



# Asthma as a Comorbid Disease in COVID-19

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## ABSTRACT

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus that causes coronavirus disease 2019 (COVID-19). In terms of asthma and COVID-19, there is also a risk of experiencing an asthma exacerbation triggered by coronavirus infection beyond the direct risk of the infection itself. As a comorbid disease, the prevalence of COVID-19 infection in asthma patients is not clear. In addition, the influence of asthma on the severity of COVID-19 has not been reported. The aim of this review was to summarize the reported worldwide data about the prevalence and the clinical characteristics of patients with asthma during COVID-19 infection.

**Keywords:** Asthma, severe asthma, asthma attack, viral infection, coronavirus disease 2019, COVID-19, SARS-CoV-2

## INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is the novel coronavirus first detected in Wuhan, China in December 2019, and causes coronavirus disease 2019 recently named as “COVID-19” by the World Health Organization (1). Since the virus has crossed international boundaries worldwide, it is considered as a pandemic.

Respiratory viruses are one of the most common triggers for asthma exacerbations, and one might anticipate that patients with chronic respiratory diseases (CRDs) would be at increased risk of COVID-19 infection. Impairment of antiviral activity and the airway epithelium may make patients with asthma more prone to have severe viral respiratory infections of the lower airways, which may lead to an increase in the risk of exacerbation. Several studies have found deficient interferon (IFN) responses in subjects with asthma, and some have suggested that IFN delay/deficiency may be detected only in more severe/less well-controlled disease (2). The relationship between this deficiency and viral infection in asthma has been the topic of interest particularly during pandemic diseases. While pandemic H1N1 influenza did not appear to cause more severe disease than seasonal influenza A virus, asthma as a comorbid disease appeared to be a significant risk factor for severe disease (3). A study of 272 patients infected with

H1N1 hospitalized in the United States of America (USA) found that 73% of the patients had a single co-morbidity on admission, of which asthma was most common (28%), followed by obesity (29%) (4). The data influenced strategies for vaccination and pre-emptive anti-viral therapy.

The new pandemic SARS-CoV-2 disease has resulted in high rates of hospitalization and intensive care unit (ICU) admission (1). Many published studies showed comorbidities as a risk factor for COVID-19 associated morbidity and mortality, as well as male gender and older age (5-7). In terms of asthma and COVID-19, there is also a risk of experiencing an asthma exacerbation triggered by coronavirus infection beyond the direct risk of the infection itself. As a comorbid disease, the prevalence of COVID-19 infection in asthma patients is not clear. In addition, the influence of asthma disease on the severity of COVID-19 has not been reported. The aim of this review was to summarize the reported worldwide data about the prevalence and the clinical characteristics of patients with asthma during COVID-19 infection.

## Prevalence of asthma in COVID-19 patients

During COVID-19 disease, almost more than half of adult patients had at least one comorbidity in many studies, whereas all ICU patients had underlying diseases (5-7).

Top comorbidities among COVID-19 infected patients were reported as cardiovascular and metabolic disorders, followed by CRDs (8). Even though COVID-19 infection is mainly a respiratory system disease, there is surprisingly a low rate of associated pre-existing respiratory comorbidities in these studies. Types of CRDs were not specifically defined in many cohorts, but asthma or other CRD seemed to be relatively less common than diabetes and cardiovascular diseases (5,6). Therefore, an

information about chronic obstructive pulmonary disease (COPD) from worldwide cohorts was added because of the lack of clear differentiation between COPD and asthma. Frequency of CRDs in COVID-19 infected patients are given in Tables I-III.

A retrospective cohort of 1,590 hospitalized patients with COVID-19 throughout China reported the prevalence of COPD as 12%, besides hypertension (56%), diabetes

**Table I. Clinical characteristics of laboratory-confirmed COVID-19 infected patients with asthma comorbidity or other chronic respiratory diseases in Asia.**

Reference, Study population, Country	Clinical characteristics	Chronic respiratory diseases (CRD)	Comment on asthma cases
Chen et al. (5) n=50 deaths in 1590 (hospitalized) All provinces, China	Median age: 69 (51-86) yrs. n=30 male 70% comorbidity; 56% HT 26% DM 16% CVD 10% Renal disease	n=6 (12%) COPD No asthma	Complications; ARDS Secondary infection Septic shock DIC
Huang et al. (6) n=41, (COVID-19 pneumonia) Wuhan, China	Median age: 49 (41-58) yrs. 73% male n=3 (7%) smokers n=6 (15%) died (5 ICU, 1 non-ICU care) n=13 (32%) comorbidity; 20% DM 15% HT 15% CVD 2% Ca 2% Liver disease	n=1 (2%) COPD No asthma	1 patient with COPD among 13 patients in ICU
Zhang et al. (10) n=140 (hospitalized pneumonia) Wuhan, China	Median age: 57 (25-87) yrs. 50.7% male n=90 (64.3%) comorbidity; 30% HT 12.1% DM 5.7% Liver disease 5% CVD 1.4% Renal disease	n=2 (1.4%) COPD n=2 (1.4%) urticaria n=16 (11.4%) drug hypersensitivity No asthma, allergic rhinitis, food allergy, atopic dermatitis	Allergic diseases, asthma, and COPD are not risk factors for SARS-CoV-2 infection
Wang et al. (8) n=138 (hospitalized) Wuhan, China	Median age 56 (22-92) yrs. 54.3% male n=36 ICU care (6 died) 46.4% had comorbidity; 31.2% HT 14.5% CVD 10.1% DM 7.2% Ca 2.9% Liver 2.9% Renal disease	n=4 (2.9%) COPD	COPD patients; n=1 (8.3%) non-ICU n=3 (1%) ICU

Table I. Cont.

Reference, Study population, Country	Clinical characteristics	Chronic respiratory diseases (CRD)	Comment on asthma cases
Chine Epidemiology Team (11) n=44,672 (confirmed cases) All provinces, China	86.6% 30-79yrs 51.4% male n=1023 (2.3%) death Comorbidity; 12.8% HT 5.3% DM 4.2% CVD 0.5% Ca	n=511 (2.4%) CRD n=32 (7.9%) death with CRD	Fatality rate %; HT: 6 DM: 7.3 CVD:10.5 CRD: 6.3 Ca: 5.6 No comorbidity: 0.9
Korea National Data (12) n=4212 (hospitalized with pneumonia, all ages) All provinces, Korea	Peak age; 20s and 50s 62% female n=22 (0.5%) death 32% comorbidity; 20% DM 15% HT 15% CVD	n=1 bronchitis No asthma	This case was a 77 yr.-f Under home isolation with confirmed positive result She was waiting for hospitalization, but her condition aggravated rapidly, and she died.

**ARDS:** acute respiratory distress syndrome, **Ca:** cancer, **CDC:** Chronic Disease Center, **COPD:** chronic obstructive pulmonary disease, **CRD:** chronic respiratory disease, **CVD:** cardio vascular disease, **DIC:** disseminated intravascular coagulation, **DM:** diabetes mellitus, **HT:** hypertension, **ICU:** intensive care unit, **IMV:** invasive mechanical ventilation.

(26%), coronary heart disease (16%), and chronic renal disease (10%) (5) (Table I). In studies from Wuhan-China, Cai et al. reported no CRD among 298 confirmed cases (9), whereas there were only one case with a history of COPD among 41 confirmed COVID-19 pneumonia cases reported by Huang et al. (6). Self-reported prevalence of asthma was zero, but the rate for COPD was 1.4% as reported by Zhang et al. (10). Wang et al. found the frequency of COPD as 2.9% in 138 hospitalized COVID-19 patients (8). The China Epidemiology Team group reported the prevalence of CRDs as 2.4% in 44,672 confirmed cases among all provinces of China (11). In the national study of Korea with a young age population, which was expected to have a higher asthma prevalence, there was only one COVID-19 case with CRD as bronchitis among 4212 confirmed cases (12).

In a comprehensive study, the prevalence of asthma and COPD were 13.6% and 2.6% in Korea, and 7.1-13.5% and 5.3-28.6% in the USA among hospitalized patients with COVID-19 (Table II) (13). Reported outcomes among COVID-19 patients of all ages from the Centers for Disease Control and Prevention (CDC) in the USA showed that the prevalence of CRDs was 9.2%, similar to the ones for diabetes and cardiovascular disease (10.9% and 9%) (14). Goyal et al. from New York City reported a low prevalence of asthma and COPD, as 12.5% and 5.1%, in contrast to hypertension (50.1%) and diabetes (25.2%)

among 393 confirmed COVID-19 adult patients (15). According to the COVID-19 associated hospitalizations network (Covid-net) of the USA, CRD (34.6%) was the third common comorbidity after hypertension (49.7%) and obesity (48.3%); however diabetes mellitus (28.3%), cardiovascular diseases (27.8%), and asthma were not in the first three conditions in the 50-64 and >65 years groups among 180 hospitalized adults (16).

In Italy, there were 42 patients (4%) with a history of COPD, and 205 (20%) cases with other comorbidities including asthma among 1591 laboratory-confirmed COVID-19 patients in the ICU (Table III) (7). In France, the prevalence of asthma and other CRD was reported as 6% and 1%, respectively, in a large cohort of pregnant women among initial reports of COVID-19 and asthma (17). In the United Kingdom, the prevalence of CRDs was 6.8% among 3802 screened people, and the authors concluded that there was no evidence of association between CRDs and being positive for SARS-CoV-2, except for being black, living in an urban area, older age, male gender, and chronic kidney disease (18). In Spain, CRD (38%), obesity (48%), and hypertension (44%) were the three most commonly associated co-morbidities among 48 patients with acute respiratory distress syndrome (ARDS) in the ICU (19).

The above studies from various parts of the world suggest that asthma is not a common co-morbidity in adults

**Table II. Clinical characteristics of laboratory-confirmed COVID-19 infected patients with asthma comorbidity or other chronic respiratory diseases in the USA.**

Reference, Study population, Country	Clinical characteristics	Chronic respiratory diseases (CRD)	Comment on asthma cases
Burn et al. (13) United States (US): n=1634 South Korea (SK): n=5172 (Hospitalized)	US: Majority male SK: Majority female HT: 32-72% US, 22% SK DM: 20-43% US, 18% SK CVD: 21-48% US, 15% SK Ca: 8-18% US, 8% SK	Asthma 7.1-13.5% US 13.6% SK COPD 5.3-28.6% US 2.6% SK	Hospitalized Comorbidities are high Hospital admissions are seen among younger and healthier people compared to seasonal influenza
CDC (14) n=7162 United States	n=12217 non-hospitalized n=5285 hospitalized non-ICU n=1069 ICU admission n=7162 complete data; 37.6% comorbidity; 10.9% DM 9% CVD 3% Renal disease	n=656 (9.2%) with CRD including asthma and COPD	Patients with CRD; 15% hospitalized in non-ICU 21% in ICU
Goyal et al. (15) n=393 (hospitalized) New York City, US	Median age: 62.2 (48.6-73.7) yrs. 60.6% male 33.1% intubated 10.2% death 66.2% discharged Comorbidity; 50.1% HT 35.8% obesity 25.2% DM 13.7% CVD	n=49 (12.5%) asthma n=20 (5.1%) COPD	IMV vs nonIMV; Asthma: 13.1% vs 12.2% COPD: 5.4% vs 4.9%
Garg et al. (16) n=1482 (hospitalized, >18yrs) US	74.5% >50 yrs. 54.4% male n=178 had complete data; 89.3% had comorbidity; 49.7% HT 48.3% Obesity 28.3% DM 27.8% CVD	n=55 (34.6%) CRD in 159 patients; n=27 (17%) asthma n=17(10.7%) COPD	Obesity was the most prevalent comorbidity, followed by CRD (primarily asthma) and DM

Ca: cancer, CDC: Chronic Disease Center, COPD: chronic obstructive pulmonary disease, CRD: chronic respiratory disease, CVD: cardio vascular disease, DM: diabetes mellitus, HT: hypertension, ICU: intensive care unit, IMV: invasive mechanical ventilation, NIMV: non-invasive mechanical ventilation, SK: South Korea, US: United States.

infected with COVID-19. Furthermore, asthma seemed to be relatively less common in patients with COVID-19 than other CRDs, and COPD was more common in elderly patients. The low prevalence of asthma cannot only be explained by the low recognition rate or underdiagnosis of CRDs, and gene expressions mediated with SARS-CoV-2 infection as angiotensin converting enzyme 2 (ACE2) and TMPRSS2 of host lung cells in induced sputum cells were not found to be different between healthy and asthma subjects (20). Furthermore, inhaled corticosteroids (ICS) were related to decreased expression of ACE2 and

TMPRSS2 in sputum cells, but there was no effect with systemic corticosteroids (21). ICSs alone or in combination with bronchodilators have been shown to suppress coronavirus replication and cytokine production (22).

### Severity of COVID-19 in asthma patients

Monitoring asthma patients for poor COVID-19 outcomes has been suggested as there are some known risk factors in asthmatics that might increase the severity of COVID-19 infection, such as decreased lung function as in severe asthma, exacerbations with viral infections, and the

**Table III. Clinical characteristics of laboratory-confirmed COVID-19 infected patients with asthma comorbidity or other chronic respiratory diseases in Europe.**

Reference, Study population, Country	Clinical characteristics	Chronic respiratory diseases (CRD)	Comment on asthma cases
Graselli et al. (7) n=1591 (ICU) Lombardy, Italy	Median age: 63 (56-70) yrs 82% male 99% had respiratory support 26% died 68% comorbidity; 49% HT 21% CVD 17% DM 8% Ca 3% Liver / kidney disease	n=42 (4%) COPD n=205 (20%) asthma among "other" comorbidities (anemia, inflammatory bowel disease, epilepsy, chronic respiratory insufficiency, etc.)	Ages of patients with COPD and asthma (with others); 0-10 yrs; n=0 and n=3 21-40 yrs; n=1 and n=6 41-50 yrs; n=0 and n=10 51-60 yrs; n=8 and n=49 61-70 yrs; n=12 and n=77 71-80 yrs; n=20 and n=55 81-90 yrs; n=1 and n=5
Kayem et al. (17) n=617 (pregnant) France	41% hospitalized 20.7% had respiratory support n=1 death 78.8% recovered 2.9% HT	6% (n=37) asthma 1% (n=6) other CRD	Asthma vs other CRD, COVID-19 severity; Non-severe 5.7% vs 0.8% Require O <sub>2</sub> 6.5% vs 1.1% Critical 8.6% vs 2.9%
de Lusignan et al. (18) n=3802 (primary care) UK	n=587 (15.4%) PCR (+) Risk factors positive for SARS-CoV-2 male gender older age >40yrs black race urban areas chronic kidney disease obesity Decreased risk with active smoking	n=258 (6.8%) CRD in 3802 tested	OR 8.90 (5.20–15.30) black race 6.00 (4.82–7.46) urban area 5.00 (3.18–7.90) >75 yrs. 1.47 (1.23–1.75) male 2.90 (2.14–3.93) chronic kidney disease 1.75 (1.40–2.20) DM 1.74 (1.36–2.20) Obesity 1.65 (1.21–2.25) CRD 1.46 (1.20–1.75) HT 1.46 (1.17–1.82) Ca
Barrasa et al. (19) n=48 (ICU with ARDS) Spain	Median age 63 (51-75) yrs. n=27 male 94% intubated 13% died 48% obesity 44% HT 38% CRD	38% COPD No asthma	Pandemic 2009 influenza A in Spain by Rello et al n=32, age=40, no ARDS 31% obesity 3% HT 16% CRD No asthma
Dreher et al. (25) n=50 (Hospitalized) Aachen, Germany	Mean age 65 (58-76) yrs. n=24 intubated with ARDS n=26 non-ICU-care Comorbidity; 70% HT 58% DM 34% Obesity	n=25 (50%) CRD; 22% COPD 14% Obstructive sleep apnea 12% Asthma	Patients with ARDS were more likely to have CRD than those without ARDS (58% vs 42%)

**ARDS:** acute respiratory distress syndrome, **Ca:** cancer, **COPD:** chronic obstructive pulmonary disease, **CRD:** chronic respiratory disease, **CVD:** cardio vascular disease, **DM:** diabetes mellitus, **HT:** hypertension, **ICU:** intensive care unit, **OR:** odds ratio, **UK:** United Kingdom.

accompanying treatment. Treatment with glucocorticoids may also be associated with a higher viral load, longer duration of viremia, and worse clinical outcomes (21).

A study on asthma and severe COVID-19 has reported 3 (14%) asthma patients admitted to the ICU with severe respiratory failure among 24 patients with COVID-19 (23). Even though these three patients had mild asthma, they had received systemic glucocorticoids within one week before ICU admission, as outpatients, for presumed asthma. Three of the 4 COPD patients needed ICU care among 138 hospitalized COVID-19 cases in Wuhan (8). The frequency of CRDs was higher among patients with ARDS and COVID-19 than observed during the H1N1 pandemic in 2009 (24). The China Epidemiology Team reported CRD in the third place among causes of fatality from COVID-19 comorbidities (11). CDC identified people with asthma as a group that may be at higher risk for severe illness from COVID-19 since CRD was in the third place among the comorbidities of COVID-19 patients with a 15% rate of hospitalization, and 21% rate of ICU care (14).

In comparison of asthma and COPD in the COVID-19 group, Goyal et al. found that patients with asthma had a higher invasive mechanical ventilation rate than COPD patients among COVID-19 hospitalizations (15). Similarly, a higher prevalence of asthma was found in ICU patients with COVID-19 than those with COPD by Graselli et al. (7). Kayem et al. also found that patients with asthma had more severe COVID-19 disease than patients with other CRDs (17). In Germany, the frequency of CRD (COPD 22%, obstructive sleep apnea 14%, asthma 12%) was in the third place (50%), after hypertension (70%) and diabetes mellitus (58%) in 50 hospitalized COVID-19 patients (25). They reported that 4 of 6 asthma patients had developed ARDS and 2 had non-ICU care, whereas the ARDS rate was almost 50% in COPD patients, and 30% in sleep apnea patients. The relatively better prognosis of asthma in COVID-19 patients compared to COPD may be related to COPD developing after age 40 and being a progressive disease with irreversible decreased lung function.

There are also contrary reports suggesting that asthma is not an independent risk factor for ARDS or fatality due to COVID-19. Zhang et al. from Wuhan reported that asthma as well as allergic diseases were not risk factors for COVID-19 infection, even though 2 hospitalized patients with COPD had severe COVID-19 pneumonia

(10). Chen et al. reported only one case with CRD who was not in the 11 fatal cases among 99 patients of COVID-19 pneumonia in Wuhan (26). The National study of Korea reported only one exitus with CRDs, as bronchitis, among all fatal patients in 4212 confirmed cases (12). Dong et al. presented no asthma, but one case with COPD, pneumonia and hypertension, in the 11 cases of coronavirus infection with underlying allergic diseases (27). In another study from China, CRDs were not found to be a risk factor for a fatal outcome of COVID-19, since there were no cases with these diseases in a retrospective analysis of 1590 hospitalized patients (5). Huang et al. reported only one patient (2% of 41) with COPD who was admitted to the ICU (6). In the pregnant women cohort from France, it was found that the most vulnerable pregnant women were those with comorbidities but asthma and other CRD did not increase the risk of developing ARDS (17). All these results support the notion that some asthma patients had a good prognosis with COVID-19. Even though the reported good prognosis of COVID-19 in asthma patients may be supported by the benign nature of asthma as a reversible inflammatory airway disease, as well as treatment with corticosteroids suppressing type 2 inflammation, and restore impaired anti-viral immunity against to SARS-CoV-2 infection (28). Further studies are needed to explain the association between asthma and COVID-19.

## CONCLUSIONS

In summary, there is no clear evidence that patients with asthma are at a higher risk of being infected with COVID-19 infection. However, they should be monitored carefully as they may have a higher risk for severe COVID-19. Clinicians should keep in mind that having asthma as an underlying disease may increase hospitalization due to COVID-19, just like other comorbidities and older age. Before drawing any conclusion, further studies are necessary to characterize the prognosis of asthma patients during COVID-19.

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