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Research Article
Coronavirus Disease 2019 (COVID-19): A Simplified Assessment of its Origin, Epidemiology and Physiological Manifestations

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Abstract

The renowned coronavirus has spread across the globe like an invisible fire in a short period and it has done so while destroying everything that it encountered, it did not differentiate between an Arab country or a Western one. All of humanity is now terrified of a virus whose genome is the size of fewer than 34 kilobases. This article aimed to provide knowledge on all relevant aspects of the current coronavirus pandemic and its causative agent, i.e., the COVID-19 virus-or more precisely, SARS-CoV-2. Its possible adverse effects on physiological functions of targets and their body functions, especially on cardiovascular and respiratory systems, have been reviewed in detail.

Key words: COVID-19, coronavirus, SARS-CoV-2, prevention of COVID-19, pandemic, viral structure, viral taxonomy

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INTRODUCTION

Nowadays, the world is concentrating on one common subject, the "Coronavirus" or "COVID-19," which has spread across the entire world at the speed of light and has caused immense panic owing to the high mortality and fatalities associated with it. Coronaviruses are a group of closely related viruses that infect both mammals and birds to cause severe respiratory disorders. They belong to the family *Coronaviridae*, subfamily *Orthocoronavirinae*, order *Nidovirales* and realm *Riboviria* as detailed in Table 1[1]. The coronaviruses are pleomorphic enveloped particles that contain single positive-sense RNA, in combination with nucleoproteins[2]. Every single RNA is almost 27-34 kilobases long. The specific characteristics of the SARS-CoV-2, which is now popularly known as the COVID-19 virus, include nucleocapsid and spiked proteins (Fig. 1). It is these proteins that give the coronavirus its name that has been derived from the terms, "crown" or "halo", to refer to its unique shape resembling a crown or a solar corona when seen under an electron microscope.

Taxonomy of the COVID-19 virus: Most known viruses are classified according to their phylogenetic relationship with viruses that have been previously recorded to infect the same host as well as their specific genotype. The viral agents that cause Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS), i.e., SARS-CoV and MERS-CoV, respectively are closely related to COVID-19 as depicted in Fig. 2. A look at their genomic sequences revealed COVID-19 to differ from them by only a few nucleotide bases, with a closer resemblance to SARS-CoV as compared to MERS-CoV. Furthermore, the spiked protein in the COVID-19

Table 1: Taxonomy of selected coronaviruses

Category	Coronavirus	Humans
Realm	*Riboviria*	
Order	*Nidovirales*	Primates
Suborder	*Cornidovirineae*	
Family	*Coronaviridae*	*Hominidae*
Subfamily	*Orthocoronavirinae*	*Homininae*
Genus	*Betacoronavirus*	*Homo*
Subgenus	*Sarbecovirus*	
Species	Severe acute respiratory syndrome-related coronavirus	*Homo sapiens*
Individuum	SARS-CoVUrbani, SARS-COVGZ-02, Bat SARS CoVRf1/2004, Civet sars CoVSZ3/2003, SARS-CoVPC4-227, SARSr-CoVBtKY72, SARS-CoV-2 Wuhan-Hu-1, SARSr-CoVRatG13, etc	Dmitri Ivanovsky, Martinus Beijerinck, Friedrich Loeffler, Barbara McClintock, Marie Curie, Albert Einstein, Rosalind Franklin, Hideki Yukawa, etc

In this list, even if no similarity is visible, all species of coronaviruses are deemed to be capable of targeting humans. Divergence decreases from the level of *Realm* to *Individuum*

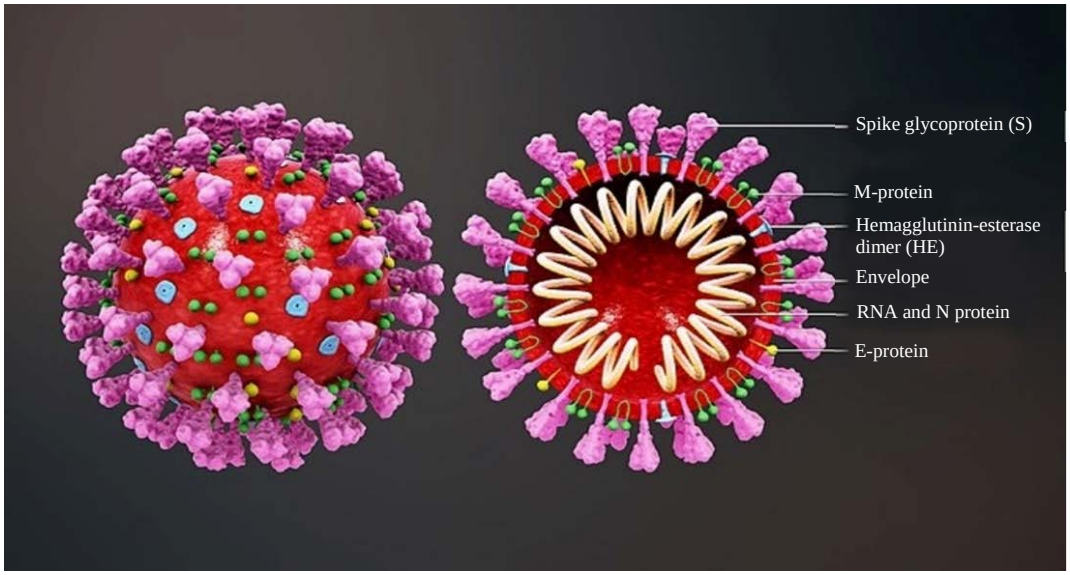

Fig. 1: Cross-sectional depiction of a coronavirus particle

Source: https://www.scientificanimations.com/coronavirus-symptoms-and-prevention-explained-through-medical-animation/

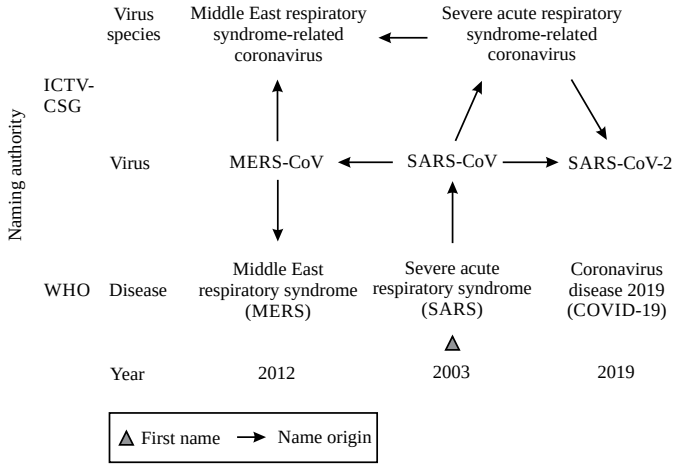

Fig. 2: Current international classification of two similar disease-causing viruses, MERS-CoV and SARS-CoV based on genomic sequences[4]

virus is much larger than that in either MERS-CoV and SARS-CoV. At this point, it should be noted that SARS-CoV and MERS-CoV are not the only viruses related to the COVID-19 virus. Currently, 39 viral species are recognized as members of the 27 subgenera, five genera and two subfamilies of *Coronaviridae* (suborder *Cornidovirineae*, order *Nidovirales* and realm *Riboviria*)[3].

It must be noted here that the name given to the species of coronavirus causing the current pandemic, i.e., COVID-19, is not its formal name. This species was named "severe acute respiratory syndrome coronavirus 2" or "SARS-CoV-2" by the International Committee of the Taxonomy of Viruses. However, to avoid confusing it with the virus that caused the SARS outbreak, the World Health Organization (WHO) introduced the name, COVID-19.

Transmission via respiratory droplets: As of now, sneezing or coughing has been reported to be the most common route of exposure to COVID-19. Respiratory droplets are suspended in the air for a short period after being released from a person until they fall on a surface. They may even adhere to the sneezer or cougher's hands from where they can translocate to their nose or mouth and thus, be transmitted to other people during physical contact. As will be discussed later, relative humidity and temperature are important factors controlling the resistance of this viral strain[4]. According to some reports, COVID-19 may persist in the atmosphere without a host from 72 hrs to 9 days, depending upon the conditions. The WHO has emphasized the role of carriers with mild cough as a significant causative factor in the rapid spread of this virus[5]. Chinese researchers investigated a specimen of the COVID-19 isolated from a patient with severe pneumonia and observed it to be viable. These researchers as well as the China Center for Disease Control, have suggested that COVID-19 can transmit across patients, even indirectly, through contaminated stools, which is why hand washing is crucial after using the bathroom to hinder its spread.

Occurrence of COVID-19 in children and evidence of potential oral spread: In a study on children infected with COVID-19, it was observed that children, who were diagnosed to be positive for the virus by Polymerase Chain Reaction (PCR) results, were asymptomatic. Furthermore, images of their chests under X-rays were either normal or exhibited only coarse lung markings with no symptoms of pneumonia. Similarly, rectal swabs from these children were recorded positive for the COVID-19 by PCR. These findings provide evidence for the speculation that fecal-oral transmission may play an important role in the spreading of COVID-19 in younger patients[6].

Effect of high humidity and temperature on COVID-19: The transmission of COVID-19 is affected by several extrinsic factors, including temperature and humidity[7]. A study carried out in China reported high temperature and relative humidity to be important for reducing the spread of COVID-19. Similar patterns are known to study against influenza viruses. The spread of COVID-19 outside of China during the ongoing pandemic reveals an interesting pattern as well, whereby regions of lower air temperature and humidity, such as Korea, Japan and Iran, suffered from major outbreaks as compared to warmer and more humid regions, including Singapore, Malaysia and Thailand. The Fig. 3 depicts the pattern of spread in different countries around the globe during the initial

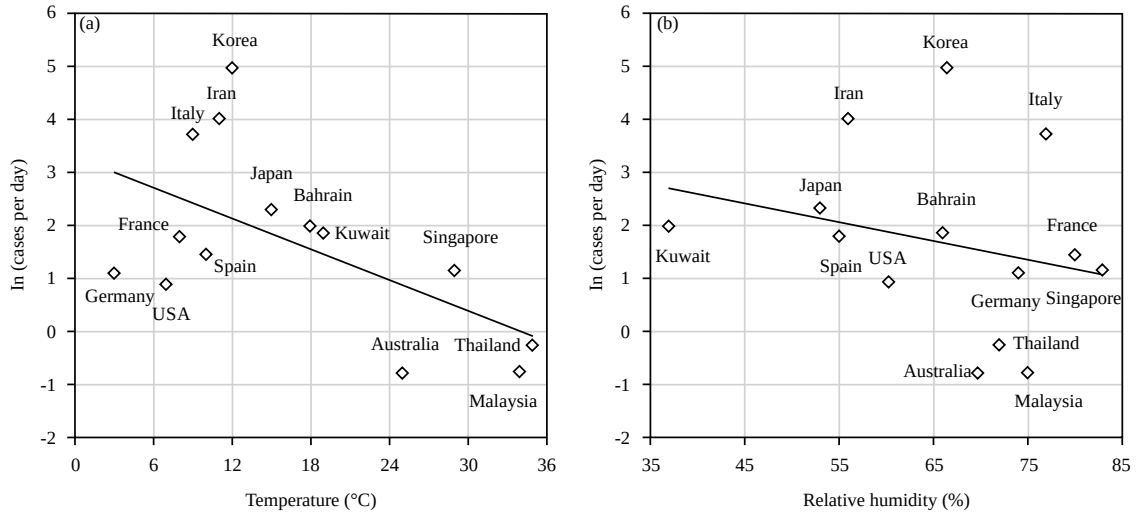

Fig. 3(a-b): Intensity of COVID-19 cases represented as a natural log of the number of COVID-19 cases versus (a) Temperature and (b) Relative humidity in regions outside of China[9]

period of the pandemic. A plot of the natural log of the average number of cases of COVID-19 per day from February 8-29 reveals that the intensity of spread is inversely related to average temperatures and relative humidity in a given region[8].

Inactivation with biocidal agents: With the increasing severity of the COVID-19 pandemic, strategies are being developed to prevent its further spread, especially in sensitive public places, such as hospitals. A major route of transmission from one person to the next is via the contamination of dry surfaces with mucous originating from the eyes, nose or mouth of an infected individual[9]. As has been mentioned earlier, COVID-19 can survive on abiotic surfaces from 72 hrs up to 9 days[10], therefore, biocidal agents, including alcohols (ethanol or propanol), benzalkonium chloride, Didecyldimethyl Ammonium Chloride (DDAC), sodium hypochlorite, hydrogen peroxide and povidone-iodine are being frequently employed as a countermeasure against the spread of COVID-19. However, the effective concentration of these disinfectants and the most suitable time of exposure varies between the viral strains. Surface disinfection has been reported to be the most effective with 0.1% sodium hypochlorite solution or 62-71% ethanol with 1 min exposure time.

The virus invades its host through a glycoprotein spike on its surface as depicted in Fig. 4. When the virus encounters the host cell physically, glycoproteins that are represented as red subunits in Fig. 4 enable it to enter the cell with the help of an Angiotensin Converting Enzyme (ACE), ACE-2. This particular enzyme is expressed in membranes of a variety of cell types, including epithelial cells of the alveoli in the lungs. Each of its two glycoprotein subunits, S1 and S2, binds to cell surface receptors and fuses with the cell membrane, respectively[11]. A Transmembrane Serine Protease (TMPRSS) in the host cell provides the means of entrance by activating the glycoprotein spike as well as by cleaving ACE-2. Activation of the glycoprotein takes place by an irreversible constitutional change in its S2 subunit, this, in turn, facilitates the fusion of the virus to the cell membrane and thus, allows it to enter the host.

Clinical features and effects of coronavirus on different body systems and organs: The incubation period of the virus within the host is expected to be 2-14 days following initial exposure. Symptoms that follow infection include fever with fatigue, dry cough, myalgias and dyspnea[13]. Other symptoms include headache, sore throat, rhinorrhea as well as gastrointestinal issues. The most commonly reported and severe symptom is the occurrence of pneumonia in COVID-19 patients. A major factor dictating the intensity of COVID-19 infection is the age of patients. Numerous studies have revealed the infection's severity to increase in individuals, who are older than 30 years. In the case of children, symptomatic infection is uncommon, however, if it occurs, it is generally mild[14]. Until now, no deaths have been recorded for children and the recovery period for young patients is generally 1-2 weeks after the initial onset of symptoms. According to a recent report by the China-WHO Joint Mission Expert Group, children under 18 years of age constitute only 2.4% of all reported cases of COVID-19.

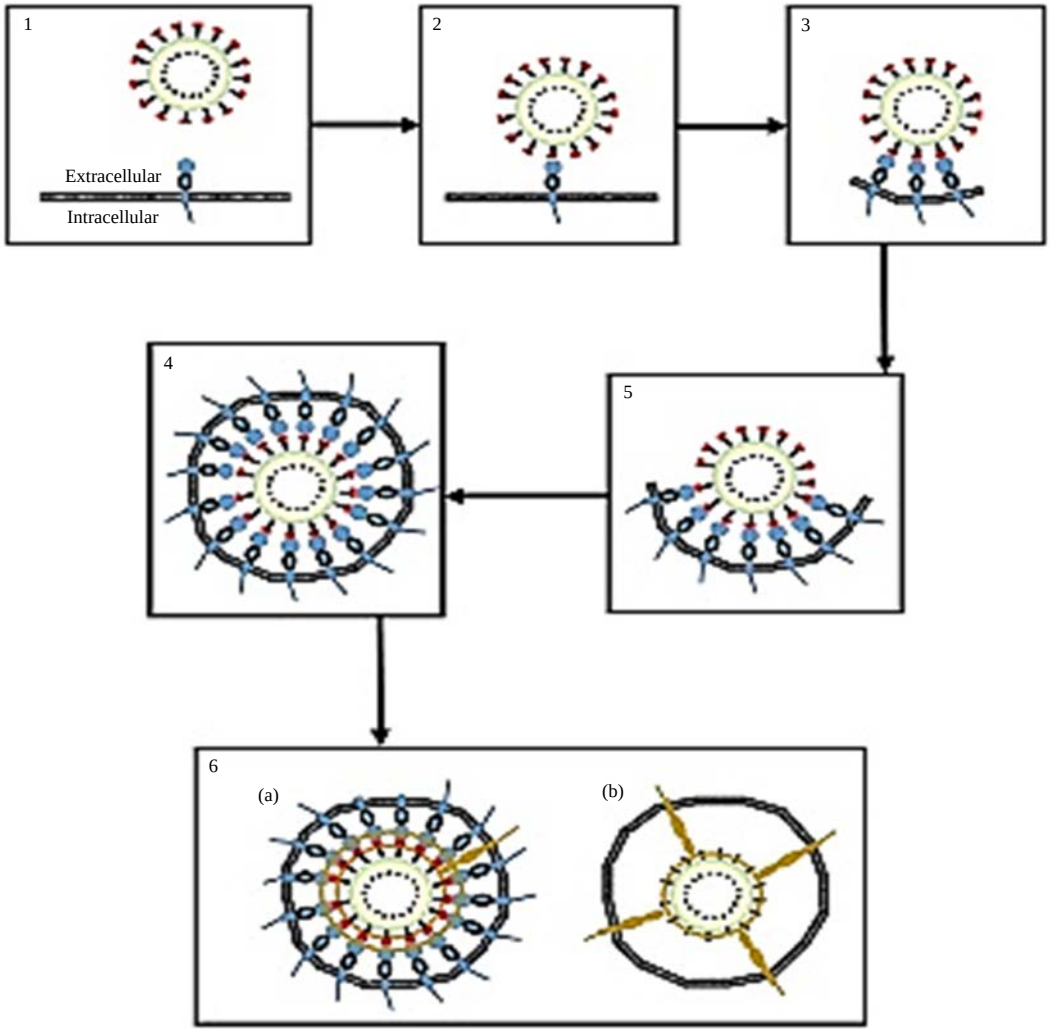

Fig. 4: Schematic representation of the steps by which the COVID-19 virus invades the host cells[12]

The deadly COVID-19 virus is a highly contagious strain of coronaviruses that manifests itself in the form of an acute respiratory disorder, along with pneumonia. However, once it strengthens, it may affect other organs, including kidneys, heart as well as the digestive, circular and nervous systems[15]. A recent study reported the COVID-19 virus to occur in the cerebrospinal fluid of infected individuals. In this study, 78 out of the total of 214 participating patients infected with COVID-19 (36.4% patients) exhibited neurological dysfunctionality. Another investigation revealed COVID-19 patients to lose involuntary control over their breathing [16]. Evidence for the presence of the COVID-19 virus in the general body circulation of patients indicates that it may reach cerebral circulation, where it is speculated to be able to easily multiplicate owing to the decreased movement of blood.

This multiplication follows its interaction with ACE2 in the cells of the capillary endothelium of infected individuals. Once it starts budding, the virus may break through the endothelial lining and eventually reach the brain. Previously, in the case of SARS-CoV, receptors of ACE2 were reported to interact with neural tissues of neurons to initiate a cycle of viral budding that eventually led to neuronal damage. However, this process took place without evident in ammation. In the same manner, COVID-19 can also access the brain and damage neural functioning by adopting a transcribrial route[17].

Effects of COVID-19 on the cardiovascular system: Cardiovascular and immune systems are heavily dependent on ACE2 for their functioning. This enzyme is also involved in proper heart function and thus, any enzymatic dysfunction may lead to the development of hypertension and diabetes

mellitus. This enzyme has been highlighted as an important receptor of several coronaviruses, including SARS-CoV and COVID-19, where the COVID-19 infection is initiated by the binding of a spiked glycoprotein on the surface of the virus to ACE2 in the host cells. Usually, this adhesion takes place in the cells of the heart and lungs. Amongst these two potential entry points, the COVID-19 largely exhibits preferential entry through epithelial cells of the alveoli that results in respiratory symptoms. Individuals suffering from cardiovascular disorders generally exhibit increased expression of ACE2[18] because of the use of renin-angiotensin-aldosterone system inhibitors. In hypertensive patients infected with COVID-19, the use of angiotensin receptor blockers (ARBs) must be carefully monitored and controlled. Similarly, patients of MERS and other coronavirus-caused diseases are more prone to suffering from acute myocarditis and heart failures, therefore, treatment methods have to be chosen carefully keeping in mind the patient's safety and overall medical history[19].

COVID-19 and the immune system: A study that aimed to elaborate the relation between the COVID-19 virus and the host's immune response exhibited that the process of infection can be categorized into three phases: Phase I is the incubation period during which the virus may either be detectable or not. Phase II is when the virus can clearly be detected but symptoms are not yet severe. Phase III is where respiratory symptoms start to show and eventually become severe[20]. Each individual's response to infection by the virus is dictated by their specific genetic makeup and immunity. When a person's immune response is impaired, the virus spreads rapidly and further infects tissues. Generally, higher and more rapid deterioration occurs in organs with high ACE2, such as intestines and kidneys[21]. Proinflammatory macrophages and granulocytes control the innate in ammation that takes place in the damaged cells of the lungs. The reason why lymphocytopenia is commonly observed in patients infected by the COVID-19 virus is the occurrence of the cytokine release syndrome (CRS), which is mediated by not only leukocytes but by T-cells as well[22].

Interferon-gamma (IFNγ) is a soluble cytokine from the type II class interferons, its major role is to provide innate immunity against the COVID-19 virus and other microbial threats faced by the body via the Natural Killer (NK) cells and Natural Killer T (NKT) as well as lymphoid cells. It is an important activator of macrophages that induces the expression of the class II type of the Major Histocompatibility Complex (MHC). Furthermore, IFNγ is crucial to the immune system because it can inhibit viral replication directly[23]. Mesenchymal stem cells may help repair severely damaged lung tissues in patients of COVID-19, however, these cells must be activated by IFNγ before they can exert their anti-in ammatory action. Generally, these cells may be not present or are not activated in severely affected patients.

Vitamin B3 that is also known as niacin or nicotinamide (soluble form of the vitamin) is highly effective in preventing damage to the lung tissue. Cross-sectional images of lungs infected with the COVID-19 virus depict white fluid-containing patches termed as ground glass. The exact composition and nature of the clear jelly in these patches is yet unknown, but hyaluronan, which is generally associated with acute respiratory distress syndrome, has been observed to be present in the fluid.

Effects of COVID-19 on the liver: Once any type of coronavirus starts spreading onwards from the respiratory system to other parts of the body, the liver is often the easiest target. However, liver damage in the case of SARS-CoV, MERS-CoV and COVID-19 is often mild. Severe cases may, however, lead to serious liver damage and may even result in liver failure. Abnormally high expression of liver enzymes is an indication of liver injury. Reports on enzyme expression and liver damage from COVID-19 patients have provided evidence of Alanine Transferase (ALT) to be a prominent enzyme exhibiting changes after infection. Furthermore, an elevation in the levels of creatinine kinase and lactic dehydrogenase have been reported. In several cases, elevation in the levels of ALT did not necessarily arise from the liver alone but was a side-effect of myositis induced by COVID-19. Hepatic dysfunction as a consequence of severe COVID-19 infection is generally followed by coagulative and fibrinolytic pathways becoming more intense, a relative decrease in platelets and neutrophils, reduced neutrophil to lymphocyte ratios and an increase in ferritin levels[15]. Furthermore, a liver biopsy of a COVID-19 patient after their death indicated the occurrence of micro-vesicular steatosis, which is a common observation in conditions of sepsis[24]. All such immunological markers are often considered non-specific indicators of inflammation, however, they still corroborate the idea of disease severity is proportional to the loss of innate immunity.

Kidneys and COVID-19: Currently, there is not much evidence to support the adverse effects of COVID-19 infection on kidneys, especially in cases of mild to moderate infections. However, kidney abnormalities have been recorded for 25-50% of persons, who were hospitalized with severe infections. In these individuals, increased excretion of proteins and red blood cells via the urine was observed. Less than 15% of COVID-19 patients exhibited a decline in the actual function

of kidneys, i.e., acute kidney injury is rare in COVID-19 infections. However, this does not rule out the long-term effects of the infection on kidney functioning.

Previously, 6 and 25% of SARS and MERS patients, respectively, were recorded to suffer from acute renal injury. Now, recent studies have revealed COVID-19 to have the same potential, which is opposite to what we had known in initial studies and cases. Kidney dysfunction is a relatively uncommon manifestation of the disease, but, if/when it occurs, it is fatal. Amongst SARS patients, 91.7% died of acute renal impairment, where their kidney tubules were severely affected by the virus. Following the outbreak, the WHO reported the widespread occurrence of inflamed kidney tubules in infected people. Similarly, COVID-19 infection is especially deadly to individuals, who are undergoing dialysis. Such individuals may be more prone to not only acquiring the infection but to exhibiting greater variations in clinical symptoms as well. A major consequence of patients requiring dialysis and also suffering from COVID-19 is their inability to self-quarantine as they have to visit dialysis centers on regular basis, which increases the risk of disease transmission to medical personnel and other patients in the facility, especially if the COVID-19 infection is asymptomatic or has not been diagnosed yet. Therefore, the Chinese Society of Nephrology, the Taiwan Society of Nephrology, the American Society of Nephrology, the Centers for Disease Control (CDC, USA) and the European Renal Association (ERA-EDTA) introduced special guidelines for dialysis units to avoid the spread of COVID-19 via these facilities.

Effects of COVID-19 on the digestive system: During the historical outbreaks of coronaviruses, SARS-CoV and MERS-CoV, a large proportion of patients suffered from diarrhea. Similarly, gastrointestinal abnormalities are commonly observed in the current outbreak of the COVID-19 virus as well, with rare cases of diarrhea and abdominal pain. The first step for a viral invasion is finding suitable receptors on the host cells, these receptors may not be present on all types of cells in a host. Both SARS-CoV and MERS-CoV can invade large and small intestinal linings, with the infections reaching the gut. Such infections eventually lead to leakage of fluids in the form of diarrhea. It has been proposed that the COVID-19 virus adheres to the same receptor as does SARS-CoV, it may enter via cells of the lungs or small intestines. As has been discussed in detail before in this review, COVID-19 is present in the stools of infected patients, which indicates that it may spread via contact with feces. However, this is only a speculation at this point[25]. The first case of COVID-19 infection that was reported in the United States had a 2 day history of nausea and vomiting, the hospital records indicated loose bowel movement on the second day that the patient was admitted to the hospital. Specimens of loose stool as well as respiratory samples, were tested to be positive for the virus[26]. It should be noted that extra pulmonary presence of the viral RNA does not guarantee that the virus is present. Further testing is required, while an initial positive culture for the virus may be due to salivary gland infection with increased chances of transmission[27].

COVID-19 and blood groups: A preliminary study was performed in China to identify patterns of dominance in blood groups of more than 2,000 participants diagnosed with COVID-19. The researchers observed blood type A to be more susceptible to being infected and developing more intense symptoms. On the other hand, people with blood type O seemed to be less prone to acquiring the disease. This finding was further strengthened by the fact that blood type O is the dominant proportion of the studied population (34%) than type A (32%), however, 41% of reported COVID-19 patients had blood type A and only 25% of them had blood type O. Overall, it was recommended that further research must be carried out to cater to the different blood types in the treatment of patients.

COVID-19 and gender: An interesting and highly significant observation reported during the current COVID-19 pandemic is the much more common spread and mortality rate of this coronavirus in men as compared to in women. According to an analysis of approximately 45,000 reported cases in China, the mortality rate was 2.8 and 1.7% in men and women, respectively[28]. Even at the level of infection by the virus, men comprised a slightly larger portion of the overall infected population, i.e., 51%. Current explanations attribute this pattern of men being more likely to suffer from COVID-19 to them being more likely to smoke cigarettes and thus, have weaker lungs or a predisposition to cardiovascular diseases.

Coronavirus infection in pregnant women may not pass from mother to newborns: A study in China that included four pregnant women as participants revealed an important finding that the COVID-19 virus may not pass from the mother to the newborn baby at the time of birth[29]. Previously, perinatal transmission of another type of coronavirus, SARS-CoV, was found to not occur in ve newborn babies from an infected mother during a community outbreak in Hong Kong in 2003. Most importantly, none of these babies developed any symptoms of SARS-CoV infection, including clinical, radiological, hematological or biochemical

abnormalities. The same observations have now been reported for COVID-19 infections using RT-PCR assays of throat swabs from three women and their newborn babies.

Prevention of COVID-19: Studies and experiences reported from all across the world have indicated one common factor to be essential in stopping-or at least slowing down-the spread of the COVID-19 virus: Good personal hygiene. Examples from our daily lives and science show that the simplest steps can often lead to the most effective results, such as the use of a ketogenic diet to lose weight[30], exercising every day to avoid hypertension in women[31] or even wearing sunscreen to protect ourselves against solar radiation[32]. In the ongoing uncertain times, we must know and practice the very basic methods of protecting ourselves. Contaminated hands permit easy virus transmission, therefore, handwashing for approximately 10-20 sec, whenever required, is the first and foremost step toward prevention. Furthermore, minimal self-contact with eyes, nose and mouth helps reduce the chances of viral transmission, hence, tissues must be used, when one coughs or sneezes. Infected individuals must wear personal protective equipment, including masks and gloves to minimize the risk of exposing others. Most importantly as has been discussed in detail in a later section, social distancing is a powerful measure against transmission. Because of the current spread, governments and travel authorities have put strict restrictions on traveling between different regions of the world to avoid the transmission of COVID-19 and to decrease the severity of this pandemic. Last but not the least, social media must play its role by highlighting the deadly effects of the COVID-19 virus and by sharing hygiene-related instructions with people as much as possible.

Hand washing: The US Centers for Disease Control and Prevention have been strongly emphasizing the necessity of washing hands with soap and water for 20 sec or more every time a person exposes themselves to the public or comes in contact with another person. This is especially important after relieving oneself in the toilet as research has provided evidence of COVID-19 being capable of transmitting from the stool. An antiviral sanitizer, such as diluted (60%) alcohol must be used to clean hands, when they are visibly dirty as well as before eating. The same must be practiced after blowing the nose, coughing or sneezing.

Respiratory hygiene: The use of masks is highly recommended for infected people because it helps reduce the release of respiratory droplets during talking, coughing and sneezing. In case masks are not available at a given moment or one chooses to not use them, the WHO suggests that people cover their faces by bending their elbow in front of their mouth and nose or use a tissue to cover themselves during coughing or sneezing, the tissue must be disposed of properly in a waste bin immediately after use to avoid exposing other people. On the other hand, it must be kept in mind that healthy people must wear masks, even if they are not themselves at high risk when they are responsible to care for another individual, who may be at risk of acquiring the COVID-19 virus. The lowest level of protection is provided by surgical masks as they are designed to protect healthy people from infected ones.

Social distancing: A major and effective means of controlling any disease that spreads as fast as COVID-19 is social distancing, which is a minimization of close physical contact. The different methods of practicing social distancing include quarantining, reduced travel, shutting down educational institutions, such as schools and universities as well as other places of public gathering, including workplaces, stadiums, theatres, shopping centers, etc. At an individual level, greetings that include touching of hands or other body parts and kissing must be avoided. During the ongoing pandemic of COVID-19, many governments and organizations all across the world have made it compulsory to practice social distancing to reduce the intensity of the outbreak. This is especially applicable to groups of high-risk individuals, including adults of 60 years or more of age, who can be readily infected due to compromised immunity or previous health conditions, such as cancer, asthma, diabetes, hypertension, etc.

Self-isolation: This is a form of social distancing, where one practice staying by themselves in closed quarters to avoid infecting others or acquiring the virus themselves. This preventative measure is recommended for individuals, who have been diagnosed positive for the COVID-19 virus or are prone to be infected. Self-isolation is highly recommended for people, who have recently traveled to a region that had numerous cases of COVID-19 occurrence or who suspect that they might have been exposed to the COVID-19 virus. According to the National Health Service of the UK, individuals exhibiting symptoms of COVID-19 must self-isolate themselves for no less than 14 days, while taking all possible measures to avoid transmitting it to others within and outside of their household.

Medications and treatment: A broad-spectrum antiviral drug currently used against beta coronaviruses is remdesivir. This

drug inhibits replication of the virus by terminating RNA transcription prematurely and thus, may exhibit activity against the COVID-19 virus as well[33]. A recent study performed in China reported chloroquine to be capable of treating COVID-19 patients and thus, it was one of the recommended antiviral drugs against this virus in China, two related drugs, hydroxychloroquine and chloroquine are oral drugs that are conventionally employed to treat malaria and some inflammatory conditions[34,35]. Chloroquine is specifically used to treat malaria and provide chemoprophylaxis, while hydroxychloroquine is used to treat several disorders, including arthritis rheumatoid, systemic lupus erythematosus and porphyria cutanea tarda. No significant positive effect was observed for the drug, lopinavir-ritonavir, in one investigation, while a study by a Korean group of physicians recommended that young healthy patients, who exhibited only mild symptoms, may use broad-spectrum antiviral medications, while older individuals or younger patients with serious symptoms may be treated with a combination of lopinavir and ritonavir or by chloroquine. Other drugs that have been successfully used to treat COVID-19 till now are remdesivir[36] and the combination of sofosbuvir and ribavirin.

A study was carried out to identify a suitable drug for the COVID-19 virus based on its phylogenetic similarity with other viruses. The goal was to repurpose already known and effective drugs for COVID-19[37]. Fifteen HCoV whole genomes were sequenced to reveal that the COVID-19 virus is 79.7% identical with the nucleotide sequence of another coronavirus, SARS-CoV. The envelope and nucleocapsid proteins of the COVID-19 virus are evolutionarily conserved regions in coronaviruses, there are 96 and 89.6% sequence identities for these regions, respectively, between COVID-19 and SARS-CoV. Based on this similarity, 16 potential general anti-coronavirus drugs were considered repurposable against COVID-19, including melatonin, mercaptopurine and sirolimus.

Aside from conventional drugs against the virus, non-conventional agents, such as selective estrogen receptor modulators, have been reported to be capable of indirectly inhibiting viral replication[38]. Research has indicated a nonsteroidal drug, toremifene, to block the spread of various coronavirus strains, including MERS-CoV and SARS-CoV. This particular drug hinders the virus from fusing with the host cells' endosomal membranes by destabilizing glycoproteins in the viral membrane that eventually inhibits replication of the virus.

Because of the important role of ACEs, ARBs have been tested for their potential role as agents against COVID-19. The Food and Drug Administration (FDA) generally recommends ARBs to be used to ameliorate hypertension and diabetic nephropathy. An important ARB, irbesartan, is reported to inhibit co-transport of polypeptides with sodium taurocholate and inhibit viral entry into the host cells. Similarly, immunosuppressant or antineoplastic agents, such as the rapamycin complex 1, help regulate the replication process in many viruses, including the coronavirus[39]. Previously, such an agent, sirolimus, was reported to reduce the infection intensity of MERS-CoV by over 60%. This drug was also used to treat severe H1N1 pneumonia and acute respiratory failure[40]. Recent *in vitro* and *in vivo* studies reported mercaptopurine to target papain-like protease, which allows it to selectively inhibit both SARS-CoV and MERS-CoV[41]. Natural antioxidants, such as vitamin E, have been employed previously to cure medical conditions[42]. Similarly, folic acid effectively reverses the chronic chemical toxicity of paracetamol by its antioxidant potential[43]. Melatonin has been used as an antiviral agent due to its anti-in ammatory and antioxidant potential[44]. What makes it important for use against the COVID-19 virus is the fact that it can indirectly regulate ACE2 expression, which is a key entry receptor for infection by COVID-19. More specifically, melatonin inhibits calmodulin, thereby stopping the virus from interacting with ACE2. In the case of SARS-CoV, inhibition of calmodulin impedes the shedding of the viral ectodomain, which is the key process by which it infects the host cells.

CONCLUSION

The coronavirus disease, more popularly known as COVID-19, has gained attention worldwide owing to its rapid spread, severity and high mortality rate, especially in older patients with a history of cardiovascular, pulmonary and kidney disorders as well as those predisposed to hypertension and diabetes. The virus affects the respiratory systems generally but it can affect other systems of the body and organs as well once it enters the host. It is demonstrated through a concise literature review that the main factor that promotes the spread of COVID-19 throughout the body is the Angiotensin Converting Enzyme 2 (ACG2) that has receptors in the lung, heart, brain, kidney and other organs and thus, can cause physiological disturbance capable of turning into serious complications. Furthermore, this review elucidates the adverse effects of COVID-19 on body organs and systems, while providing concise information on its taxonomy, transmission, modes of entrance, prevention and possible medications.

SIGNIFICANCE STATEMENT

This study compiles relevant information regarding the cause, prevention and treatment of the ongoing pandemic,

COVID-19 that can be beneficial for the general public as well as the academic community and research groups alike. This study will help researchers and laymen to understand critical aspects of COVID-19 that many individuals do not have access to in a single place. With this compilation, understanding of the severity, susceptibility and preventative methods will be enhanced.

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