

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

Hyo Geun Choi¹, Jee Hye Wee², So Young Kim³, Joo-Hee Kim², Hwan Il Kim², Ji-Young Park², Sunghoon Park², Young Il Hwang², Seung Hun Jang², and Ki-Suck Jung²

¹Hallym University Sacred Heart Hospital

²Hallym University College of Medicine

³Bundang CHA Medical Center

October 15, 2020

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

Hyo-Geun Choi¹, Jee Hye Wee², So Young Kim², Joo-Hee Kim³, Hwan Il Kim³, Ji-Young Park³, Sunghoon Park³, Yong Il Hwang³, Seung Hun Jang³, and Ki-Suck Jung³

¹ Departments of Otorhinolaryngology-Head & Neck Surgery, Hallym University

Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea

² Department of Otorhinolaryngology-Head & Neck Surgery, CHA Bundang Medical Center, CHA University, Seongnam, Korea

³ Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea

Acknowledgments

We acknowledge all the health-care workers involved in the diagnosis and treatment of COVID-19 patients in South Korea. We thank Korea Disease Control &

Prevention Agency, National Medical Center and the Health Information Manager in

hospitals for their effort in collecting the medical records. This study was supported by a grant from the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (NFR-2017R1C1B5076565).

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.

To the Editor,

Coronavirus disease 2019 (COVID-19) has rapidly spread worldwide, posing a serious public health problem. The prevalence of asthma in COVID-19 patents differs among studies, with 0.9% reported in Wuhan, China, and markedly higher prevalence rates of 9% and 14% reported in the United States (US) and the United Kingdom (UK), respectively.¹⁻³ Data from the UK showed that asthma was a risk factor for severe COVID-19; however, another study from the US showed no association between asthma and severe disease, suggesting that it is still unclear whether asthma is a risk factor for a poor prognosis.^{4,5}

Given the variability in the reports analysing 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.⁶ 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=0.009). The relative HR for mortality in participants with asthma compared with those without asthma was 2.48 (95% CI =1.21-5.08, p=0.013). After adjustment for multiple variables, the risk of mortality was 2.20 (95% CI =1.02-4.76, p=0.045) 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<0.001; HR=4.68, 95% CI=1.30-16.84, p=0.018, 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=0.003), indicating that asthma participants ranked 0.44 points higher than non-asthma participants (Table S2 and S3).

These data differ from those reported in previous studies, possibly because of the different health care 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 health care 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 severely hospitalized patients.^{2,5} 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.

In conclusion, our study provides strong evidence that asthma is associated with an increased risk of mortality and worse clinical outcomes in patients with COVID-19.

References

1. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol* 2020;146:110-118.
2. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. *Jama* 2020;323:2052-2059.
3. Zhu Z, Hasegawa K, Ma B, Fujiogi M, Camargo CA, Jr., Liang L. Association of asthma and its genetic predisposition with the risk of severe COVID-19. *J Allergy Clin Immunol* 2020;146:327-9 e4.

4. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;584:430-436.
5. Chhiba KD, Patel GB, Vu THT, et al. Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19. *J Allergy Clin Immunol* 2020;146:307-314.e4.
6. Sung HK, Kim JY, Heo J, et al. Clinical Course and Outcomes of 3,060 Patients with Coronavirus Disease 2019 in Korea, January-May 2020. *J Korean Med Sci* 2020;35:e280.

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

Characteristics	Characteristics	The participants with COVID-19	The p
		Asthma	Contr
Total number (n, %)	Total number (n, %)	96 (100.0)	3,961
Age (years old) (n, %)	Age (years old) (n, %)		
	0-9	2 (2.1)	55 (1.1)
	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, %)	Sex (n, %)		
	Male	38 (39.6)	1,685 (42.5)
	Female	58 (60.4)	2,276 (57.5)
Obesity ++ (n, %)	Obesity ++ (n, %)		
	Underweight	5 (5.2)	242 (6.1)
	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, %)	Systolic blood pressure (n, %)		
	<120 mmHg	19 (19.8)	977 (24.6)
	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, %)	Diastolic blood pressure (n, %)		
	<80 mmHg	41 (42.7)	1,491 (37.5)
	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 (8.9)
Heart rate (mean, SD)	Heart rate (mean, SD)	88.48 (13.64)	85.29 (12.1)
Temperature (mean, SD)	Temperature (mean, SD)	36.89 (0.48)	36.94 (0.48)
Past medical history	Past medical history		
	Diabetes mellitus (n, %)	17 (17.7)	475 (11.9)
	Hypertension (n, %)	21 (21.9)	808 (20.4)
	Heart failure (n, %)	2 (2.1)	38 (0.9)
	Chronic heart disease (n, %)	8 (8.3)	124 (3.1)
	Chronic obstructive pulmonary disease (n, %)	7 (7.3)	23 (0.6)
	Chronic kidney disease (n, %)	0 (0.0)	43 (1.1)

Characteristics	Characteristics	The participants with COVID-19	The p
	Any Cancer (n, %)	3 (3.1)	104 (3.1)
	Chronic liver disease (n, %)	1 (1.0)	57 (1.0)
	Rheumatic or autoimmune disease (n, %)	0 (0.0)	31 (0.0)
	Dementia (n, %)	4 (4.2)	116 (4.2)
Death (n, %)	Death (n, %)	8 (8.3)	118 (8.3)

* Chi-square or Fisher's exact test. Significance at $P < 0.05$

+ Independent t test. Significance at $P < 0.05$

++ Obesity (BMI, body mass index, kg/m^2) was categorized as < 18.5 (underweight), [?] 18.5 to < 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 non-asthma groups with subgroup analyses

Characteristics	Characteristics	HRs for death	HRs for death	HRs for death
		Crude	P-value	Adjusted
Total participants (n = 4,057)	Total participants (n = 4,057)	Total participants (n = 4,057)		
	Asthma	2.48 (1.21 to 5.08)	0.013*	2.48 (1.21 to 5.08)
	Non-asthma	1		1
Age < 50 years old (n = 2,039)	Age < 50 years old (n = 2,039)	Age < 50 years old (n = 2,039)		
	Asthma	N/A		N/A
	Non-asthma	1		1
Age [?] 50 years old (n = 2,018)	Age [?] 50 years old (n = 2,018)	Age [?] 50 years old (n = 2,018)		
	Asthma	2.33 (1.14 to 4.78)	0.021*	2.33 (1.14 to 4.78)
	Non-asthma	1		1
Men (n = 1,723)	Men (n = 1,723)	Men (n = 1,723)		
	Asthma	1.91 (0.60 to 6.10)	0.273	1.91 (0.60 to 6.10)
	Non-asthma	1		1
Women (n = 2,334)	Women (n = 2,334)	Women (n = 2,334)		
	Asthma	3.31 (1.31 to 8.38)	0.012*	3.31 (1.31 to 8.38)
	Non-asthma	1		1

Abbreviation: N/A, Not applicable

* Cox proportional hazard regression model, Significance at $P < 0.05$

+ 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.