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Editorial

Management of Chronic Respiratory Diseases in the Era of COVID-19

On December 31, 2019 the World Health Organization (WHO) China Country Office was informed of cases of pneumonia of unknown aetiology (unknown cause) detected in Wuhan City, Hubei Province of China. As of January 3, 2020 a total of 44 patients with pneumonia of unknown aetiology were reported to WHO by the National authorities in China. Of the 44 cases reported, 11 were severely ill, while the remaining 33 patients were in stable condition. According to media reports, the concerned market in Wuhan was closed on January 1, 2020 for environmental sanitation and disinfection. The causative agent was later named as severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) which caused the outbreak of novel coronavirus disease (COVID-19).[1,2] The 2019 novel coronavirus (COVID-19) outbreak was declared a public health emergency of international concern on January 30, 2020, by the WHO, which subsequently declared the COVID-19 outbreak a pandemic on March 11, 2020, requiring effective national and global mitigation measures, strong public health response and coordination. Till July 1, 2020, the SARS-CoV-2 pandemic has affected 10,512,383 individuals worldwide and 512,331 people dying from the disease with a a 4.87% case-fatality ratio (CFR). The same figure for India, which is now having the 4th highest number of cases is 585,481 with 17,400 deaths and a CFR of 2.97%.[3]

Non-communicable diseases (NCDs) comprised 71% of global mortality (41 million) of the 57 million deaths which occurred globally. NCD burden is greatest within low- and middle-income countries (LMIC), where 78% of all NCD deaths and 85% of premature deaths were registered. Cardiovascular diseases (CVDs) (31%), cancers (16%), chronic respiratory diseases (CRDs) (7%), and diabetes (3%), these four diseases are largely preventable through public policies that tackle their common risk factors: tobacco use, harmful use of alcohol, unhealthy diets, physical inactivity and air pollution.[4,5] There were 3.2 million deaths due to chronic obstructive pulmonary disease (COPD) and nearly five lakh deaths due to asthma according to the results of the Global Burden of Diseases (GBDs) Study 2017.[6] All-age prevalent cases of CRDs (*i.e.*, individuals with CRDs in 2017) were 545 million, of which about 50% due to COPD and about 50% due to asthma; all-age incident cases of CRDs (new cases of CRDs in 2017) were 62 million, mostly due to asthma (69%) and COPD (29%).[7]

The India Gobal Burden of Disease Study Collaborators showed that COPD and asthma—make the second largest contribution to the total mortality burden of India, at 10.9% (95% CI 10.0–12.0). The crude prevalence rates of these diseases increased by 29.2% (27.9–30.4) for COPD and 8.6% (6.1–11.4) for asthma in the studied period. The study reports higher crude COPD prevalence in the northern states of Jammu and Kashmir, Himachal Pradesh, Uttarakhand, and Haryana, which were a mix of lower-middle, higher-middle, and high ETL (epidemiological transition level); it is defined as the ratio of disability adjusted life years (DALYs) from communicable diseases to those from non-communicable diseases and injuries combined, with a low ratio denoting high ETL and vice versa) groups.[8] The number of cases of COPD in India increased from 28.1 million (27.0-29.2) in 1990 to 55.3 million (53.1-57.6) in 2016, an increase in prevalence from 3.3% (3.1-3.4) to 4.2% (4.0-4.4). The age-standardised COPD prevalence and DALYs rates in 2016 were highest in the less developed low ETL state group. There were 37.9 million (35.7-40.2) cases of asthma in India in 2016, with similar prevalence in the four ETL state groups, but the highest DALYs rate was in the low ETL state group. The highest DALYs rates for both COPD and asthma in 2016 were in the low ETL states of Rajasthan and Uttar Pradesh. The DALYs per case of COPD and asthma were 1.7 and 2.4 times higher in India than the global average in 2016, respectively; most states had higher rates compared with other locations worldwide at similar levels of socio-demographic index. Of the DALYs due to COPD in India in 2016, 53.7% (43.1-65.0) were attributable to air pollution, 25.4% (19.5-31.7) to tobacco use, and 16.5% (14.1-19.2) to occupational risks, making these the leading risk factors for COPD.[9] The contribution of chronic respiratory diseases to the total DALYs in India increased from 4.5% (95% CI 4.0-4.9) in 1990 to 6.4% (5.8-7.0) in 2016. Of the total global DALYs due to CRDs in 2016, 32.0% occurred in India. COPD and asthma were responsible for 75.6% and 20.0% of the CRDs DALYs, respectively, in India in 2016.[9] Besides COPD and asthma,[10] there are other CRDs which include bronchiectasis, post-TB (Tuberculosis) sequele, interstitial lung diseases (ILDs), occupational lung diseases, pulmonary hypertension, and pleural lung diseases, etc that pose significat morbidity and mortality in India.[11-20]

Virus infections are the most common causes of exacerbations in patients with CRDs as these are more vulnerable to respiratory infections. This will result in emergency visits, hospitalisations and deaths. Lower respiratory function, ineffective immunity and treatments that may increase their susceptibility to infection, are possible causes of their higher risk of unfavourable outcomes, once they have a common cold, influenza or other infections.[21-25] These difficult situations are compounded by uncertainty and one is not sure whether the worsening of respiratory symptoms are a result of the underlying disease or as a consequence of the superimposed infection.[24]

Many studies and clinical observations from various countries shows CRDs as the most frequent co-morbidities associated with intensive care unit (ICU) admissions, need for mechanic ventilation and deaths.[24,26-30]

Chronic obstructive pulmonary disease is associated with an increased risk of morbidity and mortality in community-acquired pneumonia (CAP). Alterations in local/systemic inflammatory response, impaired host immunity, microbiome imbalance, persistent mucus production, structural damage, and use of inhaled corticosteroids have been hypothesised to contribute to such risk. With respect to COVID-19, levels of angiotensin converting enzyme-2 (ACE-2), the reported host receptor of the virus responsible of COVID-19, have been observed to be increased in patients with COPD. However, early individual COVID-19 studies have not consistently reported a significantly higher rate of severe disease in COPD patients.[31] Further, there is still controversy and uncertainty regarding the actual magnitude of the risks of unfavourable outcomes and deaths attributable to COVID-19 in patients with CRDs. It is expected by some that CRDs, particularly COPD and asthma would be at increased risk of SARS-CoV-2 infection and more severe presentations of COVID-19. However, it is striking that both diseases appear to be under-represented in the co-morbidities reported for patients with COVID-19, compared with the GBDs estimates of the prevalence of these conditions in the general population; a similar pattern was seen with SARS.[32] It is postulated that this may be due to substantial under diagnosis or poor recognition of CRDs in patients with COVID-19, CRD protects against COVID-19 by some unknown immunological factors, treatment with inhaled corticosteroids alone or in combination with bronchodilators have been shown to suppress coronavirus replication and cytokine production.[32]

Besides both diseases affecting the course of each other (CRD and COVID-19), there can be other non-medical issues like lack of care and availability of hospital beds for patients of CRDs due to lock-down and closure of many hospitals with non-availability of consulting physicians in general OPD, non-availability of hospital beds for indoor care for non-COVID patients as many of the hospital beds are converted into COVID hospitals, ICU beds and oxygen delivery systems being mainly taken over for the care of COVID patients. Acute exacerbation of COPD and asthma could not get proper attention. It is mainly because of above factors and reluctance of patients themselves to attend/consult hospital because of fear of COVID. Many chronic patients will require prescriptions for continuation of their maintenance medications. Patients on rehabilitation programme will also suffer because of closure of hospitals and lockdowns as travel was resticted or banned because of curfew and non-availabilty of transport, although there was always a provision for emsergency or medical travels. Similarly, COPD patients and other CRD patients waiting for lung transplant could not be taken up because of COVID and other management issues.

As some studies have shown that COPD is associated with a significant, over five-fold increased risk of severe COVID-19 infection, patients with a history of COPD should be encouraged to adopt more restrictive measures for minimising potential exposure to SARS-CoV-2 and contact with suspected or confirmed cases of COVID-19. Clinicians should also carefully monitor all COPD patients with suspected infection and, finally, it may be advisable to consider COPD as a variable in future risk stratification models Global Initiative for Chronic Obstructive Lung Disease (GOLD) recognises people with COPD are amongst the worst affected by COVID-19 and GOLD is working with WHO to try to minimise the impact of the infection.[33] It strongly encourages people with COPD to follow the advice of the public health teams to try to minimise the chance of becoming infected and on when and how to seek help if they show symptoms of the infection. GOLD is not aware of any scientific evidence to support that inhaled (or oral) corticosteroids should be avoided in patients with COPD during the COVID-19 epidemic. Therefore, COPD patients should maintain their regular therapy. Oxygen therapy should be provided, if needed, following standard recommendations. As new information becomes available, patients are advised to continue to follow recommendations on management from the authorities.

Global Initiative for Asthma (GINA) recommends that people with asthma should continue all of their inhaled medication, including inhaled corticosteroids, as prescribed by their doctor.[34] In acute asthma attacks patients should take a short course of oral corticosteroids if instructed in their asthma action plan or by their health-care provider, to prevent serious consequences. In rare cases, patients with severe asthma might require long-term treatment with oral corticosteroids on top of their inhaled medication(s). This treatment should be continued in the lowest possible dose in these patients 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 oral corticosteroids as much as possible. Nebulisers should, where possible, be avoided for acute attacks due to the increased risk of disseminating COVID-19 (to other patients and to physicians, nurses and other personnel). The same will be true for nebulisation therapy in COPD cases. Pressurised metered dose inhaler (pMDI) via a spacer is the preferred treatment during severe attacks (spacers must not be shared at home). While a patient is being treated for a severe attack, their maintenance inhaled asthma treatment should be continued (at home and in the hospital). Patients with allergic rhinitis should continue to take their nasal corticosteroids, as prescribed by their clinician. Routine spirometry testing should be suspended to reduce the risk of viral transmission, and if absolutely necessary, adequate infection control measures should be taken.

Patients with CRDs should take appropriate preventive measures as they are at a higher risk of having a more severe infection than others. Most patients with respiratory diseases recover from COVID-19. If symptoms of a viral infection appear and patients have traveled to a high-risk area in the past 40 days, they should self-isolate at home for 14 days. They should maintain their daily care regimens and speak to their health-care providers for any specific queries about their personal health. Family members and care-givers of people with chronic diseases should take appropriate precautions and take extra care to avoid bringing COVID-19 home. They should constantly monitor patients and stock medicines and other necessary supplies that can last for several weeks. Storing extra non-perishable food can help minimise trips to the grocery store. Further, they should stock up on necessary medications and supplies that can last for a few weeks. They shuld avoid crowds and non-essential travel, should stay at home as much as possible. They should also seek prompt medical attention, if they or anyone in their family show symptoms of COVID-19. People who show symptoms of COVID-19 should avoid visiting their family members until the self-isolation period is complete.

The Global Alliance against Chronic Respiratory Diseases (GARD, https://gard-breathefreely.org/) which is a WHO network of national and international organisations, medical and scientific societies, patient organisations, institutions and agencies, recommends the action how to handle CRD and COVID into three perspectives: (1) patient level: interactions with health-care providers; (2) health-care provider level: real-time experience sharing; and (3) community level: environmental impact, air pollution.[35]

Globally, there are a large number of people with under-recognised, under-diagnosed and under-treated CRDs, most of whom have uncontrolled symptoms, on a verge of being compromised by COVID-19. Since the reflections and experiences are still evolving with the pandemic, they do not represent recommendations of any specific organisations or institutes. However, GARD believed that hey may foster deeper thoughts and considerations into how to move forward in relation to the heavy respiratory burden in times of COVID-19.

At the patient level, many with an underlying chronic condition such as asthma and COPD may opt to stay home (even when their symptoms flared up) and "suffer" rather than to seek health care. As shown in the aftermath of SARS, patients not affected by SARS but with a chronic disease presented with a higher than pre-SARS level of severity or worsened disease/symptom control.[1] With availability of digital technologies, face-to-face medical consultation, while should be encouraged, is not the only option, especially in unusual situations, such as during an epidemic or pandemic. With the wide usage of smart phones, patients and health care providers (doctors, nurses, therapists, pharmacists etc.) should be able to use readily available apps (*e.g.*, facetime) to conduct e-consultation and to provide routine and scheduled "virtual visits".[2,6,36] This may help patients reduce their anxiety, depression and loss of ability and strength in disease self-management. All attempts should be made to promote and implement health literacy measures for the general population, with a focus on COVID-19 and CRDs. The public is afraid, anxious and eager for information. Information through social media may be imprecise and misleading Very often this drives one's attention away from the most important measures for prevention, early diagnosis, home isolation and identification of signs of severity requiring medical care. All scientific bodies in the country like the National College of

Chest Physicians (India) (NCCP [I]), Indian Chest Society (ICS), Indian College of Allergy, Asthma and Applied Immunology (ICAAAI), and Association of Physicians of India (API), etc must communicate with the public, stating clearly the key messages, which are usually already advertised by the health authorities. *At the level of the health-care provider,* it must be realised that although a lot has been learnt about COVID-19 during the pandemic, there is still a lot that remains unknown or uncertain. These include the efficacy and effectiveness of various options of therapy, variant phenotypes, morbidity and mortality risks, short- and long-term disease sequelae and length of immunity. Many people are still questioning whether COVID-19 is just a respiratory disease, *i.e.* affects the lungs or it is more than that and is a systemic disease. Many observed patients who recovered from the infection continued to manifest non-respiratory symptoms and morbidities, such as amnesia, hallucinations, seizures, anosmia, dysgeusia, pulmonary embolism/thrombosis, myositis, etc. which indicates the virus may have also attacked the brain and not just the lung.

Early in the epidemic, many rushed into ventilating patients due to acute and severe respiratory failure, and many of these patients did not survive. The wide use of ventilators also created a global shortage of ventilators. With the shortage, health-care providers started to implement other treatment options including use of high dose of steroids, rotating the position of the patients (lying on the stomach *versus* on the back) and breathing exercise (in those who can do it). The use of chatbots, such as WhatsApp, Skype, Facebook Messenger and WeChat allow frontline health-care providers to communicate with each other and share their patient experiences (successes and failures) in real time and consult each other.[37-42] This collegial support within a network of professionals using social media and modern technology has shortened the distance between people, broken the barrier that stands between interactions and brought them together while they could be physically thousands of miles apart.

During these difficult times of fighting the SARS-CoV-2, health-care professionals must be highly valued, rigorously protected and explicitly reassured any health consequences of an incidental COVID-19 will be compensated. The government, the health-care systems and the population and society depend on their service and performance. *At the Community Level* the public has realised that strategies attempting to curtail the spread of COVID-19, like work from home, staying at home, closure of schools and other public places, curtailment of traffic like vehicles, trains and buses, stoppage of commercial flights, and shut down of non-essential services and business, there is a record low level of air pollution in cities all over the world. Ambient levels of nitrogen dioxide (NO_2), one of the main traffic-related pollutants in many cities, have declined significantly.[43] This "short-term" reduction in air pollution is positive news out of the pandemic, however, if this short-term "improvement" will be associated with any significant health benefits, remains to be seen. Nonetheless, it demonstrated that abating air pollution is achievable if everyone at every level (individuals, industries, government) is in it together.

The reduction seen in air pollution levels across the country and globe are only temporary due to lock-down measures of various degrees, such drastic steps of shutting down the economy to be the way to clean the air are not sustainable. To avoid pollution levels bouncing back as the economy turns a corner and the coronavirus crisis passes, there are time tested methods to achieve better air quality without putting people into hardships. To achieve this we should shift from the current highly fossil fuel dependent economy to clean energy based systems has to be adopted. More comprehensive solutions such as transitioning to clean transport and energy sources, we need to ensure that we invest heavily in renewable energy and other clean energy solutions, transform our transportation systems towards more intensive public transportation systems along with making our cities conducive to movement of people rather than just vehicles by building better infrastructure for walking and cycling friendly cities, and strengthen emission standards for polluting industries and enforce full implementation with time bound targets.

The current crisis has shown us that clear skies and breathable air can be achieved very fast if concrete actions towards reducing burning of fossil fuels are taken and we feel that this could be the turning point for India towards securing the right to breathe and life for citizens of the country.

It is possible that during these unusual times of less air pollution and extreme measures to avoid transmission of respiratory viruses in general, there is a clear decline in morbidity and mortality due to respiratory diseases unrelated to COVID-19, particularly those due to acute respiratory infections and/or exacerbations of CRDs. It is fundamental to reinforce surveillance and proceed with early analysis of databases, which may demonstrate how much the population could benefit from a more rigorous control of air pollution and transmission of respiratory viruses in general.

Tuberculosis control has suffered a lot due to lockdown. Hospitals are closed and the RNTCP (NTEP) has suffered a lot. The case notification through the Niksya portal shows a dismal and disastrous result. Till June 8, 2020, only a total of 760,565 cases (25% of the targeted number of 2,999,030 for the year) could be notified over these 5+ months. Public sector could register only 29% and private sector only 19% of their target number. For the months of March onwards, there is a precipitous fall in the number of cases: January - 196,112; February - 211,021; March - 162, 038; April - 75,789; May - 96,601 and June (till 6th) only 13,414 cases were reported. Thus, it is expected that the case notification in this year will have a drastic fall. Because of lock down and many hospitals being closed, no new registration is possible and even patients who are on treatment from the Directly Observed Treatment, short-course (DOTS) center are suffering. Many medical officers are put on COVID duty. If some patient is lucky and he could contact the DOTS center, he is given drugs for about a month or so. Supervisory visits are not possible. Gene-X-pert machines are being used for COVID testing, which are over busy and molecular testing is a big causality. Specimen transport and drug transport also does suffer. Because many hospitals and drug resistant TB (DR-TB) Centres are converted into COVID hospitals, DR-TB patients are not being admitted. It is not yet clear how patients on any form of therapy for DR-TB are getting their drugs. Interruption of treatment even for few days/weeks will affect the result of short-course chemotherapy. Research is also a big causality with issues like patient enrolment and follow-up.

There are a lot of suffering and losses due to COVID-19 and the health-care system, in general, is disturbed and in strain. It has also created a lot of social turmoil and interaction of physician and the patients is at its low. Despite this unprecedented global crisis, health-care professionals are united to combat this deadly and fast-spreading virus, finding strength, compassion, courage and solidarity among peers who are committed to prevent, manage and rehabilitate patients with this life threatening ailment, at all levels. This interpersonal synergy and team efforts were seen in many countries including India. It is motivating and invigorating to see the public in these countries openly applaud and salute the frontline health-care providers every night, expressive a unison voice that– we are in it together! This has been the motto. Besides fighting COVID-19, we need to take care of the other population needing health care to the best of our ability. According to the words of Prime Minister Narendra Modi " It is imperative to focus on both aspects, *'jaan bhi jahan bhi'*, for India's bright future, and a prosperous and healthy India".

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