

## Post-COVID sequelae: an emerging problem of pandemic

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**C**OVID-19, a pandemic caused by SARS-CoV-2, initially started from Wuhan, China and gradually spread across the world. Countries across the world are in different stages of COVID-19 with some declaring their states as COVID free while others are going through the peak of the pandemic. As more and more patients continue to recover, physicians across the world will encounter the long term complications of COVID-19. Some of these complications are infectious while others are non-infectious but they continue to cripple the lives of the people who have recovered from COVID-19. Few of these sequelae are discussed here.

### **COVID associated pulmonary Aspergillosis (CAPA):**

Fungal infections have been long known to infect patients with viral infections. H1N1 Influenza virus is already known to make host susceptible for fungal infections especially aspergillus. Invasive aspergillosis has been reported in multiple studies on patients suffering from severe influenza in intensive care unit. SARS-CoV-2 has also shown association with the development invasive and non-invasive fungal infections. A recently published study from Pakistan described the initial relationship of COVID-19 with Aspergillus infestation.<sup>1</sup> In this study, out of 23 ICU patients Aspergillus species were isolated from tracheal aspirates of nine (39.1%) patients, and of these, five patients (21.7%) were diagnosed with CAPA and four (17.4%) had Aspergillus colonisation. Another factor that can further instigate the pulmonary aspergillosis is the use of high dose of steroids which has now been recommended in severe disease. Steroids make COVID patients more susceptible to aspergillus infection and the risk becomes higher if patient has co-morbidities like diabetes mellitus. Moreover, a part of steroids, COVID

patients are also receiving IL-6 inhibitors like tocilizumab which further suppresses the immune system. So the patients receiving both steroids and tocilizumab become more prone of developing CAPA. Physicians should keep this complication in mind when encounter patients with cavities on chest imaging. Bronchoalveolar lavage (BAL) for fungal culture and galactomannan helps in confirmation of diagnosis. Early diagnosis and treatment reduces the morbidity and mortality.

### **Post-COVID pulmonary fibrosis:**

Post-COVID fibrosis is one of the irreversible insults already seen with previous Corona virus infections. Follow up chest radiographic findings in Middle East respiratory syndrome coronavirus (MERS-CoV) showed 33% of the patients developing pulmonary fibrosis and cases of pulmonary fibrosis were also seen in patients recovering from SARS-CoV.<sup>2,3</sup> Hence it is being rightly anticipated that post-COVID fibrosis will be seen sooner or later. Post-COVID fibrosis is a multi-factorial insult. Viral inflammation, aging, co-morbidities, disease severity and mechanical ventilation, all play a role in its pathogenesis. Multiple studies have documented fibrotic changes in lungs of patients suffering from COVID-19. Some of them suffered from severe disease requiring mechanical ventilation while others were spontaneously breathing not requiring mechanical ventilation.<sup>4,5</sup> Hence COVID associated pulmonary fibrosis is one of the non-infectious sequelae of COVID that we are bound to see in patients especially those with severe disease. What will be the pace of its progression and what will be the role of anti-fibrotic agents in its management still remains a dilemma. Further prospective trials are required to document its incidence and the way forward.

### Thromboembolism:

There are multiple reports on the increasing incidence of thrombotic complications in patients with COVID-19. Multiple factors are involved in the development of thrombosis which includes inflammation causing release of clotting substances like fibrinogen. The pathogenesis encircles around the Virchow's triad which includes altered blood flow, hypercoagulability of blood and vascular damage. The immune complex vasculitis along with sepsis induced coagulopathy leads to vessel wall abnormality.<sup>6</sup> Reactionary angiogenesis and microcirculation, both lead to turbulent flow.<sup>7</sup> The inhibition of clot lysing mechanism and loss of protective endothelium with its glycocalyx layer leads to hypercoagulable state. All these postulated mechanisms lead to thrombotic phenomena resulting in deep vein thrombosis and pulmonary embolism which is being readily reported in literature.<sup>8</sup> Hence one should be aware of the high possibilities of such complications since this can be fatal and early intervention can make a difference.

### Neurological and neuropsychiatric complications:

Neurological complications in COVID include cerebrovascular event, altered mental status and encephalopathy. Rare instances of seizure like activity, cerebral venous sinus thrombosis and isolated single nerve palsy have also been reported.<sup>9</sup> Multiple factors including endothelial damage, hypoxia, immune reaction, disseminated intravascular coagulation, sepsis, inflammation and septic shock are involved in its pathogenesis.<sup>10</sup>

Neuropsychiatric complications are one of the most underrated and underestimated sequela of COVID-19. It can be because of a direct viral involvement of CNS or because of the adverse psychosocial affects including quarantine, self-isolation and life style modification. Increased suicidal ideation, behavioral disorders, post-traumatic stress disorder, anxiety, headache and sleep disorders are few of the major neuropsychiatric manifestations.<sup>11</sup> Post-traumatic stress symptoms have already been reported in 7% of patients in China.<sup>12</sup> Long term consequences of these complications are still unknown. But as we recover from this pandemic, we are bound to see a surge in such complications. However, the dilemma with neuropsychiatric complications is, that it is always under diagnosed and underrated. Hence physicians need to be on their toes to diagnose such issues so that early management can be facilitated and grave consequences can be prevented.

### Summary:

COVID-19 has taken the world by surprise. It has not only affected the patients of COVID-19 but also those who are not affected by the disease. As more and more patients recover, we are stepping into an era where post-COVID sequelae will predominate and optimal management remains unclear. As physicians one should be aware of all the spectrum of sequelae so that proper diagnosis and timely management can be facilitated.

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