

Pulmonary, Critical Care and Sleep Medicine Practice in the Times of COVID-19

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ABSTRACT

On December 31, 2019, WHO informed about the cases of pneumonia of unknown etiology in Wuhan city, China. They found that it was caused by a novel strain of coronavirus (nCoV) which was not identified previously in humans. This COVID-19 pandemic has a tremendous effect on various health care services being provided by the hospitals as most of them were overwhelmed in providing care to a large number of COVID patients. In this review article, we discussed how Pulmonary, critical care and sleep medicine practice was changed during these hard times and we also wrote our opinions on the management of these patients in this COVID-19 pandemic after a thorough search of the literature.

Keywords: COVID-19, pulmonary, sleep, Critical care.

INTRODUCTION

COVID-19 is caused by novel corona virus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and now spreads rapidly across the globe. During this global pandemic of COVID-19, health care services are overwhelmed and the care of other patients is compromised as majority of the health care services are being utilized by the COVID patients. The treating physicians are also overburdened in

this pandemic and they lack time for treating their routine new and follow-up patients in the out-patient department. As on 22 June 2020 there were more than 8 860 331 positive cases in the world with case fatality rates vary widely between countries, from 0.2% in Germany to 7.7% in Italy. India currently is in fourth position in the world with total number of positive cases of more than 3.5 lakhs. ^[1]

The branch of pulmonary and critical care medicine is unique with wide array of diseases and their presentations. The symptoms of acute exacerbation of some chronic lung diseases like bronchial asthma, COPD etc. can mimic the presentation of COVID-19. So, according to the new ICMR guidelines every patient with Severe Acute Respiratory Illness (SARI) in a previously healthy or with preexisting illness should be managed as a potential suspect and must be tested for COVID-19. The safety of the treating physicians is equally important and they should wear proper personal protection equipment (PPE) when attending these patients and contact time should be minimized.

In this review article we briefly discuss about how to manage common pulmonary diseases in the present times of COVID-19 when they come for routine

follow-up, through telemedicine or they got admitted with acute exacerbation of their underlying disease.

Chronic Obstructive Pulmonary Disease (COPD):

Presently literature is not replete management of COPD patients during this COVID pandemic. Certain suggestions from leading societies can be followed for infection prevention and clinical management guidelines:

COPD patients are strongly advised to stop smoking to decrease risk of acute exacerbations and to reduce the risk of poor outcomes if patient is co-infected with COVID-19.

COPD patients who are on regular treatment (either MDI with spacer or DPI) can continue their same treatment during these times, ^[2] and they can be followed through telemedicine OPD's or can take a prior appointment to meet the specialist. Any increase in symptoms like worsening of dyspnea, cough, increase in sputum volume and purulence should be immediately reported to health care facility.

Regarding the use of inhaled corticosteroids in COPD patients, if the patient is taking ICS in some special situation according to GOLD 2020 COPD guidelines, ^[3] (patients with Absolute eosinophil count >300, H/O concomitant asthma and in people at high risk of exacerbations (2 or more moderate exacerbation or history of hospitalization with COPD exacerbation), they should continue ICS and presently there is no scientific evidence to support that ICS should be avoided in patients with COPD during the COVID-19 epidemic.

Routine use of oral steroids is not recommended in stable COPD patients. If the patient is admitted with acute exacerbation he/she should be treated as a potential COVID suspect and nasal and throat swab for SARS-coV-2 must be taken and should be managed as COVID-19 suspect patient till the report turns out to be negative.

If COPD patient is co-infected with COVID-19 and if clinically stable there is no indication for giving systemic steroids. The patient should use his own personal MDI with spacer or DPI and symptomatic treatment (for fever, myalgia, sore throat) to be given. ABG is indicated when room air saturation is less than 92%. Baseline chest radiograph can be performed and these patients can be followed up by ultrasound of the chest.

According to the standard guidelines about the use of systemic corticosteroids in patients with AECOPD, one should be treated with 5 days course and antibiotics are prescribed if only there is evidence of bacterial infection. ^[3] If the patient with AECOPD is found to have COVID-19 co-infection, according to new British Thoracic Society (BTS) guidelines, SABA or SAMA can be given through nebulizer. The rationale behind this is that the droplets are from the machine (liquid bronchodilator drug particles), not the patient. Therefore nebulization is not considered as a 'viral' aerosol generating procedure. ^[4]

A patient of COPD presenting with acute exacerbation and in type 2 respiratory failure should be considered for NIV if there are no contraindications for it as per current COPD treatment guidelines (even though NIV is not recommended for COVID alone as a bridge to IPPV). If there are contraindications he/she should be intubated and put on mechanical ventilation. ^[4]

All routine laboratory investigations including blood and sputum cultures, electrocardiogram, chest radiograph, procalcitonin and other investigations as clinically indicated should be performed.

General management includes deep venous thrombus prophylaxis, nutritional diet; stress ulcer prophylaxis and oxygen saturation should be maintained at 88 to 92%.

After discharge these patients should be followed up in long term to see for any complications.

Bronchial Asthma (BA):

Albeit asthmatics are considered as high risk cases with COVID-19 disease, there is no evidence that asthmatics are at a higher risk for contracting the illness. [5] Having said that once contracted as well, presently there is no evidence for an increased adverse outcome with asthma, however these reports are preliminary in nature and it is judicious to believe that an underlying respiratory illness is likely to complicate the management as with other respiratory viral illnesses. [6]

Patients diagnosed with BA should continue their same treatment as before and can be consulted through telemedicine for their routine follow-up.

The pandemic is notwithstanding, there is ample of evidence equating the efficacy of MDI's and nebulized medication as modes of drug delivery in asthmatics not in exacerbation. [7-9] It must be understood that even if they have been isolated/quarantined as a COVID-19 suspect he/she should continue their routine medications and with their own MDI with spacer or DPI.

Uncontrolled asthma poses a definitive risk of an exacerbation or a hospital visit, [10] which in the present times of isolation could be counterproductive. There is no evidence for a worse outcome or increased risk of contracting COVID-19 with inhaled corticosteroids and hence it is advisable to continue on inhaled corticosteroids as per routine requirement to avoid an exacerbation. As evidence is lacking for the effect of steroids with stray reports suggesting increased virus shedding, there exists an advisory for the patients on systemic steroids (which includes oral) to maintain isolation to avoid infection. [11] However, it goes without saying that patients with controlled asthma on any medication should follow local policy during a lockdown.

In rare cases, patients with severe *asthma* might require long-term treatment with oral corticosteroids (OCS) on top of their inhaled medication(s). This

treatment should be continued in the lowest possible dose in these patients who are at risk of severe attacks/exacerbations. Biologic therapies should be used in severe asthma patients who qualify for them, in order to limit the need for OCS as much as possible. [12]

In BA patients who are admitted with acute exacerbation, COVID sampling should be done and if turned out to be positive, along with all other routine treatments like bronchodilators and oxygen, the use of systemic steroids has a special role in this subgroup of patients. Recent guidance from the WHO has advised against the use of corticosteroids, if COVID-19 is suspected due to concerns that these agents may impair protective innate antiviral immune responses. This may not be appropriate in the unique case of asthma exacerbations, a syndrome associated with augmented type-2 inflammation and a disease feature that is known to directly inhibit antiviral immunity. Corticosteroids, through their suppressive effects on type-2 inflammation, are thus likely to restore impaired antiviral immunity in asthma and, in contrast to non-asthmatic subjects, have beneficial clinical effects in the context of SARS-CoV-2 infection. [13] So, therefore these patients should be given a course of systemic steroids during the period of acute exacerbation. Other treatments specific for COVID-19 should be given according to the local hospital policies. Antibiotics are recommended if there is clinical evidence of bacterial co/super-infection. As there is limited role of NIV in asthma patients with exacerbations, MV should be initiated when indicated depending upon patient clinical status and ABG analysis.

Community Acquired Pneumonia (CAP):

All patients presenting to health care facility with signs and symptoms of CAP should be asked about the contact and recent travel history. Careful recording of upper respiratory symptoms like sore throat, rhinitis, cough and fever should be done. Every patient should be treated like a potential COVID suspect until unless

proved. Apart from all routine investigations procalcitonin, C-reactive protein and nasal and oropharyngeal swab should be sent for COVID. Other specific investigations like BioFire respiratory panel should be sent depending on the clinical condition of the patient. Symptomatic treatment with oral paracetamol and anti-histaminic drugs should be given in haemodynamically stable patients. Antibiotics should be indicated only if there is evidence of bacterial infection.

If patient is clinically stable and COVID negative he can be prescribed antibiotics according to the Indian antibiotic guidelines and they can be triaged based on CURB-65 score. If COVID report came out be positive, he/she should be admitted in the health care facility and treated depending on clinical status (mild/moderate/severe). Usually mild cases require symptomatic treatment and discharged when they were afebrile for 3 days. Moderate and severe cases require admission in high dependency unit or intensive care unit and close monitoring is required. The initial hype given for the use of Hydroxychloroquine (HCQ) in treatment of COVID-19 is now contradicted by many studies due to observation that its administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death. [14] and the Lancet and NEJM also retracted their studies previously published on the use of HCQ in COVID due to its unclear benefits and potential side-effects. So, presently the role of HCQ's for treatment of COVID is a matter of debate. On 1st may 2020, US FDA issued an emergency use authorization for the investigational antiviral drug Remdesivir for the treatment of suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease based on results of ACTT – 1 trail. This drug was shown to shorten recovery in some patients in clinical trials. [15] The RECOVERY TRIAL (Randomised Evaluation of COVID-19 thERapY) is a recent randomised clinical trial to test a range of potential treatments

for COVID-19, including low-dose dexamethasone (6mg once per day for ten days), the interim results have shown that mortality can be reduced by up to one third in hospitalised patients with severe respiratory complications of COVID-19. [16] The use of Tocilizumab, a monoclonal antibody against interleukin-6 (IL-6), emerged as an alternative treatment for COVID-19 patients with a risk of cytokine storms (by monitoring levels of CRP and IL-6) recently based on the results of various small studies done in the present pandemic. [17-20]

Antibiotics are indicated if there is evidence of bacterial infection or for other indications in ICU like ventilator/hospital acquired pneumonia, urinary tract infections, blood stream infections etc.

Rapid sequence intubation should be performed in COVID patients with acute hypoxemic respiratory failure. Minimum number of personnel should be present while performing intubation and proper PPE should be used. Preferably avoid Bag and mask ventilation in COVID patients. Endotracheal tube should be clamped while performing intubation to minimize aerosol generation. Heat and Moisture Exchange (HME) filters should be kept at patient end and at the expiratory limb of the circuit. Closed suctioning should be used. American Heart Association updated CPR guidelines should be used while performing CPR on COVID-19 patients. [21] Ventilator settings (include Fio₂, PEEP, RR, TV, MV, I:E ratio, P peak, P plateau etc.) should be individualized to every patient depending on the clinical parameters and severity of illness. ABG monitoring should be done. Chest condition can be followed-up by serial ultrasound assessments. Anticoagulation protocol should be followed. General ICU care and nutrition requirements should be strictly followed. Presently as data is not sufficient in management of COVID patients every institution/hospital should have their own protocol for management. Awake proning with high flow oxygen therapy can be tried

in some patients in mild to moderate cases depend on the experience of the intensivist. [22] Non invasive ventilation is not indicated in treatment of acute hypoxemic respiratory in COVID-19 patients. Finally all ICU personnel should wear adequate PPE while attending to patients and while performing their duties.

Interstitial Lung Diseases (ILD):

The management of ILD patients needs special consideration in times of COVID-19 as this subgroup of patients has high risk of mortality if they have contracted the disease, due to underlying chronic lung disease. [23,24]

ILD Outpatient clinics – General points: If required these patients can be reviewed by telemedicine, else OPD appointment can be deferred to a later date.

If there is any deterioration in the patient's condition ask about new cough, shortness of breath, fever, muscle aches and headaches. Review travel and contact history.

Sick patients should report to emergency department.

Idiopathic Pulmonary Fibrosis (IPF) patients already on anti-fibrotic drugs:

The anti-fibrotic drugs that are used are pirfenidone and nintedanib.

This group is not thought to be at any greater specific COVID-19 risk due to their treatment. Their risks may be their age, underlying chest disease +/- other co morbidities. No need to alter drugs due to outbreak.

Patients should continue their routine ongoing treatment.

Routine OPD visits should be deferred and LFTs monitoring can be done if symptomatic.

IPF patients already on anti-fibrotic drugs and diagnosed with COVID-19:

If an IPF patient on anti-fibrotic drugs is diagnosed with COVID-19 and is admitted to a hospital, it is not considered harmful to stop the drugs for short periods of time (4-8 weeks).

NIV can be initiated to manage respiratory failure and to decrease the work of breathing.

However, the patients ILD Specialist team must supervise any re-initiation of the drugs in the recovery phase.

Anti-fibrotic drugs can be associated with deranged liver function tests and are generally not advised if creatinine clearance falls below 30mls/min.

ILD patients already on immunosuppression:

The general advice for ILD patients already initiated on immunosuppression is to keep taking them unless they are experiencing any symptoms of infection, or side effects are an issue.

Any patient on an immunosuppressant drug is at an increased risk of infection. It is thus of particular importance that ILD patients on immunosuppression should socially isolate now and may need to do for some time to come and by monitoring of blood counts if necessary.

This group may experience a higher rate of post-viral pneumonia or chance of clinical decline.

At the first signs of deterioration or symptoms of a lower respiratory tract infection this group should seek early medical advice and if appropriate be treated early with broad-spectrum antibiotics. Opinion from an ILD specialist should be taken about when/if to stop these drugs due to co-existing infection or follow the advice already given to them by their clinics.

ILD Patients already on immunosuppression diagnosed with COVID-19:

If an ILD patient on immunosuppressant drug is diagnosed with COVID-19 and admitted to hospital it is advised to stop these drugs and the steroids should be continued.

If the patients are on long-term steroids, dose increment should be considered to reduce the risk of adrenal crisis.

NIV can be given to manage respiratory failure and to decrease work of breathing.

If patient is already on HCQs or sulfasalazine, these drugs can be continued during hospitalization and local institutional antibiotic policy should be followed for treating the admitted patients.

General advice in a patient admitted with Acute Exacerbation (AE) Of ILD:

After ruling-out of infections (including COVID-19) in a patient with acute exacerbation of ILD (e.g. vasculitis, connective tissue disease-ILD), consider intravenous therapy on a case-by-case basis. Discuss risks versus benefits with the patient. Where steroid based regimes fail to control the disease, longer acting drugs such as IV cyclophosphamide may be considered (with some risks).

IV rituximab should be the last resort, due to its very long half-life, at least until pandemic is starting to resolve.

As the exacerbation of interstitial lung disease is very dreadful and associated with high mortality, prophylactic antibiotics, oseltamivir and other supportive treatment should be included in management of hospitalized patients.

Tuberculosis (TB):

In TB endemic countries like India, management of TB is very difficult in these times of pandemic. According to the 2019 world health organization (WHO) report, there were around 10 million cases globally and out of these 27% was contributed by India. [25] In this difficult time, the diagnosis and treatment of tuberculosis is a concern because of limited availability of diagnostic tools and other infrastructure related problems. In periods of lockdown due to interruption of transport and other logistics, it is difficult for the TB patients to get an un-interrupted supply of drugs from their respective Direct observed treatment short-course (DOTS) centers, may be this will reflect in the future with increase in incidence of drug resistant tuberculosis (DRTB) cases. Government of India despite

being under enormous pressure is continuously making efforts to provide uninterrupted supply of anti-tuberculosis drugs.

In these times of COVID-19 pandemic, government may make provisions, that the patients with drug susceptible tuberculosis may get full course of drugs in intensive phase (IP) for 2 months and will return to DOTS center after completion of IP for clinical assessment and for collecting drugs for continuation phase (CP). In between patients can be followed up through telemedicine from respective DOTS center and health-care facility to monitor any side effects.

The management of DR-TB is little bit complicated as some of the multi-drug resistant TB treatment regimen still use injectable drugs in the regimen, so compliance may concern in these times. But as we move towards all oral regimens in MDR-TB cases, compliance may be improved as patient can easily self administer these drugs and can be followed up by telemedicine if there are any side effects.

During follow-up, the sputum evaluation or other genotypic tests like gene-xpert and line probe assay can be done in the nearest facility or can be transported to district tuberculosis unit (DTU).

Care should also be taken for TB patients who are migrant laborers, to provide them with extra drugs to cover the period of transport and should be advised to follow up in DOTS center in their native place and the case should be transferred for further management.

Clinicians treating TB patients co-infected with COVID should know about the drug to drug interactions and potential side effects of some drugs in the regimen which cause QT prolongation leading to fatal cardiac arrhythmias. [26]

Lung Cancer:

We know that having cancer increases the risk of dying of COVID-19,

although not necessarily the risk of getting the virus and we also know that having lung cancer could increase the risk of pulmonary complications from SARS-CoV-2. According to new GLOBACON report of 2018, lung is the most common malignancy (when both sexes are combined) and is associated with highest mortality, treatment should be offered to all eligible patients. [27] The management of lung cancer requires multi-disciplinary discussion team including pulmonologist, radiologist, oncologist and radiation oncologist. From diagnosis to treatment the management of lung cancer has been entirely changed due to new innovations in diagnostic modalities and new targeted therapies. But in this pandemic as many hospitals are overwhelmed with COVID-19 cases, the management of other diseases is being compromised and lung cancer is one of them. Lung cancer is an important one because the patient family members are also of opinion that cancer is associated with poor outcomes as most of them are of primary education level according to some studies [28] and they have little knowledge about new innovations in management. So, it is the duty of the treating physicians to educate the patients and their family members about the new treatment protocols and associated improved survival rate even in advanced cases of some histological variants like adenocarcinoma of lung with driver mutations. [29] Already diagnosed lung cancer patients are followed up through telemedicine and chemotherapy and radiotherapy dates should be given so that they can get their treatment in day-care facilities or the regimen containing drugs, dose and duration should be given to them so that they can get it from nearest health care facility. Necessary laboratory investigations during treatment period to look for side effects and progression can be done from the nearest facility and followed up through telemedicine OPD and appointment can be given to them if necessary.

Early stage lung cancer patients (NSCLC stage I-IIIa) should be admitted and evaluated for surgical options because these are the subgroup of patients where survival can be improved by surgical resection. The un-resectable/metastatic NSCLC patients should be evaluated for driver mutations (EGFR mutations, Alk rearrangement and Ros1 translocations) or for expression of other markers (PD-I or PD-L1) as this group of patients can get oral treatment options and immunotherapy that may improve the overall survival. [28]

Some of the intravenous drugs used in chemotherapy regimen (like etoposide) to oral formulations reduce the hospital stay but they may affect the pharmacodynamic properties of the drug and thus should be carefully considered on patient to patient basis. [30]

Bronchoscopy in the times of COVID-19:

As bronchoscopy is aerosol generating procedure, the indications should be carefully assessed before performing the procedure. For non-malignant indications if possible other means of diagnosis with least invasive ones is preferred first. In case of malignancy the lesion should be assessed on CT scan and if it is peripheral lesion image guided (USG/CT) should be done first as it has very a low chance of aerosol generation.

If bronchoscopy is indicated the patient should have COVID negative (RT-PCR) report, preferably done 48 hours prior to the procedure. Patients should be called and admitted one day before performing the procedure. They should be asked if there are any recent upper respiratory tract symptoms, fever, contact and recent travel history, if any of them are present the procedure can be deferred to a later date (after 28 days). In those patients who are asymptomatic and had RT-PCR report can proceed with the procedure. But the intervention pulmonologist and technicians in the bronchoscopy suite should wear proper Personal protection equipment (PPE) as a negative PCR report does not totally exclude presence of infection. Only limited number of personnel should be present in

the procedure room and the patient should be adequately sedated to minimize coughing. For a patient with confirmed COVID-19 infection bronchoscopy can be deferred for 28 days and he should be reassessed again before performing the procedure. [31]

Obstructive sleep Apnea (OSA):

Sleep medicine is one area that was affected badly in this pandemic, American academy of sleep medicine strongly urges all sleep clinicians to continue postponing and rescheduling in-laboratory administration of Positive Airway Pressure (PAP) therapy and polysomnography (PSG), except in emergencies, until at least April 30, 2020.

Beginning May 1, 2020, the AASM advises sleep clinicians to implement the following strategies, depending on the local level of COVID-19 community spread as reported by state and local health department and the society recommends that in the area where community transmission was substantial and mild to moderate to postpone all sleep studies and in lab titration except in emergency cases.

In the area where the community transmission was normal or minimal the physicians can resume the sleep studies and PAP in lab titration. All patients attending to sleep lab facility should be tested for COVID-19. Only asymptomatic and test report negative patients can be taken for the sleep study and subsequent titration. [32]

All previously diagnosed patients can be followed up through the telemedicine OPD and their compliance can be checked through the soft ware or some application in the mobile phone. Patients should continue the same prescribed treatment like oral appliances and PAP therapy.

General precautions to all the patients:

- Hand hygiene
- Social distancing, use proper face mask
- Stay at home
- Continue supportive treatment like LTOT, NIV etc.
- Report to health care facility in case of any emergency (including new onset flu

symptoms or worsening of pre-existing symptoms).

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