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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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Association between asthma and clinical mortality/morbidity in COVID-19 patients using clinical epidemiologic data from Korean Disease Control and Prevention

To the Editor,

Coronavirus disease 2019 (COVID-19) has rapidly spread worldwide, posing a serious public health problem.[1] The prevalence of asthma in COVID-19 patents differs among studies, with 0.0% reported in Wuhan, China, and markedly higher prevalence rates of 17% and 14% reported in the United States (US) and the United Kingdom (UK), respectively.[2-4] Data from the UK showed that asthma was a risk factor for severe COVID-19; however, another study from the

TABLE 1 General characteristics of the participants with COVID-19 according to asthma history

Characteristics	The participants with COVID-19		
	Asthma	Control	*P*-value
Total number (n, %)	96 (100.0)	3,961 (100.0)	
Age (years old) (n, %)			
0-9	2 (2.1)	55 (1.4)	<.001[a]
10-19	0 (0.0)	175 (4.4)	
20-29	15 (15.6)	820 (20.7)	
30-39	13 (13.5)	423 (10.7)	
40-49	11 (11.5)	525 (13.3)	
50-59	13 (13.5)	788 (19.9)	
60-69	16 (16.7)	618 (15.6)	
70-79	12 (12.5)	362 (9.1)	
80+	14 (14.6)	195 (4.9)	
Sex (n, %)			
Male	38 (39.6)	1,685 (42.5)	.562
Female	58 (60.4)	2,276 (57.5)	
Obesity[c] (n, %)			
Underweight	5 (5.2)	242 (6.1)	.033[a]
Normal	30 (31.3)	1,668 (42.1)	
Overweight	31 (32.3)	922 (23.3)	
Obese I	21 (21.9)	944 (23.8)	
Obese II	9 (9.4)	185 (4.7)	
Systolic blood pressure (n, %)			
<120 mmHg	19 (19.8)	977 (24.7)	.444
120-129 mmHg	28 (29.2)	872 (22.0)	
130-139 mmHg	19 (19.8)	792 (20.0)	
140-159 mmHg	24 (25.0)	975 (24.6)	
≥160 mmHg	6 (6.3)	345 (8.7)	
Diastolic blood pressure (n, %)			
<80 mmHg	41 (42.7)	1,491 (37.6)	.501
80-89 mmHg	34 (35.4)	1,372 (34.6)	
90-99 mmHg	16 (16.7)	743 (18.8)	
≥100 mmHg	5 (5.2)	355 (9.0)	
Heart rate (mean, SD)	88.48 (13.64)	85.29 (14.94)	.038[b]
Temperature (mean, SD)	36.89 (0.48)	36.94 (0.56)	.391
Past medical history			
Diabetes mellitus (n, %)	17 (17.7)	475 (12.0)	.090
Hypertension (n, %)	21 (21.9)	808 (20.4)	.723
Heart failure (n, %)	2 (2.1)	38 (1.0)	.244
Chronic heart disease (n, %)	8 (8.3)	124 (3.1)	.012[a]
Chronic obstructive pulmonary disease (n, %)	7 (7.3)	23 (0.6)	<.001[a]
Chronic kidney disease (n, %)	0 (0.0)	43 (1.1)	.626
Any cancer (n, %)	3 (3.1)	104 (2.6)	.741
Chronic liver disease (n, %)	1 (1.0)	57 (1.4)	.998
Rheumatic or autoimmune disease (n, %)	0 (0.0)	31 (0.8)	.999
Dementia (n, %)	4 (4.2)	116 (2.9)	.532
Death (n, %)	8 (8.3)	118 (3.0)	.009[a]

[a]Chi-square or Fisher's exact test. Significance at $P < .05$

[b]Independent *t* test. Significance at $P < .05$

[c]Obesity (BMI, body mass index, kg/m^2) was categorized as <18.5 (underweight), ≥18.5 to Note <23 (normal), ≥23 to < 25 (overweight), ≥25 to <30 (obese I), and ≥30 (obese II).

TABLE 2 Crude and adjusted hazard ratios (95% confidence interval) for death in asthma and nonasthma groups with subgroup analyses

	HRs for death			
Characteristics	**Crude**	***P*-value**	**Adjusted[b]**	***P*-value**
Total participants (n = 4,057)				
Asthma	2.48 (1.21 to 5.08)	.013[a]	2.20 (1.02 to 4.76)	.045[a]
Nonasthma	1		1	
Age < 50 years old (n = 2,039)				
Asthma	N/A		N/A	
Nonasthma	1		1	
Age ≥ 50 years old (n = 2,018)				
Asthma	2.33 (1.14 to 4.78)	.021[a]	2.22 (1.03 to 4.78)	.042[a]
Nonasthma	1		1	
Men (n = 1,723)				
Asthma	1.91 (0.60 to 6.10)	.273	2.33 (0.68 to 8.02)	.181
Nonasthma	1		1	
Women (n = 2,334)				
Asthma	3.31 (1.31 to 8.38)	.012[a]	3.74 (1.35 to 10.35)	.011[a]
Nonasthma	1		1	

Abbreviation: N/A, not applicable.

[a]Cox proportional hazard regression model, significance at $P < .05$.

[b]The model was adjusted for age, sex, obesity, systolic blood pressure, diastolic blood pressure, heart rate, temperature, diabetes, hypertension, heart failure, chronic heart disease, chronic obstructive pulmonary disease, chronic kidney disease, cancer, chronic liver disease, rheumatic or autoimmune disease, and dementia.

United States showed no association between asthma and severe disease, suggesting that it is still unclear whether asthma is a risk factor for a poor prognosis.[5-7]

Given the variability in the reports analyzing the impact of underlying asthma on the prevalence and severity of COVID-19, there is a need to better characterize the relationship between asthma and COVID-19. The Korea Centers for Disease Control and Prevention (KCDC) has collected clinical data from hospitalized patients with mild to critical COVID-19 nationwide using a standardized clinical record form.[8] Using this dataset, we evaluated the association between a history of asthma and mortality and morbidity related to COVID-19. A Cox proportional hazards regression model was used for mortality, and a linear regression model was used for morbidity scores.

In this study population, 2.3% (n = 96) of the patients were diagnosed with comorbid COVID-19 and asthma, while most (n = 3,961) did not have asthma (Table 1). The mortality rate was 8.3% (8/96) in patients with asthma and 3.0% (118/3,961) in those without asthma ($P = .009$). The relative HR for mortality in participants with asthma compared with those without asthma was 2.48 (95% CI = 1.21-5.08, $P = .013$). After adjustment for multiple variables, the risk of mortality was 2.20 (95% CI = 1.02-4.76, $P = .045$) in patients with asthma compared with those without asthma (Table 2). Subgroup analyses based on past medical history showed that among the patients with asthma, those with heart failure and chronic heart disease had an elevated risk of mortality (HR = 31.61, 95% CI = 4.36-229.05, $P < .001$; HR = 4.68, 95% CI = 1.30-16.84, $P = .018$, respectively, Table S1). To assess the effect of asthma on the clinical morbidity due to COVID-19, the maximum morbidity score was obtained, and this score was used to calculate the EV for morbidity. COVID-19 patients with asthma had a higher maximum morbidity score than those without asthma (EV = 0.44, 95% CI = 0.16-0.73, $P = .003$); participants with asthma ranked 0.44 points higher than participants without asthma (Tables S2 and S3).

These data differ from those reported in previous studies, possibly because of the different healthcare systems in each country and the different characteristics of the study participants. Earlier in 2020, many countries lacked sufficient hospital beds and physicians; however, the initial peak surge in cases during the COVID-19 pandemic did not exceed the capacity of the healthcare system; during this period, ~10,000 patients were infected among ~50,000,000 Koreans. The registry used in this study includes COVID-19 patients across the spectrum of disease severity, unlike other studies, which mostly included hospitalized patients with severe disease.[5,9] As all COVID-19 patients are isolated, even those with mild cases, we postulate that the impact of host factors such as underlying diseases may be relatively greater on the outcomes. However, we could not analyze the effect of asthma-related factors such as inflammatory markers, lung function, and medications due to the limited availability of the relevant data. Specifically, severe or intrinsic asthma is considered a risk factor for a poor prognosis in patients with COVID-19; nevertheless, supporting studies are still limited and inconclusive.[7,8,10,11]

Our study provides strong evidence that asthma is associated with an increased risk of mortality and worse clinical outcomes of COVID-19. However, considering that asthma is a heterogeneous disease, further studies investigating the effects of asthma severity and asthma endophenotypes should be performed in a large cohort.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

HG Choi, JH W, and SY Kim organized and analyzed the data and prepared the manuscript. HI Kim and JY Park interpreted the results of analyzing data. SH Park made some instruction in the study. YI Hwang, SH Jang, and KS Jung worked in the writing and critical review of the manuscript. HG Choi participated in the preparation of the manuscript. JH Kim designed the study and reviewed the manuscript.

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