

Cytokine Storm Syndrome, a potential cause of death in COVID-19 patients

Letter to Editor

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Sir,
SARS-Cov-2 has infected more than three million people worldwide.[1] Its mortality rate of 3.4% is driven by lower respiratory tract infections such as pneumonia, septic shock, multiorgan failure, and acute respiratory distress syndrome (ARDS), the latter being the most prevalent.[2] With constantly evolving research regarding its pathophysiology, possible treatment regimens, and trials for potential vaccines in progress, the field of medicine is subjected to new data concerning the current global pandemic.

Cytokine storm syndrome (CSS) consists of uncontrolled systemic inflammation, vascular instability, multi-organ failure, and death.[3] Despite usually occurring in a younger population, CSS affects all age groups in COVID-19.[4] Patients with severe COVID-19 may present with CSS and develop secondary hemophagocytic lymphohistiocytosis (sHLH), which causes acute respiratory distress syndrome (ARDS).[5] A study was conducted in Wuhan, China on 41 COVID-19 patients with a median age of 49 years. All critically ill patients admitted to the intensive care unit (n=14) including those who died, recorded high levels of cytokines in their plasma, suggestive of CSS.[4] CSS illustrates elevated levels of pro-inflammatory cytokines including interleukin IL-6, IL-8, tumor necrosis factor- α , and granulocyte-macrophage colony-stimulating factor (GM-CSF). A similar cytokine surge was also observed in previous SARS-CoV and MERS-CoV epidemics.[6] CSS manifests an increase in biomarkers including erythematous sedimentation rate (ESR), serum ferritin, liver enzymes, D-dimers, C-reactive protein (CRP), and lactate dehydrogenase (LDH) levels, which serve as a basis for its diagnosis. Lymphocytopenia with reduced NK cells and T cells accompanied with splenic atrophy has also been reported in severe COVID-19. Proportionally increased cytokine levels with COVID-19 severity sheds light through a different perspective on the management and treatment of the disease.[7]

Moreover, cytokine surge is mediated by

catecholamines using the alpha-1 adrenergic receptor (α 1-AR) pathway which can be blocked using α 1-AR antagonists (e.g. prazosin), thus illustrating its potential use as a prophylactic inhibitor for COVID-19. In a retrospective analysis of 13,125 male (age 45-64) ARDS patients where five percent of them (n=655) previously used α 1-AR antagonists, results showed that the latter had a lesser ratio of needing mechanical ventilation with a 36% lower incidence of death compared to non-users.[6] Limitations to these therapies insist on the need for increased clinical trials which can be used to evaluate their effectiveness in the prevention of CSS in COVID-19 patients. We believe that critically ill patients of COVID-19 should be tested for hyper-inflammation using laboratory trends and HScore (used to diagnose CSS) to distinguish the subgroup of patients for whom immunosuppressive drug therapy could help improve mortality.[8]



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CONFLICT OF INTEREST

The author declared no conflict of interest

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