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BIOMARKERS OF COVID-19: A BRIEF REVIEW

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ABSTRACT

This article tries to understand the factors responsible for the symptoms of COVID -19 from a genome and more so proteins perspective and their respective signs. As of September 2020, the world is still widely affected due to the global coronavirus pandemic. The article tries to explore various dimensions of COVID 19, be it the proteins like cytokines or its correlation with hypoxia. It is an effort to collect and present the biomarkers currently being studied at various laboratories across the globe in an easy to comprehend manner and its scope for future studies.

KEYWORDS: COVID-19,

The COVID-19 pandemic has affected around 29 million as of September 2020. A few biomarkers have been studied in various studies conducted across the world. Sources like PubMed, Google Scholar, and PubMed have been used to compile all the information. C Reactive Protein is a plasma protein released by the liver and induced by IL-6 and other inflammatory mediators. Computer Tomography (CT) can identify lesions due to COVID-19. Cytokine release syndrome (CRS) is an exaggerated immune response involving an overwhelming release of proinflammatory mediators. This mechanism underlies several pathological processes, including acute respiratory distress syndrome (ARDS). IL-6 is produced by macrophages and rises sharply during COVID -19. White blood cells (WBCs), known as leucocytes, are a component of blood generated from bone marrow and lymphoid tissue. They are divided into two major groups, granulocytes, and agranulocytes. Within the granulocyte group are eosinophils, basophils, and neutrophils (NC), whereas lymphocytes (LC) and monocytes are present in agranulocytes. A descriptive study in China reported depleted LC levels in the majority of COVID-19 patients. In glucose metabolism, the enzyme LDH converts pyruvate to lactate. LDH secretion is triggered by necrosis of the cell membrane, hinting to viral infection or lung damage, such as pneumonia induced by SARS-CoV-2. A multi-center study involving 1099 patients reported supporting evidence correlating the extent of tissue damage and inflammation with increasing levels of LDH. D-dimer originates from the lysis of cross-linked fibrin with rising levels indicating the activation of coagulation and fibrinolysis. Early studies have associated COVID-19 with hemostatic abnormalities with one study observing elevated levels of D-dimer, the measure of coagulation, in non-survivors compared to survivors. Chronic Kidney Diseases due to COVID-19 have been observed in various studies. In COVID-19 patients, numerous cytokines and inflammation parameters are significantly increased. In particular, there are increments in the values of IL-6 and vascular endothelial growth factor (VEGF) (Huang *et al*., 2020). "Cytokine storm" indicates a very high production of cytokines enabling the inflammation mechanisms. This condition has been discovered in patients affected by ARDS, characterized by pro-coagulant state and spread intravascular coagulation and deep venous thrombosis and consequent embolism, thrombocytopenia, and critical limb ischemia (Zhang W. *et al*., 2020). The upsurge of cytokines has been described in several pathophysiological conditions, including infectious diseases, rheumatic diseases, vascular disease, and tumor immunotherapy (Irace *et al*., 2004; Andreozzi *et al*., 2007; Zhang *et al*., 2020). Furthermore, the CS has been described in previous coronavirus pneumonia, such as severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS), leading to acute lung injury, acute respiratory distress syndrome (ARDS) (National Heart Lung Blood Institute Working Group Report, 2010; Dashti-Khavidaki and Khalili, 2020; Zhang *et al*., 2020) and death (Channappanavar and Perlman, 2017; Chousterman *et al*., 2017). However, in severe COVID-19 patients, Huang *et al*. reported that the cytokines were higher than in SARS and MERS patients (Conti *et al*., 2020; Huang *et al*., 2020); in specific, IL-6 levels were the highest in severely ill patients affected by COVID-19 (Chen *et al*., 2020; Ruan *et al*., 2020; Wu *et al*., 2020; Zhang *et al*., 2020; Zhou *et al*., 2020).

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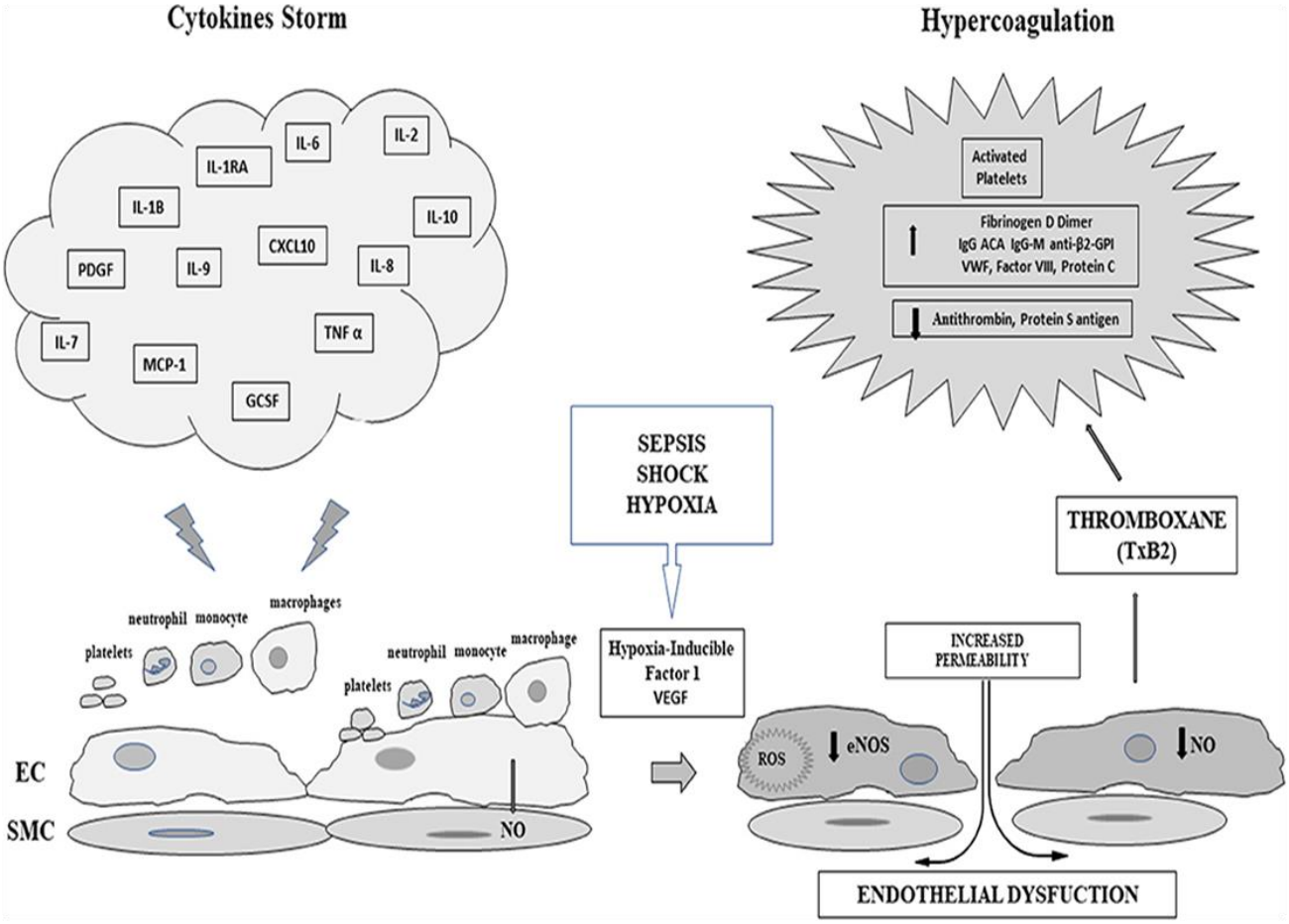
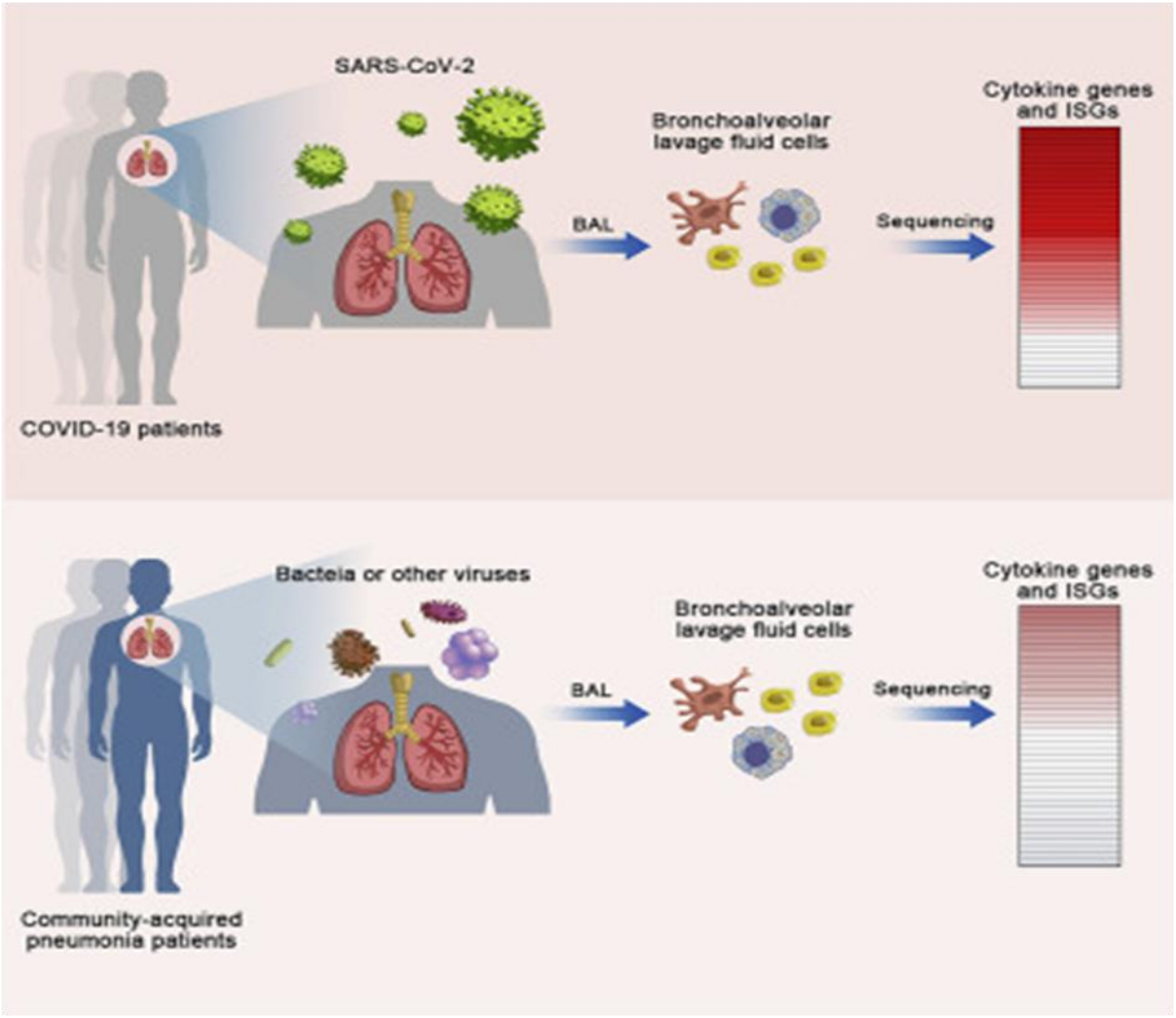
Patients with spleen atrophy, hilar lymph nodes necrosis, focal hemorrhage in the kidney show increased activity of ACE 2 receptor. Binding of SARS-CoV-2 to ACE 2 leads to its down-regulation as the virus uses the ACE 2 receptor for internalization and consequent cell damage/death. Because ACE 2 participates to the feed-back regulation of the renin-angiotensin system by counteracting ACE 1 (Chamsi-Pasha *et al*., 2014; Geng *et al*., 2020), surplus ACE 1-dependent angiotensin II production leads to noxious vasoconstrictive, proinflammatory, and pro-oxidative effects on the patient's vascular system through angiotensin receptor 1 (ATR1) stimulation not counterbalanced by the ACE 2-dependent favorable results triggered by MasR/ATR2 activation (Moccia *et al*., 2020). COVID-19-induced ACE 1/ACE two imbalance also leads to the so-called ACE 1 "shedding" phenomenon at the pulmonary vascular level, eventually improving local inflammation, pro-coagulant state, and capillary leakage, likely increasing susceptibility to SARS-CoV-2 in remote tissues (Leisman *et al*., 2020).

There are neurological complications due to COVID 19, but the neuropathological studies due to the same are very few. Most of them focus on microthrombi and acute infarcts, hypoxic changes with no specific pathology, or perivascular lymphocytic infiltration in the brainstem. There are several mechanisms leading to SARS-CoV-2 related neurological complications. There can be viral invasion through the retrograde axonal route with intracellular accumulation in endothelial cells, smooth muscle cells, pericytes, inflammatory cells (particularly macrophages), neurons, or glial cells. Another indirect process from hypercoagulability- related thromboembolism or thrombus formation within the brain or an exaggerated cytokine/ immune-mediated response to viral infection, causing damage to blood vessel walls or cells in the brain. Hypoxia, which occurs in moderate to severe COVID 19, contributes to thrombotic complications, as it is responsible for heparin resistance.

The relation between cytokine storm and endothelial dysfunction that causes sepsis during COVID-19



The expression of proinflammatory genes, especially chemokines, was markedly elevated in COVID19 cases compared to community-acquired pneumonia patients and healthy controls, suggesting that SARS-CoV-2 infection causes hypercytokinemia. Compared to SARS-CoV, which is thought to induce inadequate interferon (IFN) responses, SARS-CoV-2 robustly triggered the expression of numerous IFN-stimulated genes (ISGs). These ISGs exhibit immunopathogenic potential, with the overrepresentation of genes involved in inflammation. The transcriptome data was also used to estimate immune cell populations, revealing increases in activated dendritic cells and neutrophils.



CONCLUSION

COVID-19 is a viral pandemic that has taken the whole globe by storm. The disease can be studied under various parameters, its underlying causes, and can be correlated to blood and immune bio metabolic activities and different cells and proteins produced/depleted in the process. The objective of the article is to deliver an easy understanding of the underlying effects of a COVID-19 infection and understand those within our range of knowledge based on the reliable data from professionally written and documented sources. Keeping it in mind that these parameters can help us develop better vaccines and be a resource for future pharmaceutical research.

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