

# COPD Management during the COVID-19 pandemic

## INTRODUCTION

The COVID-19 pandemic caused by the SARS-CoV-2 virus started in December 2019 in the city of Wuhan, from where it spreads to over 188 countries in the world. An estimated 22.5 million people are reported to be infected so far with 0.79 million deaths globally. The COVID-19 disease largely affects the respiratory tract causing pneumonia in around 20%–25% cases, some of which further progress to develop severe acute respiratory syndrome. The mortality rates vary from 2% to 15% and are higher among the elderly and those with associated comorbid conditions such as hypertension, ischemic heart disease, diabetes, and chronic obstructive pulmonary disease (COPD).<sup>[1,2]</sup>

In the middle of this ongoing COVID-19 pandemic, there are an estimated 300 million cases of COPD in the community worldwide who are more vulnerable to not only catch the infection but also develop the more severe form of the COVID-19 disease and have an increased likelihood of dying from it.<sup>[3]</sup> There are an estimated 55 million cases of COPD in India, which is already the second leading cause of death and disability-adjusted life years. Physicians in India need to be well prepared to not only manage the COVID-19 pandemic but also safeguard the vulnerable population of COPD.<sup>[4]</sup>

In this manuscript, we discuss 10 important clinical issues related to COPD and COVID-19, the evidence that is currently available so far for each of these and then offers our specific recommendations. We believe that this discussion will offer practicing physicians' adequate knowledge to manage their patients of COPD better in the ongoing COVID-19 pandemic.

## **ARE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AT A HIGHER RISK OF CATCHING THE COVID-19 INFECTION? IF THEY ARE, DO THEY DEVELOP A MORE SEVERE FORM OF COVID-19 DISEASE?**

### **Description of the available evidence**

The SARS-CoV-2 virus that causes the COVID-19 disease uses the angiotensin-converting enzyme receptor-2 to enter inside the cells to cause the infection.<sup>[5]</sup> ACE-2 receptors are expressed on the apical surfaces of the polarized lung epithelial cells of both the upper and lower airways. Their numbers are significantly increased in patients with COPD compared to those who do not have COPD,<sup>[6]</sup> and this has been suggested that this accounts for not only having a greater risk of catching the COVID-19

infection but also for developing the more severe form of the disease.

A single-center, case-series study<sup>[7]</sup> reported that COPD patients were more vulnerable to develop the more severe form of COVID-19 disease than those who do not have COPD. A large case-series of COVID-19 patients from China reported a higher prevalence of COPD among patients with severe COVID-19 presentation with worse outcomes, compared to patients who did not have COPD.<sup>[8]</sup> A couple of meta-analyses have shown that patients with preexisting COPD have greatly aggravated symptoms and a 4–5.9-fold greater risk of developing severe form of COVID-19 compared to patients without COPD.<sup>[9,10]</sup>

The clinical symptomatology of COVID-19 and acute exacerbations of COPD (AECOPD) are difficult to differentiate and may potentially result in delayed or inappropriate medical intervention. Hence, there are chances of increased risk and worse prognosis of COVID-19 in patients with COPD.

### **Summary and recommendations**

Patients with COPD are at a high risk of catching the COVID-19 infection, developing a more severe form of COVID-19 disease, and a greater risk of dying from it. COPD patients should therefore be encouraged to adopt more restrictive measures to minimize potential exposures to COVID-19 and every effort must be made to reduce their contacts with suspected or confirmed cases of COVID-19. Staying at home, proper hand hygiene, and wearing a mask are crucial to reduce the risk of catching the COVID-19 disease. It is important to ensure that COPD is managed well with appropriate pharmacotherapy, vaccination (influenza and pneumococcal), and rehabilitation, and all measures must be undertaken to prevent the development of any acute exacerbation. COPD patients should not be admitted for acute exacerbations in COVID hospitals.

## **IN THIS COVID-19 PANDEMIC, HOW CAN YOU DIAGNOSE NEW CASES OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE ABSENCE OF SPIROMETRY?**

### **Description of the available evidence**

Spirometry is the gold standard diagnostic test for COPD and must be undertaken in all patients to confirm the diagnosis. However, because of the effort required to perform the test, it is an aerosol-generating procedure and therefore comes with a substantially increased risk of transmitting the infection to and from other patients

and the clinic/hospital staff. The GINA 2020 guidelines for asthma have recommended avoidance of spirometry in patients with confirmed/suspected COVID-19<sup>[11]</sup> and also postponement of spirometry within health-care facilities, unless there is an urgent need.

### Summary and recommendation

Spirometry is an aerosol-generating procedure and should be avoided in all patients with either confirmed or suspected COVID-19 and more so in regions where community transmission of COVID-19 has already taken place. Although GOLD has not yet issued any advisory on restrictions for the use of spirometry in patients with COPD for either diagnosis or management, it seems prudent to avoid this test until the pandemic is over.

Taking a good history and conducting a short and quick clinical examination will be necessary to arrive at a diagnosis of COPD. While taking a history from the COPD patient, both the patient and the physician should wear a surgical or a reliable cloth mask. The patient should be encouraged not to speak loudly and certainly not shout. The physician should sanitize his/her hands with 70% alcohol disinfectant before and after every patient and must wear gloves while examining the patient, which should be discarded immediately after the examination is over. Patients should preferably be seated on a steel round chair that can be easily disinfected with 1% sodium hypochlorite. The outpatient clinic should be well ventilated. Wherever possible, air conditioning should be avoided, as it reduces the air exchange ratio. A good history can help in differentiating COPD from other respiratory or cardiovascular causes.

## HOW SHOULD YOU MANAGE A PATIENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE WITH AN ACUTE EXACERBATION IN THIS CURRENT PANDEMIC OF COPVID-19?

### Description of the available evidence

AECOPD are crucial events that occur in the natural course of COPD and respiratory viral infections are an important cause of COPD exacerbations.<sup>[12]</sup> In general, viral infections may facilitate subsequent bacterial infection or increase the number of bacteria already present in the lower airways.<sup>[13]</sup> It is likely that the SARS-CoV-2 virus causes AECOPD.

Breathlessness in patients with COPD observed during an acute exacerbation, apart from microbial infections, could also be because of pulmonary thrombosis, which seems to be common in patients of COVID-19 with severe disease. One observational study showed a cumulative incidence of venous and arterial thrombotic complications of 31% during intensive care unit (ICU) admission of patients with COVID-19 pneumonia, with pulmonary embolism being the most common thrombotic complication.<sup>[14]</sup>

COPD exacerbations are often associated with an increased risk of myocardial infarction, stroke, all-cause mortality, and cardiovascular mortality, especially among those with an associated pneumonia.<sup>[15]</sup>

Oral corticosteroids impair induction of antiviral Type-I interferon responses to a range of respiratory viruses, effects that are likely to also occur in the context of COVID-19.<sup>[16]</sup>

### Recommendations

When a COPD patient develops a new/increased productive cough or breathlessness, it should be evaluated and treated as an acute COPD exacerbation. Presence of pneumonia, pneumothorax, pleural effusion, pulmonary embolism, pulmonary edema, and cardiac arrhythmias should all be ruled out using appropriate investigations. A chest X-ray may prove to be a very valuable tool in this diagnosis. Sometimes, a high-resolution computed tomography (HRCT) gives a lot more information than chest X-ray, and therefore where ever available and necessary, HRCT should be done. Manage the patients as per the hospital protocol and/or GOLD 2020 guidelines.

Start the treatment with short-acting inhaled beta<sub>2</sub>-agonists with or without short-acting anticholinergics. Do not start blanket antibiotic treatment for all patients. If the patient has any signs of super-added infections, pyrexia, X-ray infiltrates, and/or increase in inflammatory markers, antibiotics can be initiated considering the risk versus benefit, although systemic steroids should be used with caution but should certainly not be avoided in the context of an acute COPD exacerbation.

Although antithrombotic drugs are routinely used in the management of severe COVID-19 infection, the evidence supporting its use is weak. In a multicenter, observational study in Italy, treatment with antiplatelets or anticoagulants did not reduce the risk of ARDS or death during hospitalization (clinical impacts of preadmission antithrombotic therapy in hospitalized patients with COVID-19). We need more evidence to support the use of antithrombotic drugs in COVID-19.

Patients with AECOPD and COVID-19 may be at a high risk of cardiovascular events and mortality following the acute phase of the disease. It has been recommended that in this vulnerable period, patients be closely followed with a management plan that pays special attention to the prompt recognition of cardiovascular complications, especially in the 30 days following the resolution of the acute phase.<sup>[17]</sup>

In case of worsening of symptoms, the patient should have a discussion with the health care provider. Telemedicine/teleconsulting platforms can be used to get in touch with the patients.

## ARE THERE ANY PRECAUTIONS THAT NEED TO BE UNDERTAKEN WHILE USING NONINVASIVE VENTILATION OR HIGH-FLOW NASAL OXYGEN DURING CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS?

### Description of the available evidence

The application of noninvasive ventilation (NIV) in patients with COVID-19 in the ICU is controversial. Studies of NIV during the SARS outbreak (2003) are not necessarily applicable today due to improvements in mask design and measures to increase patient tolerance of NIV. In clinical practice, leakage (around the mask) is common and contributes to increased dispersion of droplets. NIV is generally not recommended for patients with viral infections complicated by pneumonia because, although NIV temporarily improves oxygenation and reduces the work of breathing in these patients, it does not necessarily change the natural course of the disease.<sup>[18]</sup> Considering the above factors, clinicians might not use NIV for critically ill patients with ARDS due to COVID-19 until further data from the COVID-19 epidemic are available. However, NIV can be used in patients with “mild” or “moderate” ARDS as a temporary measure under close observation monitoring for any worsening which might require invasive ventilation.

There are insufficient data to indicate whether high-flow nasal oxygen (HFNO) is as safe. Theoretically, because HFNO circuits are “leaky”, they may pose a higher risk compared to NIV (especially if the latter is used with full-face or helmet masks or with double-limbed circuits ± filters over expiratory vents/ports).

In general, in terms of disease transmission, NIV and HFNO may be similar, but the safety signal (more evidence based) is stronger for NIV.

### Recommendations

In general, if invasive mechanical ventilation (IMV) is necessary, its use is preferred over NIV. Clinical need should determine the use of NIV and HFNO. NIV is preferred over HFNO in relation to the risk of disease transmission.

A patient with COPD presenting in Type 2 respiratory failure with their exacerbation should be considered for NIV if indicated as per the current COPD treatment guidelines (even though NIV is not recommended for COVID alone as a bridge to IPPV). There are no grounds for an indiscriminate ban on the use of NIV or HFNO.

NIV should be delivered by a nonvented mask followed by a viral/bacterial filter followed by a circuit with an expiratory port. NIV is preferred over HFNO because of its lower risk of disease transmission and lower consumption of oxygen supplies. If a patient is failing to respond to noninvasive support, early transfer from NIV (or HFNO) to

IMV is advisable to prevent delay in intubation (with the exception of patients with a ceiling of care on noninvasive respiratory support).

Health-care workers looking after patients on NIV should wear full PPE (eye protection, N95 or higher respirators, gloves, and long-sleeved gowns). Patients on NIV should be managed in negative pressure facilities whenever possible. If required, patients on NIV may be managed in side-rooms, with the door closed.

## WHAT IS THE ROLE OF SMOKING CESSATION IN THE CURRENT PANDEMIC OF COVID-19?

### Description of the available evidence

It has been recently reported that the gene expression for ACE2 receptors is higher in smoker samples as compared to never-smokers.<sup>[6]</sup> In a multivariate logistic analysis, the single modifiable host factor associated with progression of COVID-19 pneumonia was current smoking (odds ratio [OR] = 14.3, 95% confidence interval [CI]: 1.6–25.0).<sup>[19]</sup> In a study comparing the severe ( $n = 173$ ) to nonsevere ( $n = 926$ ) COVID-19 cases, the percent of current and former smokers were higher among the severe cases: 17% and 5%, respectively, than among the nonsevere cases (12%, and 1%, respectively).<sup>[20]</sup> More smokers as compared to nonsmokers (26% vs. 12%) were admitted into the ICU, required mechanical ventilation, or died. Middle East respiratory syndrome coronavirus (MERS-CoV) that caused a small coronavirus epidemic in 2012–2015 presented with similar clinical features as the current COVID-19, and reports also indicated an association between smoking status and fatality rate with current smoking also more frequent among cases than among controls (37% vs. 19%, OR = 3.14, 95% CI: 1.10–9.24,  $n = 146$ ).<sup>[21]</sup>

### Recommendations

Smoking is a strong predictor of COVID-19 severity. COPD patients who smoke should be strongly encouraged to stop smoking completely during the entire course of the COVID-19 pandemic. This could involve telephone, video, or e-mail consultation support. The help of a counselor, respiratory therapist of a respiratory specialist nurse, might be sought in this endeavor.

## WHAT IS THE ROLE OF INHALED CORTICOSTEROIDS, ORAL CORTICOSTEROIDS, NEBULIZERS, AND ANTIBIOTICS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE MANAGEMENT DURING THE COVID-19 PANDEMIC?

### Description of the available evidence

While there is some evidence that use of ICS in COPD may increase the overall risk of pneumonia (both viral and bacterial), it has been recommended by the NICE Guidelines (UK) that

this risk alone cannot be a reason to change treatment in those COPD patients who are on regular ICS.<sup>[22]</sup>

Systemic corticosteroids were widely used during the outbreaks of severe acute respiratory syndrome (SARS)-CoV and Middle East respiratory syndrome (MERS)-CoV.<sup>[23,24]</sup> However, current interim guidance from WHO on clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected (released January 28, 2020) advises against the use of corticosteroids unless indicated for other reason.<sup>[25]</sup>

No clinical data exist to indicate that net benefit is derived from corticosteroids in the treatment of respiratory infection due to RSV, influenza, SARS-CoV, or MERS-CoV. The available observational data suggest increased mortality and secondary infection rates in influenza, impaired clearance of SARS-CoV and MERS-CoV, and complications of corticosteroid therapy in survivors.<sup>[26]</sup>

The University of Oxford's RECOVERY trial reported that low-dose dexamethasone reduced mortality only among COVID-19 patients requiring IMV (11.7% absolute reduction) or oxygen supplementation (3.5% absolute reduction).<sup>[27]</sup> However, the effect was only modest and the number needed to treat was large.

#### **Recommendations on use of inhaled corticosteroids in chronic obstructive pulmonary disease**

COPD patients on inhaled corticosteroids (ICS) should not discontinue ICS because of the fear of developing viral or bacterial pneumonias during the COVID pandemic.

Patients on long-term oral corticosteroids should continue to take them at their prescribed dose because stopping them can be more harmful. There is no indication for starting new oral steroids, except low-dose dexamethasone among those put on invasive ventilation or requiring supplemental oxygen.

Patients already prescribed prophylactic antibiotics should continue taking them as prescribed, unless there is a new reason to stop them (for example, side effects or allergic reaction). Avoid routine use of prophylactic antibiotics in COVID-19 infection.

Avoid nebulizers where ever possible. Pressurized metered dose inhaler via a spacer is the preferred route of drug delivery during severe exacerbations, with a mouthpiece or tightly fitting face mask if required. Best practice at all times is that inhalers or spacer devices should not be shared. Keep the inhalers and spacers in a safe place when not in use. Standard hygienic practice should be sufficient.

The quality of management of stable COPD should be upgraded to the highest standards, especially during the COVID-19 pandemic. Apart from keeping them away from potential COVID-19 infected patients, ensure adherence to appropriate pharmacotherapy (inhaled bronchodilators ± steroids), vaccination (influenza and

pneumococcal), pulmonary rehabilitation, and smoking cessation program whenever required.

#### **WHAT SHOULD WE ADVISE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON LONG-TERM OXYGEN THERAPY DURING THE COVID-19 PANDEMIC?**

##### **Recommendations**

In the absence of any specific evidence, patients currently receiving long-term oxygen therapy should continue with the same. The patient should monitor the SpO<sub>2</sub> using a pulse oximeter and maintain the same in the range prescribed by the health-care provider. In case of worsening breathlessness and declining SpO<sub>2</sub>, the patient should be advised to reach out to the health-care provider.

#### **SHOULD A PATIENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE CONTINUE PRACTICING AIRWAY CLEARANCE TECHNIQUES DURING THE COVID-19 PANDEMIC?**

##### **Recommendations**

In the absence of any evidence so far, it would be prudent to advise patients currently practicing airway clearance to continue as they were. However, several precautions need to be taken. The patient should perform airway clearance techniques in a well-ventilated room, away from other family members if possible. Other family members should be advised not to enter the room until enough time has passed for aerosols to clear.

#### **WHAT ADVICE SHOULD WE GIVE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE REQUIRING HOME NONINVASIVE VENTILATION AND CONTINUOUS POSITIVE AIRWAY PRESSURE?**

##### **Description of evidence**

There is no evidence that using continuous positive airway pressure (CPAP) increases the risk of COVID-19 infection and nothing to suggest that CPAP will worsen COVID-19. As of now, there are no data to suggest whether CPAP increases viral spread within a household. Stopping home NIV risks the return of symptoms (lethargy, headache, dyspnea, and confusion), increased patient and family anxiety, and may precipitate life-threatening acute hypercapnia, which is likely to result in hospital admission, patient exposure to COVID-19, and other infections.

##### **Recommendations for chronic obstructive pulmonary disease with obstructive sleep apnea<sup>[28]</sup>**

People with obstructive sleep apnea (OSA) should continue to use their CPAP at home as before. Stopping CPAP during the COVID-19 pandemic is not recommended, especially

for key workers, such as those with safety critical jobs and those with increased workload during the pandemic. If a CPAP user develops symptoms (or has asymptomatic proven COVID-19), then self-isolation and a discussion with their health-care provider regarding stopping the CPAP for about 2 weeks (risks versus benefit) need to be considered.

Sleeping more upright, avoiding alcohol, weight loss, and using a mandibular advancement device if available may help as alternatives to CPAP in reducing OSA a little during the period CPAP is not used. Routine hygiene is adequate for infection control including changing machine filters routinely, cleaning surfaces, cleaning mask, and tubing with hand-hot soapy water (washing up liquid) and washing hands regularly. Masks and machines should not be shared. Patients with decompensated obesity hypoventilation or COPD/OSA overlap should be provided with a nonvented mask, viral filter, and a circuit with an exhalation port, in a side room with a hospital CPAP machine.<sup>[29]</sup>

### Recommendations for chronic obstructive pulmonary disease patients on home noninvasive ventilation

Home NIV patients often have limited mobility or are housebound. Hence, they can be asked to self-isolate. There is therefore a higher risk of a carer to patient transmission. NIV does generate droplets, but using a nonvented mask with a viral filter reduces the spread significantly.<sup>[30]</sup> Patients with domiciliary NIV should bring in their machines if requiring hospitalization.

## WHAT ADVICE SHOULD WE GIVE PATIENTS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON PULMONARY REHABILITATION?

Not much is known about the long-term sequelae of COVID-19, especially in patients with COPD.

### Recommendations

Pulmonary Rehabilitation remains an important component of COPD management. Although we do not know the long-term consequences of COVID-19 on COPD, pulmonary rehabilitation should be continued as it was being practiced before. Encourage patients to undergo on-line or web-based programs and as far as possible avoid hospital visits.

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