The Chinese authorities reported a cluster of unexplained pneumonia in December 2019, with further confirmation on 7th January 2020 to be caused by the novel corona virus, renamed Severe Acute Respiratory Distress Syndrome Corona Virus type 2 (SARS-CoV2) in due course. The World Health Organization (WHO) termed the resulting disease corona virus disease-2019 (COVID-19), and declared it to be a pandemic on 12th March 2020. By the time of writing these lines, with 1.3 million diagnoses and 75,000 lives claimed, most of the healthcare systems around the world are struggling to cope with the exponential rise in demand related to this illness; daily life has come to a crippling halt in several countries with governments struggling to curtail its spread by introducing social distancing measures, lockdowns, and curfews. With the emerging data from these countries, understanding of the disease is evolving, new dimensions added day by day. Tang et al. identified two different types of Sars-CoV-2, type L (70% of the strains) and type S (30%). Predominantly, the early cases in Wuhan, were caused by the L type, with the S type becoming more prevalent subsequently, and outside Wuhan. Although the early reports suggested higher mortality associated with L-type, further data from other countries have not been conclusive. Huang et al. described the chief symptoms at onset of illness as fever (98%), cough (76%), and myalgia or fatigue (44%); less common symptoms included sputum production (28%), headache (8%), hemoptysis (5%), and diarrhea (3%). 55% of the patients developed dyspnea; 63% had lymphopenia. All the patients had pneumonia with abnormal findings on chest CT. Complications included acute respiratory distress syndrome (29%), RNAemia (15%), acute cardiac injury (12%) and secondary infection (10%). 32% patients were admitted to an ICU; 15% died. Similar incidences were confirmed in other studies reports as well. The severity of disease in confirmed cases ranged from mild to critical. Mild disease was reported in 81% cases (no or mild pneumonia), Severe 14 % (e.g. with dyspnea, hypoxia, or >
50% lung involvement on imaging within 24 to 48 h), and Critical in 5% (e.g., with respiratory failure, shock, or multi-organ dysfunction.

Zhou, et al.\textsuperscript{5} identified laboratory features associated with adverse outcomes, including lymphopenia, and raised liver enzymes, lactate dehydrogenase (LDH), inflammatory markers (e.g., C-reactive protein [CRP], ferritin), D-dimer (> 1 mcg/mL), prothrombin time (PT), troponin, and creatine phosphokinase (CPK). This points to an excessive inflammatory response, associated with critical and fatal illnesses.\textsuperscript{6}

In addition to acute respiratory distress syndrome (ARDS) in those who are critically ill, the pattern of other systems involvement has been baffling the intensivists, as being reported from several centers across the globe. The progression from dyspnea to ARDS is rapid, there is severe hypoxemia often associated with near normal respiratory system compliance, and response to conventional ARDS therapy is atypical.\textsuperscript{7} The association with cardiomyopathy, arrhythmias, acute cardiac injury, and shock, is unprecedented.\textsuperscript{3,8,9} There are conflicting reports about the extent and mechanism of acute kidney injury.\textsuperscript{10,11} There mechanism of acute liver injury in unclear as well.\textsuperscript{12} There are reports of underlying thromboembolic disease emerging from post-mortem studies.\textsuperscript{14,15}

Wenzhong, et al.\textsuperscript{16} have conducted an interesting study which could provide the missing link in the understanding of the pathogenesis of COVID-19. Through conserved domain analysis, homology modelling, and molecular docking, they compared the biological roles of certain proteins of the novel coronavirus. Their results showed that these could bind to the porphyrin, as well as coordinate attack on the 1-beta chain of hemoglobin to dissociate iron and form the porphyrin. The attack would result in a drop in hemoglobin level available to carry oxygen and carbon dioxide. The lung cells would have extremely intense poisoning and inflammatory response due to the inability to exchange carbon dioxide and oxygen frequently, which eventually would result in ground-glass appearance on the lung images. The mechanism would also interfere with the normal hem anabolic pathway, and result in human disease.

According to the validation analysis of these findings, chloroquine could prevent these proteins from attacking the hem to form the porphyrin, and inhibit their binding to porphyrins to a certain extent, effectively relieving the symptoms of respiratory distress. Favipiravir could inhibit some of these proteins from binding to porphyrin, thus preventing the virus from entering host cells, and catching free porphyrins. Because the novel coronavirus is dependent on porphyrins, it may originate from an ancient virus.

Going by this model, excessive inflammatory response leading to the hypoxia despite good lung compliance, thromboembolism involving multiple organs including heart, kidneys, and liver, could be explained. Focus of treatment would shift towards maintaining the oxygen carrying capacity of the blood, potentially with blood transfusions and super-oxygenation, potentially including hyperbaric oxygen therapy. This also has a potential to inform further research in this direction.

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AM: Concept, literature search, manuscript writing
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REFERENCES


