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# Inflammatory Response to SARS-CoV-2 Infection: Potential Immune-Modulatory and Therapeutic Strategies

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## Short Communication

Corona virus (*SARS-CoV-2*) uses angiotensin converting enzyme 2 (ACE2) present on the host cell to gain entry into the epithelial cell. ACE2 are present in the cell membranes of human respiratory and gastrointestinal epithelial cells. Lungs bear the greatest pathological burden of the viral infection compared to other organs. The major cause of COVID-19 mortality is the acute respiratory distress syndrome and respiratory failure. The histological features in the susceptible cases showed diffuse alveolar damage, thrombosis, and the presence of the inflammatory infiltrates including macrophages, lymphocytes, and neutrophils. Host immune response to the viral infection plays a major role in the inflammatory pathogenesis. The main characteristic feature of the severely infected patients is the lymphopenia and markers of the T-cell exhaustion. Presence of the inadequate levels of interferon cannot exacerbate virus and thus prolong the inflammatory response leading to inflammation induced microvascular thrombi. Following viral infection there is upregulation of the pro-inflammatory and antiviral pathways. Apoptosis leading to the loss of the type II pneumocytes is detrimental as they generate surfactant, reabsorb fluid from the surrounding airspace and function as the progenitor for the repair of the epithelial cell damage. Endothelial dysfunction or damage is common across the severely infected cases. However, the viral infection of the macrophages and dendritic cells is abortive [1].

The vascular hyperpermeability, multiorgan failure is caused by high cytokine concentrations due to overproduction of pro-inflammatory cytokines (TNF, IL-6 and IL-1β). Therefore, anti-cytokine therapies or immunomodulators for pathogen clearance is being regarded as potential strategies. Recently, two different anti-IL-1 cytokines have been described (IL-37 and IL-1Ra) which block IL-1 and these can form potential therapeutic strategy [2].

Vitamin D plays an important role in the multiple pathways involved in the host-immune response to the viral infections. The dietary and skin derived vitamin D is ultimately converted into the hydroxylated active form. The enzymatic system of the immune and non-immune cells has potential to generate or inactivate the vitamin D. Vitamin D binds to the vitamin D receptor and generates antiviral peptide called as LL-37. One of the important functions of the vitamin D is to regulate the inflammatory response and suppress the excessive. It was observed that patients severely affected by COVID-19 have insufficient vitamin D levels. One of the recent studies has confirmed that initial supplementation of the vitamin D reduced the mortality associated with COVID-19 in the hospitals. Therefore, vitamin D can be considered as the prophylactic or therapeutic adjunct in the treatment of COVID-19. Vitamin D exerts anti-inflammatory and antithrombotic effects and can be effective against immune thrombosis [3].

One of the recent studies have emphasized that the infection of *SARS-CoV-2* progresses in three stages. In the first stage is the asymptomatic viral incubation stage. The second one is the symptomatic but non-severe presence and replication of the virus and the third one is characterized by high viral load with acute respiratory infection. The study demarcated the viral infection into two phases one is the immune based defense and protection phase and the next one is the inflammation derived epithelial and endothelial dysfunction. Vitamin B3 is known to provide protection to the lungs and is suggested for use when coughing starts and intra tracheal hyaluronidase was suggested to inhibit HAS2 [4].

It was proposed that COVID-19 induced pathogenesis can be attenuated by melatonin use. Melatonin is a bioactive component is known for anti-inflammatory and anti-oxidant properties and protects against the viral acute respiratory distress syndrome. Melatonin reduces the vessel permeability and improves the sleep quality and has high physiological safety. Melatonin has been suggested as an adjuvant in treating COVID-19 induced pneumonia [5].

Controlling the inflammatory response is one of the essential strategies for viral elimination. This will block the immune pathogenesis and facilitates elimination of the viral replication. Thrombocytopenia is ubiquitously present across viral infections. The platelets can potentially worsen viral infection. Therefore inactivation of the platelets is considered as one of the therapeutic strategies and for this studies aimed at elucidating direct interaction between the platelets and virus is needed [6].

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