic regression comparing variables in patients with asthma with patients without asthma adjusted for race, sex, and BMI. Odds ratios (95% CI) are reported for these categorical variables.

†Reported *P* values for continuous variables are calculated by comparing the adjusted means in patients with asthma with patients without asthma (adjusted for race, sex, and BMI) via analysis of covariance.

(<65 years) COVID-19 patients who are otherwise shown to have a better disease course than the older patients. These data suggest that younger individuals with asthma may require extra attention because they could develop a sustained pulmonary failure with COVID-19 infection, leading to a prolonged mechanical ventilation. Per the intensive care unit protocol, all our COVID-19 intubated patients were on nebulized albuterol and most were treated with systemic steroids. To understand whether the use of bronchodilators and systemic steroids might impact the link between intubation time and asthma, we adjusted our analysis for albuterol and systemic steroids use, which did not change our findings. Patients aged 50 to 64 years with asthma showed a trend toward longer hospitalization time and overall spent 2 more days in the hospital than those without asthma in this age group. We believe that the duration of intubation is more reflective of the disease course than the duration of the hospitalization, which further depends on nonrespiratory or nonmedical issues such as placement. However, the trend toward longer hospitalization duration along with the longer intubation duration might indicate that asthma has the highest impact on COVID-19 course in those younger than 65 years.

Consistent with other series, asthma was associated with female sex and higher BMI in our study.[9,10] Obesity and sex both have been shown to affect the COVID-19 hospitalization.[2] Our analysis, which was adjusted for both obesity and sex, indicates that asthma is independently linked to intubation duration. This is clinically important because obesity, another predictor of poor outcome in COVID-19 patients,[2] occurs more frequently in individuals with asthma.[9,10] Therefore, coexistence of these 2 factors places patients at a markedly higher risk of a worsened disease course from COVID-19. This needs to be considered by all health care providers when triaging COVID-19 patients or counseling patients with asthma about COVID-19.

The main limitation of our study is that the asthma diagnoses were self-reported in some cases. All the included individuals in our study were questioned whether they had "asthma" as part of an algorithm for COVID-19 assessment. Furthermore, in 73% of cases, we could find previous clinical documentation on individuals' health and medical history such as primary care or specialty visit notes, up-to-date medications lists, and other workup for asthma in the medical records. These 73% were either established patients at our health system or another health care system across Chicago who were part of "Care Everywhere" EPIC feature. Therefore, we were able to confirm the diagnosis of asthma by reviewing the detailed past medical history of most of our series by chart review. There was no difference in the rate of asthma in patients with existing detailed past medical history and the rest of the series who were asked and reported their asthma status as part of our COVID-19 algorithm. The overall rate of asthma in our series (25.8%) is above the national average rate for asthma (8%-11%) in adults.[3] One possible explanation could be that patients with a history of asthma reached out for testing for COVID-19 more than others, because of their concern and overlapping symptoms. This higher rate calls for population-based studies to investigate whether asthma is a risk factor for COVID-19.

In summary, our study in a large cohort of patients indicate preexisting asthma as a predictor of intubation duration in COVID-19, especially in patients younger than 65 years.

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