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Understanding COVID-19: A COMPREHENSSIVE REVIEW

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ABSTRACT: The 2019 novel coronavirus (2019-nCoV), commonly known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or coronavirus disease 2019 (COVID-19), was first revealed in late 2019 in Wuhan city, Hubei province, China. It was subsequently spread globally and thereby declared as a pandemic by WHO in March 2020. The disease causes severe acute respiratory illness and is highly contagious due to the fast-onward transmission. As of the mid of November 2020, the disease has affected 220 countries with more than 16 million active cases and 1.3 million deaths worldwide. Males, pregnant women, the elderly, immunosuppressed patients, and those with underlying medical conditions are more vulnerable to the disease than the general healthy population. Unfortunately, no definite treatment is available. The aim of this review was to understand the mechanism of entry of virus inside human body and its effects on various organs.

Key Words: covid-19, life cycle, immune system

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogen responsible for coronavirus disease 2019 (COVID-19), has caused morbidity and mortality at an unprecedented scale globally1 . Scientific and clinical evidence is evolving on the subacute and long-term effects of COVID-19, which can affect multiple organ systems2 . Early reports suggest residual effects of SARS-CoV-2 infection, such as fatigue, dyspnea, chest pain, cognitive disturbances, arthralgia and decline in quality of life3–5 . Cellular damage, a robust innate immune response with inflammatory cytokine production, and a pro-coagulant state induced by SARS-CoV-2 infection may contribute to these sequelae6–8 . Survivors of previous coronavirus infections, including the SARS epidemic of 2003 and the Middle East respiratory syndrome (MERS) outbreak of 2012, have demonstrated a similar constellation of persistent symptoms, reinforcing concern for clinically significant sequelae of COVID-19 (refs. 9–15). COVID-19 is an enclosed RNA virus that is distinctly present in people and animals. The virus belongs to the Nidovirales order that consists of families, namely, Roniviridae, Arteriviridae, and Coronaviridae [16,17]. At the same time, the Coronaviridae family is divided into two, which include Torovirinae and Coronavirinae. Further, the Coronavirinae subfamily is classified as into alpha-, beta-, gamma-, and delta- COVs [16]. These viruses have virus-related RNA genome that measures from 26 to 32 kilobases in dimension, and this makes it possible to isolate them from different animal species. Moreover,

the coronaviruses can be seen under the electron microscope as it possesses a crown-like appearance. Ideally, the extensive spreading and associated health risks of the disease make it an essential pathogen. Primarily, human types of coronavirus are linked to minor clinical symptoms. Simultaneously, the World Health Organization (WHO) have conducted studies and lab research to identify the new strain of COV, designated as COVID-19 [3-22]. On the other hand, the International Committee on Taxonomy of Viruses referred to the disease-causing virus as the SARS-CoV-2 virus. As a result, the way the illness spread from person-to-person has made it a public threat [18].

Mechanism of Cell Entry and Life Cycle of the Virus

The virus enters the host's cell through angiotensin-converting enzyme 2 (ACE2) receptors present on the cell membrane of the cells of several tissues, particularly of the lower respiratory tract (LRT), heart, kidneys, and gastrointestinal tract (GIT).19 The entry is also facilitated by TMPRSS2 protease or endosomal cathepsin L present on host's cells. The viral S protein consists of S1 and S2 subunits. The S1 binds ACE2 receptors through the RBD region, while S2 and TMPRSS2 or cathepsin L complex promote membrane fusion between the virus and the host cell. The entry is followed by the release of viral RNA, translation of ORF, production of nonstructured proteins, and formation of viral replication transcriptase complex. The complex initiates genome replication and subgenomic transcription. The viral structural proteins (S, E, M, and N) are encoded, including certain accessory proteins. Afterward, translation proteins are assembled at the endoplasmic reticulum-Golgi intermediate compartment (ERGIC). Here, the S protein may also be modified by furin. The viral particles are thereby released from the host's cell through exocytosis.20 This is the same mechanism as that observed previously for the SARS-CoV virus (Imai et al., 2010; Hoffmann et al., 2020; Wan et al., 2020). Some studies have found that the ACE2 receptor affinity of SARS-CoV-2 is more efficient than that of SARS-CoV(2003) but less efficient than its 2002 strain. It is believed that any mutation on the receptor-binding domain (RBD) of S protein could make the virus more pathogenic. However, some mutations other than the receptor interaction sites in RBD of S protein have been discovered, but the role of such mutations in its pathogenicity is still not clear21

Immune System:

The immune system works as a defense system and plays a key role in the prevention of pathogenic attacks throughout the body; however, uncontrolled or impaired immune response may result in harmful tissue damage . Overwhelming of the inflammatory response is considered to be initiated as a result of the antagonism effect of interferon by SARS-CoV-2 to promote its replication inside the cell. Interferon (IFN) response is considered directly related to viral load. An increase in type 1 IFN response causes decreased viral load and vice versa. It has been observed that a decrease in total T cell count causes a declined function of these cells in COVID-19 patients . However, increased levels of cytokines such as interleukins (IL-6, IL-1β, IL-2, IL-8, and IL17), granulocytes like granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM- CSF), interferon gamma-induced protein 10 (IP10), monocyte chemoattractant protein-1 (MCP1), macrophage inflammatory proteins-1 alpha (MIPα), and tumor necrosis factor (TNF) along with C-reactive proteins, D-dimers, and ferritin are reported in COVID-19 infection. Cytokines are responsible for shock and severe tissue damage to different organs, and slow healing of lungs is observed in patients with elevated IL-6 level. Another unique characteristic of hypercoagulation has also been commonly noticed in serious COVID-19 patients . The cytokine storm and sepsis are considered the primary cause of death in about 28% of severe cases of COVID-19 . But these immunological changes are often restored, particularly in mild to medium cases. Simultaneously, individuals with robust immunity and without comorbidities may successfully eliminate the virus before the exacerbation of immune overreaction.22

Summary of post-acute COVID-19 by organ system

Pulmonary

• Dyspnea, decreased exercise capacity and hypoxia are commonly persistent symptoms and signs

• Reduced difusion capacity, restrictive pulmonary physiology, and ground-glass opacities and fbrotic changes on imaging have been noted at follow-up of COVID-19 survivors

• Assessment of progression or recovery of pulmonary disease and function may include home pulse oximetry, 6MWTs, PFTs, high-resolution computed tomography of the chest and

computed tomography pulmonary angiogram as clinically appropriate

Hematologic

Thromboembolic events have been noted to be <5% in post-acute COVID-19 in retrospective studies

• The duration of the hyperinfammatory state induced by infection with SARS-CoV-2 is unknown

•Direct oral anticoagulants and low-molecular-weight heparin may be considered for extended thromboprophylaxis afer risk–beneft discussion in patients with predisposing

risk factors for immobility, persistently elevated d-dimer levels (greater than twice the upper limit of normal) and other high-risk comorbidities such as cancer

Cardiovascular

•Persistent symptoms may include palpitations, dyspnea and chest pain

•Long-term sequelae may include increased cardiometabolic demand, myocardial fbrosis or scarring (detectable via cardiac MRI), arrhythmias, tachycardia and autonomic dysfunction

• Patients with cardiovascular complications during acute infection or those experiencing persistent cardiac symptoms may be monitored with serial clinical, echocardiogram and electrocardiogram follow-up

Neuropsychiatric

• Persistent abnormalities may include fatigue, myalgia, headache and cognitive impairment (brain fog)

•Anxiety, depression, sleep disturbances and PTSD have been

reported in 30–40% of COVID-19 survivors, similar to survivors of other pathogenic coronaviruses

• The pathophysiology of neuropsychiatric complications is mechanistically diverse and entails immune dysregulation, inflammation, microvascular thrombosis, iatrogenic effects of medications and psychosocial impacts of infection

Renal

• Resolution of AKI during acute COVID-19 occurs in the majority of patients; however, reduced e GFR has been reported at 6months follow-up

• COVAN may be the predominant pattern of renal injury in individuals of African descent

•COVID-19 survivors with persistent impaired renal function may benefit from early and close follow-up in AKI survivor clinics

Endocrine

• Endocrine sequelae may include new or worsening control of existing diabetes mellitus, subacute thyroiditis and bone demineralization

• Patients with newly diagnosed diabetes in the absence of traditional risk factors for type 2 diabetes, suspected hypothalamic–pituitary–adrenal axis suppression or hyperthyroidism

should undergo the appropriate laboratory testing and should be referred to endocrinology

Gastrointestinal and hepatobiliary

• Prolonged viral faecal shedding can occur in COVID-19 even after negative nasopharyngeal swab testing

• COVID-19 has the potential to alter the gut microbiome, including enrichment of opportunistic organisms and depletion of beneficial commensal

Dermatologic

• Hair loss is the predominant symptom and has been reported in approximately 20% of COVID-19 survivors MIS-C

• Diagnostic criteria: <21 years old with fever, elevated inflammatory markers, multiple organ dysfunction, current or recent SARS-CoV-2 infection and exclusion of other plausible diagnoses

•Typically affects children >7 years and disproportionately of African, Afro-Caribbean or Hispanic origin

• Cardiovascular (coronary artery aneurysm) and neurologic (headache, encephalopathy, stroke and seizure) complications

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