

COMMENTARY

The Impact of COVID-19 on Asthma Patients: Current Knowledge and Future Perspective

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ABSTRACT

The pandemic of CoronaVirus-19 (COVID-19) is an alarming situation worldwide as it poses a considerable threat to the healthcare system. Various study results suggested the effect of COVID-19 on non-communicable diseases (NCDs) including asthma. The present study aims to review, describe and assess the impact of COVID-19 on asthma patients. The results of the current review suggest a non-significant impact of asthma on COVID-19 outcomes. However, the impact of COVID-19 on asthmatics is complex that may vary according to the clinical severity, patient age, or genetics in different populations. Hence it is needed to conduct studies with a large number of cohorts in different populations that may provide us with conclusive results. The use of corticosteroids is not recommended, but some studies suggested that by monitoring certain factors corticosteroids can be used for COVID-19 patients suffering from asthma. The future care of asthmatic patients in COVID-19 should include self-management, remote interventions, and social distancing.

Keywords: Asthma, Covid-19, Genetics, Treatment.

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INTRODUCTION

Asthma is defined as a non-communicable, chronic inflammatory, and complex heterogeneous respiratory disorder. It is characterized by airway inflammation, hyperresponsiveness, mucus hypersecretion obstruction of airflow, and bronchial muscle spasm leading to cough, breathlessness, and chest tightness.^{1,2} It is a multifactorial disorder involving both environmental and hereditary risk factors. The microbes in the environment have also shown a crucial role in genetically susceptible individuals. Globally, it is considered as a major public health challenge as over three hundred million individuals are known to be affected by this fatal disease.³

The coronavirus-19 (COVID-19) pandemic is an alarming situation as it still poses a major burden on the health care systems.⁴ It began in early December 2019 and was reported as a new coronavirus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in Wuhan, China, and after that rapidly spread around the globe.⁵ It is one of the key pathogens that primarily targets the human airway system. The viral symptoms start to appear after the incubation time of 5.2 days. The sign and symptoms of this disease include cough, fever,

fatigue, headache, dyspnoea and other clinical features associated with pneumonia and confirmed by the chest CT scan.⁶ Currently, by using the phylogenetic analysis, it is classified as a β -coronavirus from group 2B. Its major targets in the lungs, is the angiotensin converting enzyme 2 (ACE2).⁷

Asthma is considered a risk factor for the coronavirus morbidity. Respiratory viruses, including the SARS-CoV-2 are also responsible for causing asthma complications.⁸ Moreover, the complex relationship between the respiratory viral infections may trigger or worsen the asthma symptoms; likewise, in asthmatic patients the impaired immune response against the viral infection may result in a poor outcome.⁹ There is a scarcity of data regarding the impact of COVID-19 in asthmatic patients, thus there is a need of the hour to analyze the available data. The present study aims to review the impact of coronavirus on asthmatic patients, including the genetic predisposition and treatment strategies.

METHODS

We searched the relevant literature till September 2021 by using different keywords and MeSH terms. The

various online electronic databases, including Ovid, MEDLINE, Cochrane Library, Web of Science, PubMed, and EMBASE were used for literature selection. We included articles that were published in English language.

EFFECT OF ASTHMA COMORBIDITY ON COVID-19 OUTCOMES

Although in asthmatic patients there is high susceptibility to airway viral infections, some evidence suggests that the frequency of asthma among COVID-19 patients is low. The reason for this low prevalence may be the effect of inhaled corticosteroids or the decreased expression of ACE 2; however, the protective role of inhalation therapy remains under consideration. The association between SARS-Cov-2 and asthma remains uncertain due to lack of literature regarding the clinical profile of asthma patients hospitalized for COVID-19.¹⁰ Song et al suggested that COVID-19 patients with comorbid asthma ranged from 0-12% and 1.5 to 5% for chronic obstructive pulmonary disease (COPD). They also reported the difference in disease severity between COPD and asthmatic patients. The COPD patients in this study had severe illness as compared to the asthmatic patients. However, the expression of ACE2 was found to be lower in asthmatic patients than the controls and COPD patients.¹¹

Similarly, asthma was a non-significant risk factor for the mortality in patients suffering from COVID-19. But a high mortality rate was reported in asthma patients with acute exacerbation before COVID-19.¹² The meta-analysis of 131 studies performed by Liu et al. in 2021 also reported the variation in the prevalence of comorbid asthma in COVID-19 patients. Its prevalence ranging from 1.1% to 16.9% in different countries. Moreover, asthma was not associated with the worse prognosis or severity of COVID-19.¹³ Lovinsky-Desir et al. analyzed the electronic health records of the patients in the New York Presbyterian Hospital network and the results also indicated a low risk of asthma impact on the severity of COVID-19 regardless of the obesity, age or other high-risk comorbidities.¹⁴

Hussein et al. conducted a meta-analysis including 107, 983 patients from the North America and Europe. The results of this study were also consistent with the previous studies as there was non-significant association of asthma and outcomes of COVID-19. However, asthmatic patients had lower mortality risk and recovered better than non-asthmatics. The best explanation for these findings would be the use of inhaled corticosteroids or the lower expression of ACE2 in the alveoli and nasal epithelia.¹⁵ A multi-center retrospective study, including 502 COVID-19 patients

also reported comparable outcomes. As among those 502 COVID-19 patients, 430 were non-asthmatic and 72 were asthmatic patients. The analysis of this study also revealed a non-significant association between asthma and COVID-19 severity.¹⁶

COVID-19 RISK AND ASSOCIATION OF ASTHMA AND ITS GENETIC PREDISPOSITION

The determination of genetic predispositions is important in the development of risk-stratification, treatment and prevention of COVID-19. Zhu et al. constructed a polygenic risk score (PRS) for each asthma group. The association between the overall genetic risk and asthma is represented by the sum of all risk alleles. Moreover, they found an association between the risk of severe COVID-19 and PRSs for asthma. However, the results of this study also showed a non-significant relationship between outcome and the severity of COVID-19 and genetic predisposition for asthma. All these results may suggest the complex interplay between the host response, pathogens, and environment or may include the limited discriminatory performance of the polygenic risk score in the pathobiology of the COVID-19.¹⁷ Another study conducted by Peters et al. showed that the transmembrane protease serine 2 (*TMPRSS2*) and *ACE2* were similar in both asthma cases as well as controls. Stratification analysis suggests that these genes expressions were higher in male gender, African ethnicity, and diabetic patients. Moreover, both *ACE2* and *TMPRSS2* showed lower expression after treatment with inhaled corticosteroids (ICS).¹⁸

In a recent study, it is reported that the levels of the *FURIN* and *ACE2* differ by molecular or clinical phenotype. Also, there is a strong relationship between the sputum *FURIN* expression and neutrophilic inflammation, thus it may ultimately suggest a greater potential for mortality and morbidity outcomes from COVID-19 in neutrophilic severe asthma. Moreover, the levels of *TMPRSS2* in bronchial biopsy samples were positively related to the blood neutrophils whereas in bronchial brushing specimens *TMPRSS2* levels were positively associated with the body mass index (BMI) and male gender while the *FURIN* levels showed a significant association with the blood neutrophils and male gender.¹⁹ Kasela et al. also found that *ACE2* was higher in subjects with obesity, hypertension, and active smokers and the truncated, non-binding *ACE2* isoform is strongly associated with interferon related inflammation.²⁰

EFFECT OF COVID-19 ON ASTHMATIC PATIENT'S TREATMENT AND FUTURE CARE

The impact of COVID-19 is similar to other coronaviruses

as it is anticipated to exacerbate asthma however, the accurate immunopathological mechanisms are not fully understood. The present asthma guidelines that are prescribed for hospitalized patients in acute exacerbations include the oral corticosteroids. Although the World Health Organization (WHO) recommended that it is better not to use corticosteroids in COVID-19 patients, however, with the caveat this treatment can be used if there is underlying COPD and asthma.²¹ Moreover, there is the risk of more severe exacerbations in asthmatic patients after the withdrawal of the inhaled corticosteroids and a recent meta-analysis was conducted for the COVID-19 outcomes in patients suffering from chronic respiratory diseases. The results of this study also suggested not abandoning the well-established inhaled corticosteroids treatment in asthmatic patients. Thus, there is an urgent need to elucidate the impact of inhaled corticosteroids in addition to the clinical and demographic characteristics that determines the effect of SARS-Cov-2 in asthmatic patients.²²

A research study results showed that the asthmatic patients without COVID-19 receiving the inhaled corticosteroids in high doses showed a high risk of mortality as compared to the patients taking a short-acting beta-agonist (SABA).²³ Moreover, in the severe steroid-dependent asthmatic patients without COVID-19 the inhaled sodium cromoglycate gives better results as it improves the lung functions and reduce the oral corticosteroids use to a mean of 3.68mg/day. Hasan et al. further suggested the use of corticosteroids based on COVID-19 severity in patients with concomitant asthma as this therapy may prove beneficial in critical disease or acute respiratory distress syndrome (ARDS).²⁴

Many regulatory bodies made several restrictions, thus resulting in poor access to the basic diagnosis of respiratory diseases during COVID-19. The testing should only be performed if it is needed for immediate treatment decisions. Many screening protocols have now become mandatory before entry into different workplaces. Due to the increased risk of viral transmission and aerosolization, many patients are switching from nebulizer treatment to meter-dose therapy. In addition, insufficient availability of routine medicines could lead to an increased morbidity rate in asthma patients. Furthermore, social distancing, hand washing and increase awareness may prove beneficial in reducing the exposure to asthma triggers and the burden in this population.²⁵

Boyce et al stated that all aspects of asthma care would be expected to disrupt due to limited face-to-face care

during the COVID-19; additionally, various diagnostic tools used in asthma are considered aerosol generating diagnostic tool that would further hinder asthma care. However, remote interventions and self-management during this period may prove beneficial for asthma care.²⁶ Taquechel et al conducted research on the viral testing and paediatric asthma health care utilization. The results of this study showed changes in health care utilization during the COVID-19 pandemic, including reduced systemic steroid prescriptions and reduced admissions. Further findings suggested that 61% of all visits and the highest used asthma encounter modality is video telemedicine while 19% increase in telephone encounters.²⁷ During COVID-19 it is recommended that adherence to daily controller medications is important for asthmatic patients as it is associated with better outcomes along with a reduced risk of respiratory exacerbations. In addition, there is a decrease in incidental exposure to the virus in well managed asthmatic patients and ultimately helps the health care providers to focus attention on critically ill patients.²⁸

LIMITATIONS

The literature on the impact of COVID-19 on asthmatic patients is scarce thus, this current study contributes to provide better insight into the relationship between COVID-19 and asthma, including therapeutic strategies and genetic contributions. However, certain limitations should be taken into account:

- * First, we only included the literature that was published in the English language.
- * Second insufficient information is available, particularly regarding the clinical severity of asthma and the role of genetics.
- * Third many studies included had a sample size; thus, for more conclusive findings there is a need to conduct prospective studies with large sample sizes.

CONCLUSION

The current evidence reveals an overall non-significant association of asthma with COVID-19 outcomes. However, in some groups, its genetic predisposition showed certain impact on COVID-19 outcomes. The use of corticosteroids shows promising results for the asthmatic patients suffering from the coronavirus-19. Furthermore, the best practices for future prevention includes social distancing, self-management, hand washing, social awareness, and remote interventions.

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