Asthma and COVID-19 - A systematic review

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Short report

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Abstract

**Background.** Severe coronavirus disease-19 (COVID-19) presents with progressive dyspnea, which results from acute lung inflammatory edema leading to hypoxia. As with other infectious diseases that affect the respiratory tract, asthma has been cited as a potential risk factor for severe COVID-19. However, conflicting results have been published over the last few months and the putative association between these two diseases is still unproven.

**Methods.** Here, we systematically reviewed all reports on COVID-19 published since its emergence in December 2019 to June 30, 2020, looking into the description of asthma as a premorbid condition, which could indicate its potential involvement in disease progression.

**Results.** We found 372 articles describing the underlying diseases of 161,271 patients diagnosed with COVID-19. Asthma was reported as a premorbid condition in only 2,623 patients accounting for 1.6% of all patients.

**Conclusions.** As the global prevalence of asthma is 4.4%, we conclude that either asthma is not a premorbid condition that contributes to the development of COVID-19 or clinicians and researchers are not accurately describing the premorbidities in COVID-19 patients.

Background

COVID-19 was first reported in December, 2019 in Wuhan, China, and rapidly spread across the globe (1). It has affected more than 54 million people and has led to the death of over 1.3 million as of November 16, 2020 ([www.who.org](http://www.who.org)). Severe patients present fever, dry cough, dyspnea, and fatigue, which are commonly associated with the development of pneumonia and acute respiratory distress syndrome (ARDS) (2). Advanced age, ischemic and congestive heart disease, hypertension, diabetes, and chronic obstructive pulmonary disease (COPD) are the most important independent predictors of death (2, 3). As with other infectious diseases affecting the lungs, asthma has been cited as a potential risk factor for severe COVID-19 (4-8). This association could be putatively explained on the basis of an abnormal immune response occurring in the context of the allergic condition and an abnormal respiratory function (9, 10). However, no previous study has addressed this question looking into all studies that described the clinical features of COVID-19.

Here, we systematically reviewed all studies published on COVID-19 since its emergence in December 2019 to June 30, 2020, looking into the description of asthma as a premorbid condition and its putative association with severe progression of the disease. We show that out of 161,271 patients diagnosed with COVID-19 and having their premorbid conditions described, only 1.6% were reported as previously diagnosed with asthma.

Methods
This is a systematic review of the diagnosis of asthma as a premorbid condition in patients with COVID-19. The report was organized according to the Preferred Reporting Items for Systematic Reviews (11). Two authors, NFM and CPJ, independently identified cross-sectional and longitudinal studies published before June 30, 2020, that reported on the prevalence of asthma as a premorbid condition of severe COVID-19 by systematically searching PubMed-NCBI, Google Scholar, Scopus and Web of Science databases. As previously reported, PubMed-NCBI alone covers more than 90% of MEDLINE providing a widely accessible biomedical resource (12). For database searches, language of the article was restricted to English. Search terms included the following: COVID-19 (COVID, COVID 19) or nCov or novel coronavirus or Sars-Cov-2 in the title and clinical characteristics or asthma anywhere in the text. Three authors, EM, EPA, and LAV, resolved eventual discrepancies by discussion and adjudication.

We found 1,069 articles that met the initial inclusion search criteria. All articles were assessed by authors and 598 were excluded (Supplementary Table 1) due to one or more of the following criteria: editorials; metanalyses; systematic reviews; commentaries; letters to the Editor; no description of patient’s clinical characteristics or premorbid conditions; duplicated articles and main text in a language other than English. We found 99 studies duplicated, which were also excluded accordingly, allowing us to analyze only in one of the both versions. The remaining 372 articles were included in the study. Supplementary Table 2 depicts the details of all articles analyzed.

Two authors, NFM and CPJ, independently extracted the following data from each article using a standardized form: study design; number of patients with COVID-19; mention of any respiratory disease; number of patients with any respiratory disease; mention of asthma; number of patients with the previous diagnosis of asthma. The entire body of the articles was presented descriptively.

Results

Figure 1 is a schematic representation of search, inclusion and exclusion of articles. Our search criteria resulted in the identification of 1069 articles that were pre-selected for detailed analysis resulting in the exclusion of 598 articles (Suppl. Table 1) due to one or more of the following reasons: editorials; metanalyses; systematic reviews; commentaries; letters to the Editor; no description of patient’s clinical characteristics or premorbid conditions; and main text in a language other than English. The remaining 372 articles (Suppl. Table 2) described the clinical aspects of 161,271 COVID-19 patients. Two hundred and one studies mentioned the existence of other respiratory premorbidities except for asthma. Although asthma was mentioned as a underlying disease in 67 studies, only 52 articles have described the exact number of the COVID-19 patients with asthma (Table 1). The other 15 studies presented asthma together with other respiratory diseases, making it impossible to identify the number of COVID-19 asthmatic patients. There was a total of 40,948 COVID-19 patients included in the studies mentioning asthma, of which 8,439 were previously diagnosed with asthma. In most of the studies describing other respiratory illnesses, COPD was the leading diagnosis. The United States was the country with the largest number of studies describing asthma, followed by China, France, Spain and the United Kingdom (Figure 2A).
Thus, according to current COVID-19 clinical records, 6.4% of patients included in articles describing the clinical characteristics of COVID-19 patients and citing asthma were previously diagnosed with asthma (Fig. 2B). If all studies providing any clinical description of COVID-19 comorbidities are taken into consideration, asthma was present in only 1.6% of patients (Fig. 2C).

**Discussion**

Asthma is a highly prevalent, chronic, non-communicable disease that affects up to 4.4% of the world’s population (http://www.globalasthmareport.org; https://www.who.int/news-room/q-a-detail/asthma). Its recurrent nature leads to frequent hospitalizations and high mortality, ranging from 2 to 4/100,000 (13). Respiratory viruses can trigger asthma exacerbations, which can increase the severity of the infectious condition (14). In the past, coronaviruses have been implicated as triggers of asthma exacerbations (15, 16); this is also true for influenza virus (17). However, as for the new coronavirus, SARS-CoV-2, there is still controversy regarding the putative role of asthma as a premorbid that could worsen disease progression (7, 8, 18).

Here, we evaluated all studies on COVID-19 published since its emergence up to June 30, 2020. We showed that asthma was described as a premorbid condition in only 1.6% of all patients. These numbers are far less than expected considering the prevalence of asthma in the world (http://www.globalasthmareport.org; https://www.who.int/news-room/q-a-detail/asthma) and could suggest that having asthma as a premorbid condition either represents no risk for COVID-19 or could be a protective factor against the development of the disease. However, there are some aspects that should be considered as potentially impactful for the findings herein reported. First, the prevalence of asthma varies across the globe, ranging from 21% in Australia to less than 2% in China, Kazakhstan and Vietnam (19). Likewise, the most common risk factors for COVID-19, obesity, diabetes and hypertension, have distinct prevalences in different countries (www.who.org). Thus, the geographical origin of the studies could have influenced the results. However, as the studies included in this systematic review were mostly originated from countries presenting a wide range of prevalences for both asthma and the main comorbidities for COVID-19, we believe this factor plays a minor role in the reported findings.

Another aspect that could explain our results is that asthma treatment with inhaled corticosteroids allied to improved therapeutic and prophylactic adhesion has increased over the years, resulting in the reduction of respiratory distress episodes and allergy associated immunological imbalance (20-23). Moreover, allergy and asthma international associations were efficient to rapidly produce and release COVID-19 guidelines that provided advice for health professionals involved in the care of asthma patients, as well as for reaching the general public (24-27). These actions could have beneficially impacted on the control of asthma and also influenced patients to follow social isolation procedures; thus, mitigating the risk of contracting COVID-19.

It has been suggested that the particular inflammatory environment in the bronchioalveolar system of asthma patients could lead to a reduced expression of SARS-CoV-2 receptor, angiotensin converting
enzyme 2 (ACE2), rendering asthma patients protected from the infection (28-30). This could be due to the fact that interleukin-13 (IL-13), a cytokine involved in eosinophil recruitment to the bronchial epithelia (31), is capable of reducing ACE2 expression in bronchial ex-vivo human samples (28). In line with these findings, it has been reported that progressive increase in blood eosinophil counts is related to COVID-19 recovery. Thus, if proven correct, these data could suggest that only patients with allergic asthma are protected from COVID-19, as recently suggested (32, 33). However, currently available data provides no sufficient detail regarding asthma etiological classification and further studies would be required in order to provide advance in this issue.

The main weaknesses of this systematic review rely on the facts that we included publications covering the initial 6 months of pandemics and as new data is published on a daily basis, some changes in the frequency of asthma could appear; moreover, readers should keep in mind that some reports show that in certain pocket populations, asthma could be an important comorbidity for COVID-19 (34). The reasons for these apparent discrepancies should be a focus of further studies.

Thus, as for the data analyzed in this systematic review, asthma does not seem to be an important premorbid condition in COVID-19 patients; or, conversely, it could be a protective factor, as previously proposed (18). The findings herein reported could be an epidemiological truth that should be further explored in mechanistic studies or could be due to the fact that researchers are not properly investigating and describing the premorbidities in COVID-19 patients. Whatever the reasons, the medical community should be aware of the implications of missing the diagnosis of a potentially severe respiratory disease such as asthma that could worsen the prognosis of COVID-19 patients.

Declarations

Ethics approval and consent to participate. The study does not require ethical approval because the systematic review is based on published research and the original data are anonymous.

Consent for publication. Authors are the sole responsible for the publication of this study.

Availability of data and materials. Data are available upon request.

Competing interests. Authors have no competing interests to declare.

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Authors’ contributions. NFM and CPJ performed article search and first round of inclusions. EM, EPA and LAV performed second round of inclusion. LAV and NFM performed statistics analysis. LAV and NFM wrote the manuscript. All authors read manuscript and provided approval.
Acknowledgements. We thank our grant providers.

References


**Table**

Table 1. **Details of the articles that mention asthma.**
Clinical characteristics and outcomes of COVID-19 hospitalized patients with diabetes in the United Kingdom: A retrospective single centre study

Clinical characteristics of COVID-19 in Saudi Arabia: A national retrospective study

Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State

Clinical Profiles, Characteristics, and Outcomes of the First 100 Admitted COVID-19 Patients in Pakistan: A Single-Center Retrospective Study in a Tertiary Care Hospital of Karachi

Intracerebral haemorrhage and COVID-19: Clinical characteristics from a case series

Covid-19 in Critically Ill Patients in the Seattle Region — Case Series

Clinical Characteristics and Outcomes of Hospitalized and Critically Ill Children and Adolescents with Coronavirus Disease 2019 (COVID-19) at a Tertiary Care Medical Center in New York City

Using Machine Learning to Predict ICU Transfer in Hospitalized COVID-19 Patients

Early outcomes after hip fracture surgery in COVID-19 patients in New York City

Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19

Clinical characteristics and outcomes of patients with coronavirus disease 2019 (COVID-19) and rheumatic disease: a comparative cohort study from a US ‘hot spot’

Clinical characteristics of 182 pediatric COVID-19 patients with different severities and allergic status

Characteristics of Emergency Department Patients With COVID-19 at a Single Site in Northern California: Clinical Observations and Public Health Implications

The epidemiology of reverse transmission of COVID-19 in Gansu Province, China.

COVID-19 in Solid Organ Transplant Recipients: A Single-Center Case Series from Spain

Presenting characteristics, comorbidities, and outcomes of patients infected with COVID-19 and Mycoplasma pneumoniae in the USA

Characteristics and Clinical Outcomes of Adult Patients Hospitalized With COVID-19 - Georgia, March 2020

Clinical Characteristics of Covid-19 in New York City

A novel risk score to predict diagnosis with coronavirus disease 2019 (COVID-19) in suspected patients: A retrospective, multicenter, and observational study

Individualizing Risk Prediction for Positive Coronavirus Disease 2019 Testing: Results From 11,672 Patients

Multisystem Inflammatory Syndrome in Children Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection (MIS-C): A Multi-institutional Study from New York City

Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population-based cohort study

The Epidemiological and Clinical Characteristics of 81 Children with COVID-19 in a Pandemic Hospital in Turkey: an Observational Cohort

Clinical characteristics and outcomes of COVID-19 hospitalized patients with diabetes in the United Kingdom: A retrospective single centre study

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The Epidemiological and Clinical Characteristics of 81 Children with COVID-19 in a Pandemic Hospital in Turkey: an Observational Cohort
<table>
<thead>
<tr>
<th>Authors</th>
<th>Title</th>
<th>DOI</th>
<th>COPD (Yes/No)</th>
<th>COPD Yes</th>
<th>Sample Size</th>
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<tbody>
<tr>
<td>Zhao M, et al.</td>
<td>Comparison of clinical characteristics and outcomes of patients with coronavirus disease 2019 at different ages</td>
<td>10.18632/aging.103298</td>
<td>Yes</td>
<td>COPD: 23 (2.3%)</td>
<td>Yes</td>
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<tr>
<td>Zhou X, et al.</td>
<td>Clinical Characteristics of Coronavirus Disease 2019 (COVID-19) Patients with Hypertension on Renin-Angiotensin System Inhibitors</td>
<td>10.1080/10641963.2020.1764018</td>
<td>Yes</td>
<td>COPD: 3 (2.7%)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Figures**
Figure 1

Schematic representation of search, exclusions and inclusions of articles.
Figure 1

Graphic representation of the geographical origin of the studies analyzed in the systematic review (A) and the proportion of patients with previous diagnosis of asthma among COVID-19 patients included in studies citing asthma (B) and among all COVID-19 patients described up to June 30, 2020 (C).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

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