COVID-19 - An Acute Infective Illness with Long-term Consequences!

Anupam Prakash

The novel coronavirus-2019 (nCOV-2019), cause of COVID-19, has gripped the world like none other in recent times. It is a pandemic of enormous proportions, bound to create a lasting impact on mankind, significant enough to classify the 21st century in to a pre-COVID era, an eventful COVID era, and a yet-to-come and evolving post-COVID era. Like most respiratory viral illnesses, COVID-19 is largely a self-limiting illness with 80-85% patients being asymptomatic or mildly symptomatic. However, the high infectivity of this virus coupled with no previous exposure to it among human beings led to alarming numbers being infected in a matter of days across continents. Even a low overall mortality of 2-3% became a large number in absolute terms, because of the high number of people affected across continents, with consequent overwhelming of health resources and infrastructure, of even the most developed nations.

While managing COVID-19 patients, there have been several typical observations. The clinical picture of severe acute respiratory infection (SARI)- like illness due to COVID-19 was different from the typical acute respiratory distress syndrome (ARDS) encountered in the pre-COVID era. Firstly, the patients were relatively comfortable despite being hypoxic, what is termed as ‘Happy hypoxia’.

Radiologically, there were peripheral lung opacities. Those who were on ventilators, required high flow oxygen and it was difficult to reduce oxygen flow rates, and very high PEEPs became the order of the day. Survival of COVID pneumonia patients requiring ventilatory support is universally poor till date. Some patients continued to have fever and at times high-grade fever even till the 10th day of illness despite not having COVID pneumonia. Patients who had comorbidities specially diabetes, cardiovascular diseases, obesity and elderly individuals were considered to have poor outcomes, but there were elderly patients who walked back home, and there were even young people without comorbidities who succumbed. An autopsy series indicated predominant pattern of lung lesions to be Diffuse Alveolar Damage (DAD) consistent with that seen in ARDS, but an important finding was the presence of platelet-fibrin thrombi in small arteries fitting in a coagulopathy.1

But does COVID-19 have long-term consequences?

Viral illnesses do have long-term complications in one form or the other, like subacute sclerosing panencephalitis (SSPE), post-encephalitic neurological deficits, post-herpetic neuralgia and post-polioymylitis residual paralysis. But what about acute viral respiratory illnesses! Respiratory viruses like the avian influenza A (H7N9) virus infection showed interstitial changes and fibrosis on pulmonary imaging persisting even at 2 years post-discharge, though the ventilation and diffusion dysfunction improved, but the restrictive and obstructive patterns persisted in these patients. Quality of life of these influenza survivors who had ARDS was also poorer than those without ARDS.2 In severe acute respiratory syndrome (SARS, caused by coronavirus), reticular pulmonary opacities were reported to be present at 2 weeks after symptom onset, and persisted in 50% of the patients beyond 4 weeks. A follow-up study showed that maximal recovery of function occurred in the first 2 years, though 4.6% still had interstitial abnormality at 15 years. With MERS long-term data is not available, but radiological abnormalities did persist beyond 4 weeks.

As early as May 2020, reports3 started emanating that lung damage in COVID patients may be associated with long-term impairment. In our clinical practice also we are encountering patients, who are difficult to wean off oxygen or ventilator even after 2 -3 weeks, and many patients in spite of becoming COVID-negative have had to be discharged on domiciliary oxygen. The magnitude of SARS-CoV2 infection is much more enormous compared to earlier coronavirus afflictions, and COVID related pulmonary fibrosis could be a stark reality, and a contributor to significant morbidity and incapacitation in the long-run. The postulated mechanisms for COVID-related lung injury and subsequent fibrosis include- (i) viral antigen triggered cytokine release syndrome, (ii) drug-induced pulmonary toxicity, (iii) high-airway pressure and hyperoxia-induced acute lung injury secondary to mechanical ventilation. The major risk factors for severe COVID-19 are also shared by idiopathic pulmonary fibrosis (IPF), viz. increasing age, male gender, and comorbidities such as diabetes and hypertension.4 Fibrosis occurs more with severe and prolonged disease, and we are well-aware that ARDS is a known risk factor for pulmonary fibrosis.5 Besides, it is evident in clinical practice that those who have pre-morbid lung disease fare poorly if they develop COVID pneumonia. They are likely to have increased tendency to develop pulmonary fibrosis. In India, the pre-morbid lung disease status is also worsened by the higher prevalence of tuberculosis and there has been a relation observed between COVID-19 and tuberculosis, indicating double trouble for the patient.6

Continuing inflammation is supposedly at the core of an acute...
pulmonary insult leading on to progressive fibrosis and a slower recovery. SARS-CoV2 binds to ACE2 receptors in the body, using the spike protein present on its surface. ACE2 receptors are not only present in the lung, but also on the heart, blood vessels, gut, kidneys and the nervous system. Therefore, a similar process of chronic inflammation can continue at all these sites, resulting in late complications of COVID-19.

Apart from COVID lung wherein arterial thrombi are reported,1 stroke (cerebrovascular thrombosis) and myocardial infarctions (coronary thrombosis) have been witnessed in patients post-discharge. Acute cardiac injury is observed in 8-12% patients and could be due to direct viral damage or cytokine-mediated.2 How many of these patients actually develop cardiomyopathy or worsening of atherosclerosis/plaque instability will only be known in times to come. However, arrhythmias have been reported to continue post-discharge as well, and some of our patients have even succumbed during sleep post-discharge from the hospital.

In our clinical experience dealing with COVID-19 patients, we find that like other viral illnesses, post-viral fatigue syndrome is a distinct possibility, and in COVID-patients it can last 3-4 weeks or even longer. Patients are finding it difficult to join back duties and feel fatigued. Also, COVID-19 illness has sort of predisposed to a post-traumatic stress disorder (PTSD), with immense psychological burden due to social isolation, fear of illness/death, disruption of the usual settled daily routine, loss of wages, and fear of insecurity. The gamut of psychosocial problems varies widely from panic attacks, phobias, hallucinations, acute anxiety, mood disorders and depression. Difficulty in concentration and confusion (brain fog) at times have also been observed. Worsening of motor and non-motor symptoms of Parkinson’s Disease has been reported4 and also cases of Guillain Barre syndrome, though the latter may be part of usual occurrence. ACE2 binding by nCoV-2019 can cause angiotensin dysregulation, innate and adaptive immune pathway activation and hypercoagulability resulting in organ injury and AKI. Cross talk between injured lungs, heart and the kidney further propagates AKI,5 and AKI is a well-known risk factor for chronic kidney disease (CKD) in future. The heart, the kidneys and the nervous system are all vital organs in addition to the lungs, and what sequelae will remain in COVID-19 patients will be discernible only in the times to come.

Coronaviruses are credited with contributing to new terminologies in the medical dictionary in the 21st century, beginning with SARS, MERS and now COVID-19. Though lung fibrosis as a sequelae has been witnessed with influenza and earlier coronavirus illnesses (SARS and MERS), but the mammoth numbers afflicted with SARS-CoV-2 (novel Coronavirus) causing a COVID-19 pandemic is bound to contribute to extensive lung fibrosis morbidity, and has the potential to cause atherothrombotic cardiovascular and cerebrovascular sequelae, and possibly CKD.

References