

Editorial

COVID-19 Crisis: Pulmonary and Extra-Pulmonary Complications would Last for Long Time in Foreseeable Future

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COVID-19 is currently one of the greatest problems the world is facing. A viral disease by nature, it emerged in city of China named Wuhan. Within few months it turned to be a global health emergency. It is an acute respiratory infection whose impact on world is somewhat similar to that of Spanish flu of 1918.¹ To date, this infection has killed approximately 600,000 people in 216 countries and the number is rising.² This virus affects multiple organs with varying degree of severity including respiratory, gastrointestinal, neurological, cardiovascular and hematological systems. This article will provide insight about the multiple organ complications of COVID-19 and the prognosis with different organ involvement.

COVID-19 is enveloped RNA virus with spike glycoproteins. These spikes facilitate the entry of virus inside the target cells via ACE2 receptor. This receptor expression is not variable amongst people and it is the immune system which determines the severity and spectrum of disease.³ However, there is upregulation of ACE2 receptors in smokers making them vulnerable to get a more severe disease than nonsmokers.⁴

Lungs are one of the most frequently involved organ in COVID-19 infection. Symptomatic patients have much more lung involvement compared to asymptomatic ones. A study conducted on Diamond cruise ship showed that 79% of symptomatic and 54% of asymptomatic patients had abnormal lung findings on CT scans.⁵ The clinical presentations in case of pulmonary involvement are highly variable. They range from milder signs and symptoms of common flu, cough, fatigue, fever to more severe signs of massive pneumonia. Acute respiratory distress syndrome, the most sinister complication, can occur if there is severe lung attack.⁶ Imaging

studies show that ground glass appearance occurs on X-ray which may be bilateral and involve multiple lung lobes. Ground glass appears hazy on radiology with intact bronchial and vascular markings. This appearance is followed by consolidation in lungs if disease progresses to pneumonia. Other less common findings include: septal thickening, bronchiectasis and pleural thickening at advanced stages of disease. In very severe cases pneumothorax and pleural effusion have been seen but they are uncommon.

The incidence of thrombotic complications is high in patients with severe disease. Mortality due to these complications is very high. Multiple factors could lead to these complications like immobilization, inflammation and hypoxia. A study has shown that 31 percent of patients in ICU due to COVID-19 developed thrombotic complication which is very high percentage by any standards. Another study done on Intensive Care Units of three Dutch hospitals has again shown that cumulative incidence of thromboembolic events was 49 percent despite the fact that all of them were receiving prophylactic treatment with thrombolytic drugs.⁶ Italy is one of the countries which were badly affected by COVID-19. Similarly, cumulative rate of 21 percent thromboembolic events had been recorded and half of them were developed within one day of hospitalization.⁷ It is important to prevent the thrombotic events which include arterial thrombosis, venous thrombosis, ischemic stroke, pulmonary embolism, myocardial infarction and, in severe case, disseminated intravascular coagulopathy. Both morbidity and mortality increase with their development and are associated with poor prognosis. The hospital stay is also prolonged which burdens the health system increasing the cost of impact of this disease. Other viral diseases are also known to

increase the coagulopathy. Von Willebrand activity is increased in patients and lupus anticoagulant also becomes positive in them. Multiple studies have suggested that the anticoagulation dose should be increased to counter these complications. D-dimers are elevated as well, therefore, they should be regularly monitored in moderate to severe pneumonia. It has been observed that as the acute respiratory distress syndrome progresses, D dimers become more elevated as well. Prothrombin time, activated partial prothrombin time and other biomarkers for inflammation like C reactive protein, erythrocyte sedimentation rate and interleukin-6 are also elevated.

COVID-19, like other viruses, can cause myocarditis as well. There are a number of case reports which have shown development of cardiac arrest due to myocarditis. Autopsy findings have confirmed it by demonstrating mononuclear infiltration in the cardiac muscles. Development of fulminant myocarditis leading to death has been reported. Electrocardiogram has also showed abnormal findings. Troponin I and other cardiac markers were raised in these patients.

Kidney is another organ which has not been spared by novel coronavirus. The incidence of acute kidney injury in studies varies from 0.5 to 7 percent and the percentage increases in patients admitted in intensive care units for treatment of COVID-19. Up to 23 percent patients in intensive care units developed kidney injury. Early monitoring of renal functions tests are vital for monitoring. Serum creatinine and blood urea nitrogen are raised. Some patients present with hematuria and proteinuria. As expected, the prognosis of patients is deteriorated if kidney injury occurs. A meta-analysis done to find out survival in patients developing kidney injury has calculated hazard ratio of 9.81.⁸ Postmortem findings have also demonstrated evidence of renal injury. Autopsy findings include diffuse injury to proximal tubules with tubular necrosis and aggregation of erythrocytes and lymphocytes macrophage complexes in the interstitium.

Some patients with COVID 19 develop gastrointestinal symptoms. Viral shedding in feces has been reported as well. Gastrointestinal symptoms include decrease or loss of appetite, nausea, vomiting, diarrhea and abdominal pain. In a study in Hong Kong, 17 percent patients experienced gastrointestinal symptoms. Stool RNA testing of virus demonstrated that 48.1 percent of them had virus in feces. This fecal shedding continues for few days even after respiratory symptoms have settled.

The most commonly experienced symptom is diarrhea in adults whereas children experienced vomiting in majority of cases. There is increase in duration of disease due to gastrointestinal symptoms but no increase in mortality has been recorded. There are few case reports of upper gastrointestinal bleed which might be due to COVID related coagulopathy.

Liver, the largest organ in the body, has been affected by novel coronavirus. Different studies suggest that liver abnormalities between 2 to 11 percent.⁹ Alanine aspartate and amino transferase levels rise during infection period. Multiple factors could be responsible for these hepatic findings including drug toxicity, cytokine response, immune mediated injury and hypoxic injury occurring in cases of severe pneumonia. The outcome of patients does not get worse with hepatic involvement and raised enzyme levels. However, there are exceptions in those who have preexisting liver disease.

The nervous system involvement requires more studies for establishing facts and figures. Neurological symptoms like headache, unstable gait and altered consciousness have been reported. A few case reports of patients developing encephalopathy as a result of COVID infection are on record as well. Cerebral hemorrhage and infarcts may occur due to coagulopathy of COVID, increased prothrombin time and ACE 2 receptor signaling which result in decreased blood pressure.

COVID-19, as already discussed, is capable of involving multiple organs. The morbidity is increased in multiple organ involvement that leads to multi organ failure. Hyper inflammatory response of body and ACE 2 enzyme causes multiple organs involvement. Acute respiratory syndrome sometimes progresses to multi organ failure. Multidisciplinary approach is essential for these patients in tertiary care hospitals.

Having discussed the various devastating effects of COVID-19 on different vital organs of the human body, it is evident that COVID-19, though primarily a respiratory tract illness, is capable of manifesting its symptoms in various other vital organs too. It is, therefore, essential that all cases of COVID-19 should be viewed from a multidisciplinary approach. Holistic lab examinations, continuous monitoring and comprehensive clinical care are absolutely essential for patients who exhibit severe symptoms. According to public health professionals, though the spread of the virus in Pakistan is on a downward trajectory as portrayed by the official figures, it is

important not to declare victory too early and to keep practicing precautions.

References

1. Baker SR, Bloom N, Davis SJ, Kost KJ, Sammon MC, Viratyosin T. The unprecedented stock market impact of COVID-19. National Bureau of Economic Research; 2020 Apr
2. <https://covid19.who.int/>
3. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19). In Statpearls [internet] 2020 Mar 8. StatPearls Publishing.
4. Cai G, Bossé Y, Xiao F, Kheradmand F, Amos CI. Tobacco smoking increases the lung gene expression of ACE2, the receptor of SARS-CoV-2. American journal of respiratory and critical care medicine. 2020 Apr 24(ja).
5. Inui S, Fujikawa A, Jitsu M, Kunishima N, Watanabe S, Suzuki Y, Umeda S, Uwabe Y. Chest CT findings in cases from the cruise ship "Diamond Princess" with coronavirus disease 2019 (COVID-19). Radiology: Cardiothoracic Imaging. 2020 Mar 17;2(2):e200110.
6. Klok FA, Kruip MJ, Van Der Meer NJ, Arbous MS, Gommers DA, Kant KM, Kaptein FH, van Paassen J, Stals MA, Huisman MV, Endeman H. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis. Thrombosis research. 2020 Apr 30.
7. Lodigiani C, Iapichino G, Carenzo L, Cecconi M, Ferrazzi P, Sebastian T, Kucher N, Studt JD, Sacco C, Alexia B, Sandri MT. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. Thrombosis research. 2020 Apr 23.
8. Ali H, Daoud A, Mohamed MM, Salim SA, Yessayan L, Baharani J, Murtaza A, Rao V, Soliman KM. Survival rate in acute kidney injury superimposed COVID-19 patients: a systematic review and meta-analysis. Renal Failure. 2020 Jan 1;42(1):393-7.
9. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. The lancet Gastroenterology & hepatology. 2020 May 1;5(5):428-30.