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

Short title: Association between asthma and mortality/morbidity of COVID-19

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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.

Abstract

Background: The role of asthma as a risk factor for coronavirus 2019 (COVID-2019) morbidity and mortality is inconclusive and not fully understood. The primary objective was to evaluate the association between asthma history and mortality of COVID-19, and the secondary objective was to analyze the risk of COVID-19-related outcomes among patients with asthma compared to those without.

Methods: Using clinical epidemiologic data from Korean Disease Control & Prevention, the risk for COVID-19-related morbidity and mortality were compared in patients with asthma and those without asthma among the participants who were confirmed to have COVID-19. A Cox proportional hazards regression model was used for mortality, and a linear regression model was used for morbidity scores.

Results: The hazard ratio for death of patients with asthma versus those without was 2.48 (95% confidence interval (CI) 1.21-5.08, P=0.013) and 2.20 (95% CI 1.02-4.76, P=0.045) after full adjustment. The comorbidity of asthma was associated with an increase in the maximal morbidity score of COVID-19 compared to no asthma (estimated value of morbidity score (EV) = 0.44, 95% CI 0.16-0.73, P=0.003).

Conclusion: Asthma is associated with an increased risk of mortality and morbidity in the Korean nationwide COVID-19 registry.

Keywords: asthma, COVID-19, morbidity, mortality

Introduction

Coronavirus disease 2019 (COVID-19) has rapidly spread worldwide and become a serious problem to public health.[1] The manifestations vary from asymptomatic to severe pneumonia along with additional complications, including death.[2] Community spread is rapid because the virus transmits easily, even in asymptomatic patients, and remains viable in respiratory droplets and fomites. Since the World Health Organization announced that coronavirus was a global concern, worldwide cases are close to 17 million, with more than 660,000 deaths in a half-year.[3 4]

There is an ongoing need to characterize risk factors for COVID-19 morbidity and mortality; however, the epidemiologic characteristics are not yet fully known. Comorbidity is present in 15% to 60% of inpatients with COVID-19, and a chronic condition has been found in most patients that died from COVID-19.[4-6] In order of their relative mortality rates, the chronic conditions include cardiovascular disease, diabetes, chronic kidney disease, chronic pulmonary disease, obesity, and cancer.

Asthma has not been consistently identified as a significant comorbidity for COVID-19. Regarding the comorbidity rates of asthma in COVID-19, the prevalence of asthma was merely 0.9% in patients from Wuhan, China, compared to the markedly higher prevalence rates of 9% from the United States and 14% from the United Kingdom (UK).[7-9] Furthermore, it is also unclear whether asthma is a risk factor for the clinical outcomes of COVID-19. Data from the UK Biobank have shown that adults with asthma had a higher risk of severe COVID-19, which is much higher in nonallergic asthma.[10] Two contrasting results were reported from the US: one showed that asthma is an independent risk factor for intubation, and the other showed no association between asthma and worse outcomes of COVID-19 despite a similar health care system in the same country.[11 12]

Given the variability in the reports analyzing the impact of the underlying condition of 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 a registry to collect clinical data of patients hospitalized with COVID-19 across the country using a standardized clinical record form (CRF), and this registry includes mild to critical conditions of COVID-19 among hospitalized patients, which makes this population ideal for investigating the impact of asthma on the outcomes of COVID-19.[5] Thus, the primary objective was to evaluate the association between asthma history and mortality of COVID-19, and the secondary objective was to analyze the morbidity of COVID-19-related outcomes among those with asthma compared to those without asthma.

Materials and Methods

Ethics

The ethics committee of Hallym University Sacred Heart Hospital (2020-07-032) approved this study. Written informed consent was waived by the Institutional Review Board. All analyses adhered to the guidelines and regulations of the ethics committee of Hallym University Sacred Heart Hospital.

Study Population and Participant Selection

Clinical epidemiological data of all participants with confirmed release of isolation among confirmed cases of COVID-19 by April 30, 2020, were used. The data were collected by the Centers for Disease Control and Prevention of Korea. Patients with COVID-19 confirmed by PCR were released from isolation after complete recovery. Confirmed patients without symptoms were determined to be completely recovered if the PCR result was negative twice in a row at 24-hour intervals on day 7 after definitive diagnosis. Confirmed patients with symptoms were determined to be completely recovered if they had no fever without taking antipyretic drugs, if the clinical manifestations were improved and if the PCR result was negative twice in a row at 24-hour intervals 7 days after definitive diagnosis.

Asthma participants were selected if the participants were COVID-19 confirmed cases with accompanying symptoms of asthma or a past medical history of asthma from a total of 5,628 participants (n = 128). The control group was selected from total participants who were not asthma participants (n = 5,500). Participants who did not have accompanying symptoms or past medical histories were excluded (n = 4 for asthma participants, n = 370 for control participants). Participants who did not have BMI records were excluded (n = 28 for asthma

participants, n = 1,169 for control participants). Finally, 96 asthma participants and 3,961 control participants were selected (Fig. 1).

Exposure (Asthma)

Asthma was defined if the participants were confirmed to have COVID-19 with accompanying symptoms of asthma or if they had a past medical history of asthma.

Outcome (Mortality)

During the follow-up, the event of death was recorded.

Outcome (Morbidity Score)

The maximum morbidity during hospitalization was defined by the following continuous variables: 1: no limit of activity, 2: limited activity but no oxygen, 3: oxygen with nasal prong, 4: oxygen with facial mask, 5: noninvasive ventilation, 6: invasive ventilation, 7: multiorgan failure or the need for extracorporeal membrane oxygenation (ECMO) therapy, and 8: death.

Covariates

Age groups were divided into 10-year intervals: 0-9, 10-19, 20-29…, and 80+ years old (total of 9 age groups). Systolic blood pressure was divided into 5 groups: <120, 120-129, 130-139, 140-159, and ≥ 150 mmHg. Diastolic blood pressure was divided into 4 groups: <80, 80-89, 90-99, and ≥100 mmHg. Obesity was measured using BMI (body mass index, kg/m^2), and BMI was divided into 5 groups: < 18.5, ≥ 18.5 to < 23, ≥ 23 to < 25, ≥ 25 to < 30, and ≥ 30. Heart rate and temperature were measured; missing systolic blood pressure and diastolic

blood pressure [n = 33 (0.81%)] were replaced with 120-129 and 80-89 mmHg, respectively, and temperature [n = 23 (0.56%)] and heart rate [n = 9 (0.22%)] were replaced with the mean values of each variable from the final selected participants.

Accompanying symptoms and past medical histories were checked as follows: diabetes mellitus, hypertension, heart failure, chronic heart disease, chronic obstructive pulmonary disease, chronic kidney disease, cancer, chronic liver disease, rheumatic disease or autoimmune disease, and dementia.

Statistical Analyses

The general characteristics between the asthma and control groups were compared using the chi-square or Fisher's exact test for categorical variables and independent *t* test for continuous variables.

To analyze the hazard ratios (HRs) with 95% confidence intervals (CIs) of asthma compared with nonasthma for death, a Cox proportional hazards regression model was used. In this analysis, crude and adjusted models (adjusted 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) were calculated.

To analyze the estimated value (EV) of asthma compared with nonasthma for maximum morbidity, a linear regression model was used. In this analysis, crude and adjusted models (adjusted 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) were calculated.

For the subgroup analyses, we divided the participants by age and sex (<50 years old and ≥ 50 years old, men and women) to confirm these associations according to age and sex. The division of the age groups was determined by the median value of the total number of participants. We performed further subgroup analyses according to past medical histories (S1, S2 Table).

Two-tailed analyses were performed, and significance was defined as a P value less than 0.05. SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used for statistical analyses.

Results

Participant characteristics

The demographic and clinical characteristics of COVID-19 patients with and without asthma are summarized in Table 1. In this study population, 2.3% of the study population (n=96) was diagnosed with comorbid COVID-19 and asthma, and most patients with COVID-19 (n=3,961) did not have asthma. The proportion of the elderly individuals was higher among patients with comorbid asthma than among those without asthma ($p<0.001$). The proportion of overweight, obese I, and obese II participants was higher among those with asthma than among those without asthma ($p=0.033$). At the time of diagnosis of COVID-19, vital signs were similar between the two groups except heart rate. Chronic heart disease and chronic obstructive pulmonary diseases (COPD) were more common in those with asthma than in those without asthma. The mortality rate was 8.3% (8/96) in patients with asthma; however, it was 3.0% (118/3,961) in those without asthma, which was significantly higher in patients with asthma than in those without ($p=0.009$).

The association between asthma and the mortality of COVID-19

The analysis of the association between asthma and COVID-19 death is summarized in Table 2. The relative HR for death in participants with asthma versus those without asthma was 2.48 (95% CI =1.21-5.08, $p=0.013$). After adjustment for multiple variables, such as age, sex, obesity, vital signs, and past medical history, the risk of death was 2.20 (CI =1.02-4.76, $p=0.045$) in patients with asthma. In the subgroup analyses according to age and sex, the risk for death was higher in the age ≥ 50 or female groups of patients with asthma than in those without asthma in both crude and adjusted models. Further analyses of past medical history showed that patients with heart failure and those with chronic heart disease had a risk for COVID-19 death (HR= 31.61, 95% CI = 4.36-229.05, $p<0.001$ and HR = 4.68, 95% CI =

1.30-16.84, p=0.018, respectively, Table S1). Patients with asthma without diabetes, COPD, chronic liver disease, rheumatic disease and autoimmune disease or dementia showed a higher risk for death than those without asthma (Fig. 2A).

The effects of asthma on COVID-19 disease morbidity during hospitalization

To assess the effect of asthma on the clinical morbidity of COVID-19, maximal morbidity was scored during admission, and this score was used to calculate the EV for morbidity using a linear regression model. This score was associated with an increase in maximal morbidity of COVID-19 participants with asthma compared to those without asthma (EV = 0.44, 95% CI = 0.16-0.73, p=0.003). This means that asthma participants were treated as ranking 0.44 higher than nonasthma participants. Similar to the HR for death, the subgroups of age ≥ 50 years old and the female group had increased EVs for maximal morbidity score (EV = 0.62, 95% = CI 0.12-1.12, p=0.014, and EV = 0.45, 95% = CI 0.12-0.78, p=0.007). However, after adjustment for multiple variables, EV decreased from 0.44 to 0.25 with marginal statistical significance (95% CI = 0.00-0.51, p=0.048). Further analyses with past medical history showed that asthma with heart failure or cancer was associated with an increase in the maximal morbidity score compared to those without asthma in the adjusted model (Table S2). Asthmatic patients without diabetes, COPD, and chronic kidney disease had significantly higher EVs than those without asthma (Fig. 2B).

Discussion

In this study, we investigated the association between asthma and mortality as well as clinical outcomes of COVID-19 using the nationwide COVID-19 registry. Asthma was associated with mortality, with an HR of 2.20 (95% CI = 1.02-4.76) compared to those without asthma. Furthermore, asthma was associated with clinical outcomes, showing a 25% increase in morbidity score in patients with asthma compared with patients without asthma. In particular, the subgroups of age ≥ 50 years old or women from among the patients with asthma were more vulnerable. When the patients had both asthma and heart failure, the mortality and disease severity of COVID-19 were increased compared with those without asthma.

Possible explanation for our results (asthma as a risk factor for mortality of COVID-19)

The mortality of patients with asthma in COVID-19 was 2.2-fold higher than that of those without asthma, even after fully adjusting for comorbidities, including well-known risk factors such as obesity, cancer, or chronic kidney disease, indicating that asthma itself was associated with increased mortality. A large English cohort study (n=17, 425, 445) found that asthma was associated with an increased risk of in-hospital death from COVID-19 with an HR of 1.63 (95% CI = 1.55-1.71) and that the risk was higher in those with recent oral corticosteroid use than in those without (HR = 1.13, 95% CI = 1.01-1.26).[13] Recent Korean data using a different cohort have shown that allergic rhinitis and asthma, especially nonallergic asthma, were associated with worse clinical outcomes of COVID-19.[14] On the other hand, data from New York City have shown that comorbidities of asthma or COPD have a lower association with critical illness in patients admitted to the hospital.[6] In Italy, the COVID-19-related mortality rate in patients with severe asthma was 7.7%, lower than that in the general population of Italy, 14.5%.[15] This discrepancy could be explained by the following reasons: first, the baseline characteristics of the patients were different between

studies. This registry covers a range of COVID-19 illnesses. However, most studies are based on hospitalized patients who need more intensive care, so the effect of asthma on the mild illness of COVID-19 could be excluded. Second, each country has a different healthcare system and surge capacities in the first wave of the pandemic. In the earlier period of this year, many countries suffered from a lack of hospital beds and physicians due to widespread viruses. These factors could affect mortality, and indeed, the case fatality rates of the US and [16]Italy were 26.0% (405/1,591) and 24.3% (665/2,741), respectively.[6 17] However, the surge of the COVID-19 pandemic did not exceed the capacity of the health care system in Korea in the initial peak periods in that ~10,000 patients were infected among ~50,000,000 Koreans, and the mortality rate of COVID-19 in Korea might be lower than that in other countries.[18]

Possible explanation for our results (asthma as a risk factor for susceptibility to SARS-CoV-2 infection)

This registry has shown that the prevalence of asthma among COVID-19 patients was 2.3%, which is comparable to the prevalence of the general population of this country, ranging from 1.6% to 2.2%.[19] Recent data released from New York and Dublin indicated that the rate of comorbid asthma in COVID-19 was similar or slightly higher than the prevalence of asthma in the general population (9.0% and 8.8%, compared with 10.1% and 7%, respectively)[20 21]. However, early China and Italy data have shown contrasting results in that the prevalence of asthma in COVID-19 was lower than that of the general population (0.9% and 1.9%, compared with 4.2% and 6.0%, respectively).[7 22 23] These discrepancies could be partly explained by different policies for restriction, tracing, and quarantine, health care system capacities, and the number of enrolled patients in each study. Based on our data, mortality was higher among patients with asthma than among those without asthma (8.3% vs 3.0%, P=0.009), although asthma comorbidity in this registry was lower than that in patients

from Western countries, indicating that the impact of asthma on COVID-19 illnesses is complicated.

Not only demographic but also biological factors influence susceptibility to SARS-CoV-2 infection and severity of COVID-19. The S (spike) protein of SARS-CoV-2 binds the ACE2 (angiotensin-converting enzyme 2) receptor to mediate virus attachment to host cell membranes, and virus-cell entry also depends on S protein priming by host cell proteases, including TMPRSS2 (transmembrane protease, serine 2). Previous studies have shown that ACE2 expression was lower in patients with allergic sensitization and asthma and inversely associated with type 2 inflammation, suggesting the possibility of a protective effect during COVID-19 infection in asthmatic patients.[7 24 25] However, a recent study has shown that ACE2 and TMPRSS2 gene expression was similar between asthma patients and healthy controls.[16] Instead, specific subgroups such as comorbidity of diabetes or African American people have shown higher expression of ACE2. In addition, not only ACE2 and TMPRSS2 but also additional host molecules, including ADAM17, cathepsin L, CD147, and GRP78, may also function as receptors for SARS-CoV-2.[26] These reports have suggested that different biological responses in the specific subgroups or races of patients with asthma may determine the risk factors for COVID-19 morbidity.

Limitations and strengths of this study

This study has several limitations. First, the diagnosis of asthma was based on patients' histories, which might be inaccurate and underdiagnosed. However, the original data came from the standardized CRF and were collected by health care providers in the specialized institutions for COVID-19. In addition, the overall prevalence of asthma from this registry is comparable to that of the general population, implicating good reliability of the diagnosis. Second, there were no data for lung function and asthma medication history in this registry.

We demonstrated that asthma was associated with both mortality and morbidity of COVID-19; however, we cannot analyze our data according to asthma severity. Although there are no published data to support this determination, the Centers for Disease Control and Prevention and the National Institute for Health Research state that patients with moderate-severe asthma could be at greater risk for more severe disease.[27 28] As lung function and asthma medication requirements are important factors to determine asthma severity, further studies should be performed using these parameters to precisely evaluate the impact of asthma on the morbidity and mortality of COVID-19. Third, smoking data were missing in this registry. Mechanistic studies demonstrate that ACE2 is an interferon-stimulated gene and upregulated by viral infections. As smokers' lungs harbor higher levels of ACE2, the overabundance of ACE2 may partially explain why smokers are significantly more likely to develop severe SARS-CoV-2 infections.[29 30] Epidemiologic studies about the effect of smoking on COVID-19 are scarce to date; however, as smoking is often associated with hypertension, diabetes, COPD, and obesity as confounders, smoking status should be considered for future studies.

Nonetheless, this study has some strengths. First, we included laboratory-confirmed cases ranging from mild to critical severity of illness, which is different from other studies that include more severe cases. As a strict restriction measure is the current policy of South Korea that all COVID-19 patients can be treated in a quarantine state, the impact of host factors such as underlying diseases may be greater on the outcomes. Second, we assessed the severity and treatment of all participants in this study. Third, this dataset is reliable, as it is based on a nationwide registry and collected from CRF, which was developed and maintained by the national committee and government.[5]

Conclusion

In conclusion, our study provides strong evidence that asthma is associated with an increased risk of mortality as well as worse clinical outcomes of COVID-19. However, considering that asthma is a heterogeneous disease, further studies including asthma severity and asthma endo-phenotypes should be performed in a large cohort.

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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, %)			<0.001*
0-9	2 (2.1)	55 (1.4)	
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, %)			0.562
Male	38 (39.6)	1,685 (42.5)	
Female	58 (60.4)	2,276 (57.5)	
Obesity ‡ (n, %)			0.033*
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, %)			0.444

<120 mmHg	19 (19.8)	977 (24.7)	
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, %)			0.501
<80 mmHg	41 (42.7)	1,491 (37.6)	
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)	0.038†
Temperature (mean, SD)	36.89 (0.48)	36.94 (0.56)	0.391
Past medical history			
Diabetes mellitus (n, %)	17 (17.7)	475 (12.0)	0.090
Hypertension (n, %)	21 (21.9)	808 (20.4)	0.723
Heart failure (n, %)	2 (2.1)	38 (1.0)	0.244
Chronic heart disease (n, %)	8 (8.3)	124 (3.1)	0.012*
Chronic obstructive pulmonary disease (n, %)	7 (7.3)	23 (0.6)	<0.001*
Chronic kidney disease (n, %)	0 (0.0)	43 (1.1)	0.626
Any Cancer (n, %)	3 (3.1)	104 (2.6)	0.741
Chronic liver disease (n, %)	1 (1.0)	57 (1.4)	0.998
Rheumatic or autoimmune disease (n, %)	0 (0.0)	31 (0.8)	0.999
Dementia (n, %)	4 (4.2)	116 (2.9)	0.532
Death (n, %)	8 (8.3)	118 (3.0)	0.009*

* 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	HRs for death			
	Crude	P-value	Adjusted†	P-value
Total participants (n= 4,057)				
Asthma	2.48 (1.21 to 5.08)	0.013*	2.20 (1.02 to 4.76)	0.045*
Non-asthma	1		1	
Age < 50 years old (n = 2,039)				
Asthma	N/A		N/A	
Non-asthma	1		1	
Age ≥ 50 years old (n = 2,018)				
Asthma	2.33 (1.14 to 4.78)	0.021*	2.22 (1.03 to 4.78)	0.042*
Non-asthma	1		1	
Men (n = 1,723)				
Asthma	1.91 (0.60 to 6.10)	0.273	2.33 (0.68 to 8.02)	0.181
Non-asthma	1		1	
Women (n = 2,334)				
Asthma	3.31 (1.31 to 8.38)	0.012*	3.74 (1.35 to 10.35)	0.011*
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.

Table 3 Crude and adjusted estimated value (95% confidence interval) for maximum morbidity score during hospitalization in asthma and non- asthma groups with subgroup analyses

Characteristics	Estimated value for maximum morbidity score			
	Crude	P-value	Adjusted†	P-value
Total participants (n= 4,057)				
Asthma	0.44 (0.16 to 0.73)	0.003*	0.25 (0.00 to 0.51)	0.048*
Non-asthma	1		1	
Age < 50 years old (n = 2,039)				
Asthma	0.06 (-0.09 to 0.21)	0.457	0.07 (-0.07 to 0.22)	0.330
Non-asthma	1		1	
Age ≥ 50 years old (n = 2,018)				
Asthma	0.62 (0.12 to 1.12)	0.014*	0.24 (-0.21 to 0.68)	0.303
Non-asthma	1		1	
Men (n = 1,723)				
Asthma	0.44 (-0.07 to 0.96)	0.090	0.29 (-0.19 to 0.70)	0.055
Non-asthma	1		1	
Women (n = 2,334)				
Asthma	0.45 (0.12 to 0.78)	0.007*	0.26 (-0.01 to 0.58)	0.256
Non-asthma	1		1	

Abbreviation: N/A, Not applicable

* Linear regression, 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.

Figure legend

Fig. 1. A schematic illustration of the participant selection process that was used in the present study. Of a total of 5,628 confirmed COVID-19 cases, 96 asthma participants and 3,961 control participants were selected.

Fig. 2A. Hazard ratio for death in asthma participants compared to nonasthma participants by subgroup.

Fig. 2B. Estimated value for maximum morbidity score in asthma participants compared to nonasthma participants by subgroup.