

Chronic Obstructive Pulmonary Disease and COVID-19: A Double Trouble

JYOTI BAJPAI¹, SURYA KANT², AJAY KUMAR VERMA³, AVISHEK KAR⁴



ABSTRACT

Coronavirus Disease 2019 (COVID-19) is a respiratory and systemic illness that may progress to severe Acute Respiratory Distress Syndrome (ARDS). There is a pressing need to identify clinical predictors of severe COVID-19 which can help in risk stratification and prognostication. The COVID-19 pandemic tends to have more severe clinical presentation in older age group and in chronic diseases; Chronic Obstructive Pulmonary Disease (COPD) is one of them. COPD is the common cause of high mortality and morbidity worldwide. It is obvious to fear for patients with underlying COPD. Acute episode of exacerbation and COVID-19 pneumonia are the two pivotal differential diagnoses in contemporary era, in patients of COPD presenting with worsening dyspnoea. Mortality rate have been higher among COPD group of patients with the development of hypoxemia. Literature shows that pre-existing COPD worsens the risk of COVID-19 progression and leads to poorer prognosis. Even after recovery from the acute event, proper adherence to maintenance therapy for COPD (inhalational agents) continues to be of paramount importance and remains the standard of care. Because COPD remains a subset that is highly vulnerable for adverse outcomes with COVID-19 infection, preventive therapy should be directed towards—attenuation of contact with droplets, proper hand hygiene and maintenance of adequate nutritional status. The aim of this brief review is to know the burden and impact of COPD on COVID-19 pandemic and challenges in diagnosis and management of COPD patients.

Keywords: Angiotensin converting enzyme 2 receptor, Coronavirus-2019, Prognosis, Respiratory illness, Steroids

INTRODUCTION

The COVID-19 has emerged as the biggest pandemic of century. It is a systemic illness with a prominent respiratory component in upto 15-20% cases leading to severe respiratory failure necessitating ventilatory support [1]. Coronavirus belongs to beta group and family is *Coronaviridae*, it is comparable to viruses that caused Severe Acute Respiratory Syndrome (SARS), which had a deadly disease in 2002, and Middle East Respiratory Syndrome (MERS), in 2012 [2]. Coronavirus first case was reported from Wuhan city in China in December 2019. Since then, COVID-19 cases have been rising around the globe, and it is related to a large number of morbidity and mortality [2]. Since SARS-CoV-2 is a freshly known virus, there's no pre-existing immunity within the human community; additionally, there's no definitive cure to interrupt or inactivate this virus. These obliquities create a lot of concern for vulnerable members of the community, which embody people with immune issues, co-existing co-morbidities, and old folks. In recent analysis, high blood pressure (16.9%), cardiovascular diseases (3.7%), Diabetes (8.2), urinary organ disease (1.3%), malignancy (1.1%), smoking, and COPD (1.5%) were among the significant underlying illness among hospitalised patients with COVID-19 [3]. COPD as a risk factor for COVID-19 infection remains dubious. A study of 140 hospitalised patients of COVID-19 showed that asthma, and COPD were not the risk factors [4]. However, some studies have showed that COPD patients are likely to have a higher risk of more severe illness [5,6]. COPD patients may be affected in many ways during the COVID-19 pandemic. Viral infections are the most important cause of exacerbation and leads to hospitalisation. The elderly age, cognitive impairment, similarity of symptoms of COVID-19 and COPD and use of aerosol generating devices in the management of COPD are the most important challenges faced by physicians [7].

Pathogenesis

The most common respiratory component of COVID-19 is arterial hypoxemia. Hypoxemia along with increased alveolar-to-arterial

oxygen gradient indicates either ventilation–perfusion mismatch or intrapulmonary shunting which is the cause for respiratory failure in COVID-19 patients [8]. COVID-19 primarily affect the alveolar epithelial cells of lung. Although most infections with COVID-19 are thought to be subclinical or mildly symptomatic, it may result in ARDS and occasionally into multiorgan failure [9]. Smokers are more susceptible to the infection. It has been cited that people who smoke have unregulated Angiotensin Converting Enzyme 2 (ACE2) in remodelled cell types, which is constant with consequences of SARS [10]. Smoking is the most common risk for COPD [11].

Prevalence of COPD in COVID-19 [Table/Fig-1] [3,12-15]

The COPD is a common preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. Chronic infections are the common cause of Acute Exacerbation of COPD (AECOPD), which can result in respiratory failure in many patients. In India, the disease is prevalent in 4.2% of the population of over 35 years of age [16]. COPD is currently the third leading cause of death in the world [16]. More than three million people die of COPD annually, accounting for 6% of all deaths globally and 5 lacs in India [16]. There are 93 million people suffering from COPD in India. Of them, around 37 million suffer from asthma and about 56 million from COPD [16]. Different health services and chronic diseases have been mostly affected by COVID-19 and COPD is one of them. A study of 1,099 patients with COVID-19 in China concluded that COPD was detected in 1.1% patients [3]. Different ratios have been recorded in studies from around the world due to the COVID-19. The incidence of COPD has been reported to be 2-3% among patients who developed COVID-19 pneumonia in the first reports from China, where the pandemic originated [17]. According to a meta-analysis prevalence of COPD was 0.95% (95% confidence interval: 0.43-1.61) in hospitalised patients with COVID-19 [12].

Author	Number of patients	Study type	Prevalence of co-morbidities	COPD group	Smoking history
Guan WJ et al., [3]	1099 patients confirmed COVID-19 from 552 hospitals in China	Observational	23.7% had at least one co-existing illness (e.g., hypertension and COPD).	1.1% patients had COPD, most of them (3.5%) had severe COVID-19.	12.6% were current smokers and 1.9% were former smokers.
Wang B et al., [14]	1558 samples from 6 retrospective studies; 324 (20.8%) severe group cases and 1234 non severe group	Meta-analysis		COVID-19 patients with COPD had a 5.97-fold higher risk of progression than patients without COPD.	
Zhao Q et al., [13]	11 studies included; resulted in a total of 2002 patients and 334 meeting the definition of severe COVID-19.	Meta-analysis		Presence of COPD is associated with a nearly four-fold higher risk of developing severe COVID-19. Death was reported in 6 of 10 (60%) of patients with COPD and 80 of 233 (34.3%) of non COPD patients. The pooled Odds Ratio (OR) of COPD for death was 1.93 (95% CI: 0.59-7.43).	Smoking increases the risk of severe COVID-9 (fixed-effects model; OR=1.98; 95% CI: 1.29-3.05) by around two-folds.
Lippi G et al., [15]	7 studies were included; 1592 COVID-19 patients, 314 of which (19.7%) had severe disease	Meta-analysis		COPD was found to be significantly associated with severe COVID-19 (OR: 5.69 (95%CI: 2.49–13.00), COPD is associated with a significant, over five-fold increased risk of severe COVID-19 infection.	
Emami A et al., [12]	10 studies were included; 3,403 hospitalised patients with COVID-19 infection	Meta-analysis	The pooled prevalence of hypertension, cardiovascular disease, smoking history and diabetes were 16.3%, 12.11%, 7.63% and 7.87%, respectively.	The incidence rate of COPD in hospitalised COVID-19 patients was 0.95%.	The pooled prevalence of SARS-CoV-2 infection in hospitalised patients with history of smoking was estimated as 7.63%.

[Table/Fig-1]: Different studies showing burden and impact of COPD in COVID-19 [3,12-15].

COPD as Risk Factor

The presence of persistent COPD is associated with an increased hazard of mortality in sufferers with community-acquired pneumonia because of local/systemic inflammation, compromised host response, or increased mucus production in sufferers with COPD [18]. The risk of development of coronavirus pneumonia in COPD patients compared to the normal population is not as high as expected, but the affected cases manifest significant differences in terms of monitoring in the intensive care unit, intubation, and mortality when compared to non COPD patients. A study showed the risk of developing severe COVID-19 infection in a patient with pre-existing COPD was two fold higher than in patients without COPD [13]. A meta-analysis investigating the risk factors associated with patients with COVID-19 found that, patients with COPD have a 5.97-fold increased risk [14]. COPD patients with confirmed COVID-19 have a mortality rate of 60% as shown in a meta-analysis [19]. The overall Case Fatality Rate (CFR) was 2.3%, in confirmed cases of COVID-19 [20]. In people with chronic respiratory disease, the CFR was reported as 6.3% [15].

Challenges Faced by Physicians

The management of a COPD patient during the pandemic is a great challenge for both patients and physicians [Table/Fig-2]. The most important challenge faced by physicians is to differentiate the clinical symptomatology of COVID-19 and AECOPD, which may potentially result in delayed and inappropriate management. COPD and COVID-19 both are bi-directional. Presence of both in a patient is a diagnostic and therapeutic challenge for physician. Presence of fever is the most common presenting symptom in COVID-19 patients, about one third of cases, while not being among the most frequent findings of COPD exacerbation. Dry cough is also a common symptom in isolated COVID-19 rather COPD with COVID-19 patients [21]. Computed Tomography (CT) thorax one of the primary imaging tool that has been used to diagnose and support the diagnosis of COVID-19. The complete categorisation of definitive and possible COVID-19 cases may be possible on radiological basis but not confirmatory. At this point, multidisciplinary approach including the radiologist and the clinician plays an important role to make a definitive diagnosis of COVID-19 and exclude the other causes. The most consistent radiological features are emphysema, bronchiectasis, peribronchial thickening, air trapping, pulmonary oedema and viral pneumonia in patients with COPD and COVID-19 pneumonia [22]. A comparison of images with previously

obtained images would also be helpful at this point. The detection of coronavirus by Polymerase Chain Reaction (PCR) is diagnostically important and also a confirmatory test in COPD with COVID-19.

Difficult to differentiate symptoms of COVID-19 and AECOPD.
Hesitation to treat AECOPD with steroids in COVID-19.
Restriction to use nebuliser therapy due to aerosolisation concerns with COVID-19.
Decreased access to medications and shortages of many classes of inhaler medications.
Limit to use of Non Invasive Ventilation (NIV) in COPD due to aerosolisation concern with COVID-19.
COPD patients are failing to seek care due to fears about contracting COVID-19.
Emergency Departments and hospital volumes have decreased substantially for a variety of critical conditions due to 'lockdown'.
Delayed presentation to the hospital may lead to more severe presentation of AECOPD.

[Table/Fig-2]: Challenges in the management of COPD.

*AECOP: Acute exacerbation of COPD

Impact of COVID-19 on COPD

The COPD patients are at higher risk of getting infected so they all have to take extra care of themselves. In the recent COVID time COPD patients also don't want to visit hospitals unless there was an emergency. Acute exacerbation is the most common indication for hospital visit in COPD patients, but fear of contracting COVID-19 infection may keep them away from the hospitals and leads to delayed presentation with worsening of their symptoms [23]. The wait times at the hospitals has become much longer, communication and relationships with healthcare providers has decreased which may result in fewer adherences to self-management measures. The Global Initiative for Obstructive Lung Disease (GOLD) guideline 2020 came amid this pandemic and recommend that inhalational therapy should be continued in patients with COPD during the COVID-19 [23]. Stabilisation of symptoms, avoid exacerbation were especially important in this pandemic period in the follow-up of patients with COPD. COPD patients should maintain their regular therapy. Inhaled Corticosteroid (ICS) combined with bronchodilators have to be continued in patients of COPD with COVID-19 infections. There is evidence to suggest that taking ICS may be beneficial in dealing with virus infections, specifically those due to coronavirus. An in-vitro study showed that the combination of budesonide, glycopyrronium and formoterol has inhibitory effect on the replication and cytokine production of human coronavirus HCoV-229E [24]. The corticosteroids have anti-inflammatory,

anti-fibrotic, and vasoconstrictive effects. Corticosteroids like hydrocortisone, dexamethasone and methyl prednisone have beneficial effects on short-term mortality and reduction in need for mechanical ventilation in COVID-19 patients [25].

Oxygen therapy should be provided if needed, following standard recommendations. Vaccination against influenza and pneumococcal disease are not contraindicated in COPD with COVID-19 patients. To continue a stable course of disease, COPD patients should be encouraged to quit smoking and get vaccinated. Active cigarette smoking increases mortality due to COVID-19 pneumonia by approximately 14 times [13]. Stable COPD patients should continue their medication and for follow-up they may prefer online as well as offline consultation from their treating physician. Inhalational therapy is the mainstay treatment for COPD patients. They should continue their inhalers like Metered Dose Inhaler (MDI), Dry Powder Inhalers (DPI) and nebulisers. For patients who must visit a hospital or have worsening of symptoms it is recommended that an appointment be made beforehand and during hospital visit they must use mask and follow social distancing too. These patients should follow good respiratory hygiene too. E-consultation, online health services and tele consultation are the cornerstone for the management of these patients.

CONCLUSION(S)

Caring for patients with COPD and COVID-19 poses special challenges for healthcare workers. Current clinical practice and evidence on how to treat COVID-19 effectively in patients with COPD is limited. Patients with COPD may show a poor outcome when infected with COVID-19. They should continue their medication and for follow-up they have to use online/offline consultation from their treating physician. Non pharmacological treatments like vaccination, smoking cessation and pulmonary rehabilitation also plays an important role in the management of COPD patients with COVID-19.

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PARTICULARS OF CONTRIBUTORS:

- Senior Resident, Department of Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India.
- Professor and Head, Department of Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India.
- Additional Professor, Department of Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India.
- Senior Resident, Department of Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Surya Kant,
King George's Medical University, Lucknow, Uttar Pradesh, India.
E-mail: skantpulmed@gmail.com

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