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Article Review

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On the novel coronavirus (COVID-19): a global pandemic

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HIGHLIGHTS

- COVID-19 has been declared a global health emergency.
- COVID-19 probably transmitted from bats or another host.
- Preventative measures are to be practiced.
- Efforts to develop and validate medications for COVID-19 are underway.

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ABSTRACT

Coronaviruses (COVs) are viruses transmitted through droplets of sputum from an infected person. Analyses identify COVs as zoonotic pathogens, possibly resulting from human-animal contact at animal markets. They share overlapping genetic characteristics with the avian influenza viruses from China. COVs released from humans through droplets of sputum and may land on various surfaces, which poses exposure risks; as studies have shown the virus can exist intact for a relatively long period of time (several days). The recent highly pathogenic COVs outbreak (COVID-19) emerged in Wuhan, China in 2019, include Severe Acute Respiratory Syndrome (SARs-COV). This highly transmittable disease causes pneumonia and other severe respiratory illnesses similar to SARS and MERS; it has a global mortality rate of about 6.13%. The virus has rapidly become a global pandemic, causing major global issues, including health, economic, and age-preference, among other issues. This text summarizes the nature of the emerging COVID-19 global pandemic while analyzing several factors concerning the etiology of the virus. This is done in an urgent effort to educate and provide relevant information about the virus.

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1. INTRODUCTION

Coronaviruses (COVs) belong to the Coronavirinae subfamily. COVs are single, positive stranded RNA viruses with genome ranging from 26 to 32 kilobases (kbs) in length. Corona means crown. The name, coronavirus, is derived from the appearance of the virion [1,2] which has a crown-like shape with spikes on the outer surface (Figure 1). Divided into low pathogenic (LP-COVs) and highly pathogenic (HP-COVs), six COVs are known to cause human diseases. LP-COVs are responsible for 10-30% of upper respiratory tract infections and caused minor respiratory diseases. Meanwhile, HP-COVs, which include Severe Acute Respiratory Syndrome (SARs-COV) and Middle East Respiratory Syndrome (MERS-COV), caused fatal pneumonia and infected lower respiratory airways. In 2002, SARs-COV appeared in China, infected 8,098 people, and caused 774 deaths.[3] This resulted in approximately a 9.6% mortality rate before it was controlled in 2003. The MERS-COV first appeared in Saudi Arabia; then, it surfaced in 26 other countries, and caused 2,494 reported cases. With 858 recorded deaths since 2012, MERS-COV had a 34.4% mortality rate.[4] Recently, a novel β-coronavirus (COVID-19) is shown to be highly transmittable and shares SARs-COV-like illness. Initial investigations showed that the virus emerged in Wuhan City, Hubei province in China (Table 1) in December 2019. As health officials were unable to contain the virus, it rapidly spread to all provinces in China and subsequently to multiple countries and territories (Figure 2). In late January 2020, the World Health Organization (WHO) declared the virus as a global pandemic.[5]

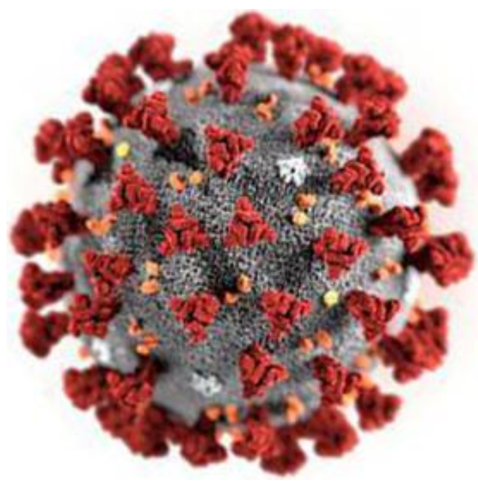

Figure 1. Microscopic illustration of the COVID-19 virion showing the spike ornaments on the outer surface.[1,2]

Many reports suggested that exposure to COVID-19 came from the Wuhan Seafood Market where wild animals are sold. Wild animals, such as bats, raccoons, snakes, bamboo rats, pangolins, and others, are suggested to be the original source of COVID-19. An intermediate source of origin and transfer to humans is not yet known. Altogether, these COVs are of serious concern to public health.[6] They lead to respiratory tract infections, resulting in pulmonary failure and fatality. In the case of COVID-19, the virus can survive and remain infectious for 2 hours to 9 days in various type of materials.[7,8] With an incubation period of 2-14 days after exposure (infection),[9,10] everyone is prone to the virus, while elderly individuals are more susceptible to experience severe illnesses, including death. Certain individuals are asymptomatic; they, along with individuals in which the virus is in the incubation period, are reported as the primary sources of infection and transmission. Transmission (direct and indirect)[8,11] can occur in various ways. This includes mucus and respiratory droplets from coughing and sneezing, which can all be suspended in air and on surfaces.

Table 1. A tabular comparison of coronaviruses outbreak outlying potential reservoirs, origins, and global data

	SARs-COV [3]	MERS-COV [4]	COVID-19 [12]
Infected	8,098	2,494	6,057,853
Deaths	774	858	371,166
Mortality rate (%)	9.60	34.4	6.13
Potential Reservoirs	Bats; Civet cats	Dromedary camels	Bats; Pangolin
Date	Nov. 2002-July 2003	Sept. 2012-Nov. 2019	Dec. 2019-
Origin	Guangdong, China	Saudi Arabia	Wuhan, China
Affected countries	26	27	<120

All data presented in this text were collected from covidgraph.com and WHO Situation Report-133.[12] At the time of this writing, COVID-19, with a mortality rate of 6.13% – became a global pandemic affecting 6,057,853 individuals in more than 120 countries and territories (Figure 2). Currently, the United States (USA) has become the new epicenter of the virus with a mortality rate of about 5.48%.

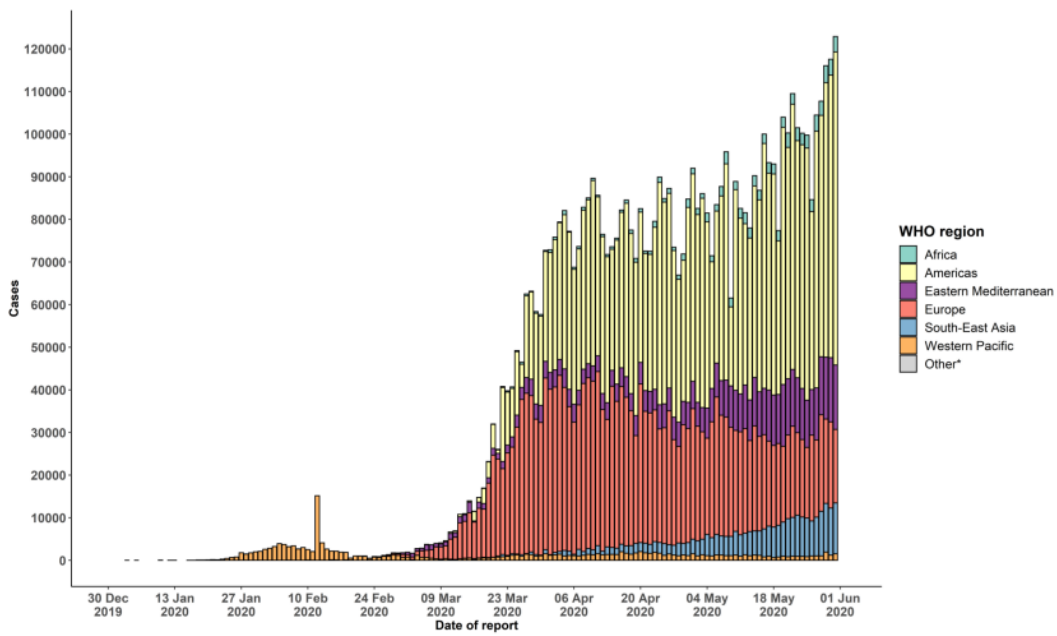

Figure 2. Geographical spread of COVID-19 showing reported cases as of 1 June 2020.[12]
For more details, see WHO COVID-19 Situation Report–133.

Among all reported case-fatality, New York, New Jersey, Illinois, California, and Massachusetts represent the top five states with the most fatalities. Altogether, the data shows that elderly individuals have a higher chance of infection. The mortality rate of COVID-19 (17-38%) is higher in elderly individuals with chronic diseases. Analyzing the data from New York state (Figure 3), the number of reported cases reached 375,133 and the death toll reached 24,133. Male represents 51.6% of the total cases while female represents 48.4%, however the death toll is much higher among male (60.9% death) compared to female (39.1%). Further analysis based on age groups shows the median infected age is 51 years old while individuals >75 are the most affected and vulnerable to COVID-19. Given the nature of the virus – highly contagious – it is important to protect these individuals from the virus by limiting direct interactions with and follow proper guidelines given by health officials. Currently, there are no available drug medications or vaccines to combat this pandemic. As transmission can occur among all age groups, the need to understand the nature of COVID-19 and its characteristics are critical in response to this global outbreak.

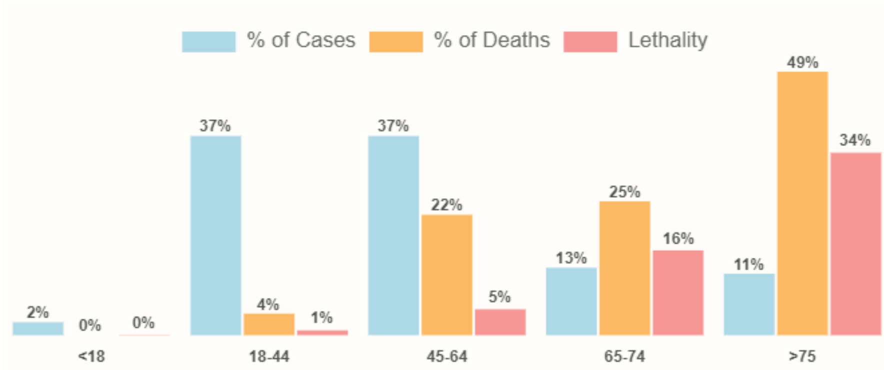

Figure 3. COVID-19 reported cases, deaths and lethality among various age groups in New York, USA.

2. REVIEW METHOD

All data presented in this text were collected using online resources from covidgraph.com, WHO Situation Reports, and U.S. Center for Disease Control and Prevention. A number of journal articles, news reports and papers available online were also used for sourcing information. All materials used for this publication are published in English. Searches were restricted to focus mainly on SARS-CoV-2, COVID-19, and a few articles searched with the keyword “coronavirus”. All data are properly cited throughout this publication. Knowing that data and information periodically are being made available, readers are encouraged to remain updated with more recent data and information following WHO, CDC, and public health officers.

3. RESULTS AND DISCUSSION

Zoonotic Pathogens

In light of zoonosis, a large number of diseases are due to human-animal contacts, causing local and global epidemy. A selected number of zoonotic diseases are briefly discussed in this text to further evaluate the consequences of zoonosis pathogens. Human-animal contact includes hunting, slaughtering, selling and cooking which pose a great risk of infection to a number of viruses– not only COVs. The handling and processing of animals –including wild animals, opens the door for more deadly pathogens that these animals may harbor. A chain of transmission can occur from human-animal contact and human-human transmission can follow. This is the case of many epidemics, including the avian influenza virus (i.e., H1N1) and numerous COVs (i.e., SARS, MERS). To minimize such epidemics, many researchers suggested not to aggregate various animal species, mammals, and birds in relatively closed environment (i.e., meat markets).[13,14,15]

The zoonotic origin of COVID-19 shares overlapping etiological characteristics with Ebola, as they are both transmitted from animal to human. Following recent studies, the full-length genome of COVID-19 was reported.[10] Its genome and spike glycoprotein showed 96.11% and 92.86% identity to *Rhinolophus affinis* bat coronavirus (BTA-COV) in Wuhan, respectively.[16,17] Bats, also known as flittermouse, with over 1,200 species, comprise about 20% of all mammalian species. They are classified under the order of *Chiroptera* and are found all across the world but Antarctica.[18] It is of interest to note that all continents except Antarctica have shown the presence of COVID-19.[19]

Bats are nocturnal. They can either be insectivores (insect-eater) or frugivores (fruit-eater), whereas other bats (i.e., vampire bats) practice hematophagia (feeding on blood). Surprisingly, bats provide numerous benefits to humans. For instance, their wastes, guano, are collected and used as fertilizer, since guano contains high levels of essential nutrients (nitrogen, phosphate and potassium) for plant growth. In addition, bats are a food source across Asia. However, they are natural reservoirs of various zoonotic pathogens.[20] Nearly 200 coronaviruses are identified in various bats species.[21] Many studies suggested that bats are a common reservoir for SARs-COV[22]; and the main bat reservoirs were identified in 2003.[23] Various bats species (i.e., *Taphozous perforatus*, *Rhinopoma hardwickii* and *Pipistrellus kuhlii*) are suggested to be the source of MERS-COV.[24] While not yet confirmed, studies suggest that the COVID-19 global outbreak was transmitted from bats to humans. This might occur directly or indirectly via an unknown, intermediate vector.[25,26] While more studies are needed for confirmation, a recent study showed Pangolin (armored anteater) as the intermediate host of COVID-19 virus.[27,28,29] Other studies suggested fish as the potential reservoir of infection from human-animal contact. Altogether, these studies demonstrated human-human transmission of COVID-19 through droplets from direct or indirect contact.[8,30,31] Developing tests at hospital settings showed that the virus is nosocomial, affecting 41% of patients based on incidence and transmission from asymptomatic carriers.[31,32,33,34,35,36,37]

Previously, the Asian palm civet cat (*Paradoxurus hermaphroditus*), a member of the *Viverridae* group, was reported as the reservoirs of SARs-COV from a wild animal market in Guangzhou, China.[38,39,40] The successful identification of this reservoir was pivotal in controlling the virus while suspending all trades of civet cats.[41] Therefore, the need to identify the reservoirs of the emerging COVID-19 outbreak is needed in order to take significant control of the disease and minimize mortality rate.

MERS-COV also has zoonotic origin. Numerous animals and birds were originally tested to identify MERS-COV's actual reservoirs. Results indicated dromedary camels as the actual reservoir (Table 1). Poultry markets in China were tested as the reservoirs for various type of influenza viruses. Learning from various studies concerning COVs and avian influenza, the authors suggested the following measured below in order to combat the virus and identify its reservoir. First, researchers should conduct serological testing of all animals sold at the Wuhan market prior to the widespread disease. This could provide information about the reservoirs and identify if other animals exposed to the virus have developed antibodies against COVID-19. Next, there is a need to investigate the seroconversion from any exposed animals. This is to confer protective immunity against the virus.

Preventative Measures

To decrease the global effect of COVID-19, government agencies, public health officials, and infection controls personnel need to urgently assess the nature of the virus while providing relevant information to the public. From previous experiences associated to MERS and SARs-COV, the World Health Organization (WHO) has been very critical in responding and recommending infection control interventions. This greatly helps to reduce risk of transmissions which include avoiding contact with affected individuals and wild animals, taking protective measures, and frequent handwashing. The WHO along with the US Centers for Disease Control and Prevention (CDC) have shared many preventative actions to minimize the risk of infection.[42,43] This includes various measures such as social distancing to slow down the rate of transmission (maintain 6 feet, 2 meters, away from each other), sneezing in clothing or disposable tissues, practicing cough etiquette (cover coughs), frequently decontaminating surfaces (i.e., door handles etc.), sheltering-in-place if required, and self-quarantining following domestic and international travels. This is in addition to not kissing (or other intimate social interactions), hugging, or handshaking. In consideration of these measures and the nature of the virus, many businesses are forced to be nonoperational, thus leading to global economic disaster, as the stock market has thus far shown.[44] These efforts are made to reduce the global impact of the virus, allow healthcare administrators and public health to better characterize the nature of the virus. This could greatly afford researchers to develop vaccines, therapeutics, and diagnostics measures in response to the virus in a timely manner. Health officials should constantly engage in circulating information, guidance and clarifying misinformation to the public. While the internet remains as the major source to relate and spread information, the public should be aware of fake news circulating the internet. The authors recommend individuals to follow credible sources for information (i.e., CDC, WHO, etc.).

Potential Treatments

Viruses bind to host receptors on target cell surface to generate infection. A recent study showed SARs-COV-2 (known as COVID-19) and SARs-COV use angiotensin-converting enzyme A (ACE-2) to gain entry into the cells.[45] ACE-2 can affect many tissues and organs in the human body since it is present in human's epithelia and small intestine including liver, lung, stomach, ileum, colon, and kidney.[46] This implies that coronaviruses can infect multiple organs (gastrointestinal and upper respiratory tracts). Identifying possible routes of COVID-19 infection could significantly have an impact on treatment of the virus. In this context, researchers have recently reported that the main target cell of COVID-19, AT2 cell is shown to express relatively low levels of ACE-2 in the lung.[45,47,48,49] This implies that COVID-19 may rely on co-receptors or other protein membranes to integrate into cell membrane, deposit its nuclear material, have that nuclear material integrated into host receptors on target cell surface, and have the host cell reproduce the viral particles until that host cell is dead and other cells are infected.[50] This is facilitated through the transmembrane protease serine 2 (TMPRSS2) for priming, where the virus is activated.[51] In this context, inhibition of TMPRSS2 could block cell entry by COVID-19, reduce the virus replication, and present a possible therapeutic pathways.

Currently, there is no effective treatment for COVID-19 and other COVs (i.e., MERS-COV); this is a significant obstacles facing the world. In the absence of known vaccines or medications, researchers are engaged in ongoing efforts to develop and validate medications to combat COVID-19 global pandemic. A number of vaccine candidates (~120) are now in clinical trials; and others are under testing. At the same time, researchers have focused on repurposing many drugs and traditional herbal medicines to combat the most severe cases of infection. Drug repurposing relies on the investigation of existing drugs for new therapeutic purposes.[52,53] This provides an effective way to rapidly recognize drugs with known side effects to be used while new drugs are under preparations.

Repurposing drugs such as hydroxychloroquine/chloroquine, used to prevent and treat malaria, in addition to autoimmune disease (rheumatoid arthritis, lupus, and porphyria cutanea tarda), is found to inhibit the replication of many DNA and RNA viruses– as in many coronaviruses.[54,55,56] The China National Center for Biotechnology Development (CNCBD) reported that infected patients (about 100) treated with chloroquine have showed improvements in their lung and decline in fever. In addition, these patients rapidly recovered when compared to the control groups. With the promising results from these studies, the Chinese Government proposed chloroquine as the front line drug treatment for the severe COVID-19 outbreak.[57,58,59,60] Ten clinical trials are underway to investigate the chloroquine as an anti-COVID-19 therapy.[61] While the drug is well known,[62,63] adverse side effects from COVID-19 patients treated with chloroquine need to be investigated. In the meantime, chloroquine remains as the available drug to fight the disease in China and other countries are suggested to use it. However, ongoing researches have shown that the use of hydroxychloroquine/chloroquine might be detrimental to COVID-19 infected patients.

In addition to chloroquine, teicoplanin can be an alternative drug for the treatment of COVID-19.[64] Teicoplanin has been found to significantly inhibit cellular entry of Ebola virus, SARs-COV and MERS-COV.[65] This antibiotic drug also shows efficacy against Staphylococcal infections, hepatitis C virus, HIV virus and influenza virus.[65,66] Further investigations are needed for the inclusion of teicoplanin as a potential repurposing drug for the treatment of COVID-19 global outbreak.

Remdesivir, a purine nucleoside analogue, is a broad-spectrum antiviral medicine developed by Gilead Sciences; it was previously used to treat Ebola and Marburg virus infection.[67] The medication was found to show antiviral activity against other single-stranded RNA viruses, such as respiratory syncytial virus and COVs.[68,69,70] Remdesivir is currently in clinical trials in Nebraska and China on hospitalized patients with COVID-19 to evaluate its safety and efficacy. Although this medication has been administered to patients, there is no available data on whether it can improve clinical outcomes.

Interferon Alfa-2B is an antiviral medicine used to treat hepatitis B and C, certain types of cancer, and genital warts. The medication was developed in Cuba; it is currently in clinical trials to treat COVID-19 patients in China, where the virus originally emerged.[71,72] Due to the absence of a general treatment, repurposing drugs such as those described above are suggested as potential treatments for patients infected with COVID-19, while researchers are investigating actual treatments.

Table 2. Medicinal Plants with Therapeutic Histories

Plants	Bioactive/antiviral compounds	Therapeutics
Zingiber officinale	Gingerol; Shogaols	Human respiratory syncytial virus
Allium sativum	Allicin	Influenza virus
Euphorbia hirta	Afzelin; Quercitin; Myricitrin; Rutin; Garlic acid; Caffeic acid	Asthma conjunctivitis
Curcuma longa	Curcumin	Dengue virus; Hepatitis C virus; Zika virus, Chikungunya virus
Olea europaea	Oleuropin	Herpes; mononucleosis; hepatitis virus; rotavirus; bovine rhinovirus; canine parvovirus; feline leukaemia virus; Respiratory syncytial virus; Parainfluenza type 3 virus
Aloe vera	Emodin; Chrysophanol; Aloe-emodin	Human respiratory syncytial virus
Allium Cepa	Quercetin; Isorhamnetin; Kaempferol; Myricetin	Human immunodeficiency virus (HIV); Herpes simplex virus type 1; Poliovirus type 1; Para-influenza virus type 3; Potato virus
Garcenea Kola	Kolaviron	Influenza virus; Hepatitis; Diarrhea; Laryngitis; Bronchitis; Gonorrhoea; Chest colds; Caughs
Echinacea	Caffeic acid	Colds; Influenza; Lung conditions; Candidiasis; Influenza A virus; Herpes simplex virus; Polio virus

Note: See reference [73] for a comprehensive review

In addition to repurposing drugs, various plants containing bioactive compounds have shown to be effective against previous coronaviruses. These plants include *Zingiber officinale*, *Allium cepa*, *Allium sativum*, *echinacea*, *euphorbia hirta*, *Garcenea kola*, *Curcuma longa*, *Aloe vera* and *olea europaea* (Table 2). The natural compounds from these plants could have potency to inhibit TMPRSS2, thus reducing the virus (COVID-19) replication. Research to better understand the mechanism of these herbal medicines are not yet fully available. However, herbal medicines have been produced in higher demands due to their use against COVID-19 (i.e., Madagascar). Countries such as China, Thailand, Bolivia, Tunisia, India, Haiti, Madagascar, and Nigeria have their respective traditional herbal medicine against the virus.[73,74,75,76,77,78,79] In a study reported by the National Health Commission of the People's Republic of China, of the 74,187 patients treated with traditional herbal medicines, nearly 90% of them have recovered. This further proves the potential use of herbal medicines to fight COVID-19 while given researchers more time to develop potential vaccines.

4. CONCLUSION

The novel coronavirus disease (COVID-19) is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARs-COV-2). To date, the virus remains a global health issue, affecting 6,057,853 individuals with 371,166 confirmed deaths (6.13 % mortality rate) in more than 120 countries and territories. This emerging virus continues to cause a public health issue, economic disaster, physiological distress–including discrimination, and limit human activities.[80,81]

While the source of the virus and its immediate host remain controversial, researchers are engaged in ongoing efforts to develop and validate medications to combat the COVID-19 global pandemic. Due to the absence of a general treatment, many repurposing drugs and traditional herbal medicines are suggested as potential treatments for patients infected with COVID-19.

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