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COVID-19: a conundrum to decipher

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Abstract. – OBJECTIVE: Recent worldwide outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of respiratory coronavirus disease 2019 (COVID-19), is a current, ongoing life-threatening crisis, and international public health emergency. The early diagnosis and management of the disease remains a major challenge. In this review, we aim to summarize the updated epidemiology, causes, clinical manifestation and diagnosis, as well as prevention and control of the novel coronavirus SARS-CoV-2.

MATERIALS AND METHODS: A broad search of the literature was performed in "PubMed" "Medline" "Web of Science", "Google Scholar" and "World Health Organization-WHO" using the keywords "severe acute respiratory syndrome coronavirus", "2019-nCoV", "COVID-19, "SARS", "SARS-CoV-2" "Epidemiology" "Transmission" "Pathogenesis" "Clinical Characteristics". We reviewed and documented the information obtained from literature on epidemiology, pathogenesis and clinical appearances of SARS-CoV-2 infection.

RESULTS: The global cases of COVID-19 as of April 2, 2020, have risen to more than 900,000 and morbidity has reached more than 47,000. The incidence rate for COVID-19 has been predicted to be higher than the previous outbreaks of other coronavirus family members, including those of SARS-CoV and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The main clinical presentation of SARS-CoV-2 infection ranges from asymptomatic stages to severe lower respiratory infection in the form of pneumonia. Most of the patients also presented with fever, cough, sore throat, headache, fatigue, myalgia and breathlessness. Individuals at higher risk for severe illness include elderly people and patients with a weakened immune system or that are suffering from an underlying chronic medical condition like hypertension, diabetes mellitus, cancer, respiratory illness or cardiovascular diseases.

CONCLUSIONS: SARS-Cov-2 has emerged as a worldwide threat, currently affecting 170 countries and territories across the globe. There is still much to be understood regarding SARS-CoV-2 about its virology, epidemiology and clinical management strategies; this knowledge will be essential to both manage the current pandemic and to conceive comprehensive measures to prevent such outbreaks in the future.

Key Words:
COVID-19, SARS-CoV-2, Coronavirus, 2019-nCoV, SARS.

Introduction

The recent outbreak of novel coronavirus is of grave international concern. Although zoonotic in its origin, an evolved strain of coronavirus can be fatal for humans. Coronaviruses SARS-CoV and MERS-CoV, in particular caused especially detrimental effects on humans. Recently identified novel Coronavirus (2019-nCoV or SARS-Co-V-2) is the seventh coronavirus known to infect humans[1]. The origin of the SARS-CoV-2 is believed to have been in the Wuhan City of Hubei Province of China, which now has spread over to the rest of the world.

The majority of the patients in local hospitals in China presented with the severe infection of the lower respiratory tract in the form of pneumonia of unknown etiology[2]. Many of these patients were confronted with the Huanan seafood market in Wuhan City, known to have a lot of exotic live animals and their parts. It is suspected that coronavirus likely crossed over from this market to

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humans. On December 31st 2019, China notified the World Health Organization about the outbreak of virus and soon after the seafood market was closed[2]. On 7th January 2020, the infectious organism was identified as a strain of coronavirus with >95% homology to bat coronavirus and > 70% similarity with SARS-CoV-1. Although the origin of SARS-CoV-2 has been postulated to be from bat coronavirus, still the intermediary carrier from which it has crossed over to humans remains uncertain. Current suspects as an intermediary carrier for human transmission of this virus include pangolins and snakes. The series of events for progression of COVID-19 to become a pandemic[3] are shown in Figure 1.

An increasing number of patients were put under surveillance with similar complications of severe respiratory distress and an exponential increase in the number of cases was reported thereafter. Modelling studies had reported 1.8 days for the epidemic doubling[4]. It was identified that the people who were not exposed to the seafood market also presented with similar types of symptoms, raising some doubt about the transmission of the virus *via* human-to-human contact[5]. Comprehensive surveillance is necessary to attenuate the human-to-human transmission, which can foster viral genome mutation and the potential for increase virulence. The outbreak has spread substantially to encompass most countries of the world to infect > 900,000 people, including >47,000 deaths as of April 2, 2020 (Figure 2).

Basic Reproductive Number (R_0) of SARS-CoV-2

The basic reproductive number is the average number of secondary cases produced by one infected individual introduced into a population of susceptible individuals, where an infected individual has acquired the disease, and susceptible individuals are healthy but can acquire the disease. Here, concerning COVID-19 cases, it will be difficult to precisely estimate the R_0 for the SARS-CoV-2, as limited population screening has made it difficult to identify the exact number of infected cases during the epidemic. The other factors affecting the R_0 are environmental circumstances, demography, and statistical methodologies. Presently, the estimated R_0 for SARS-CoV-2 has been estimated to be 2.4-3.58 days; in comparison to other deadly viruses (Table I).

Comparison of SARS-CoV-2 with Other Family Members Infective to Humans

To date, seven coronaviruses have been identified that are known to infect humans *via* zoonotic

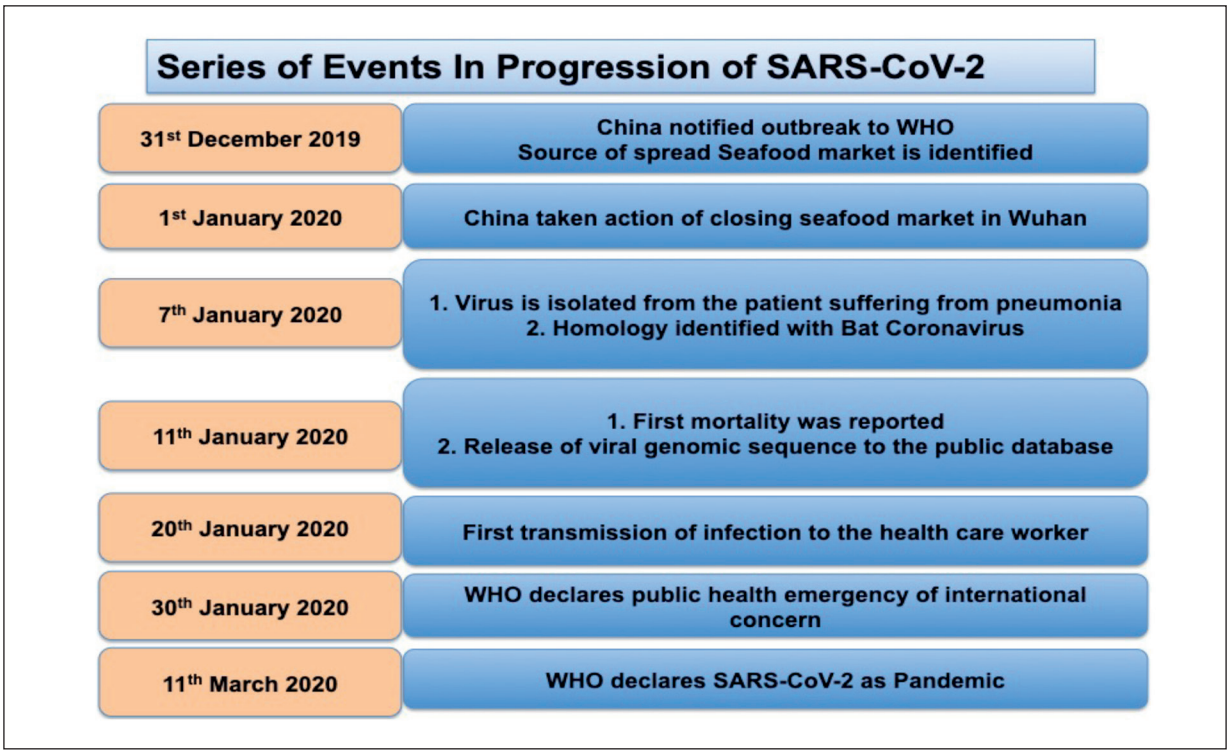

Figure 1. Series of events in the progression of COVID-19.

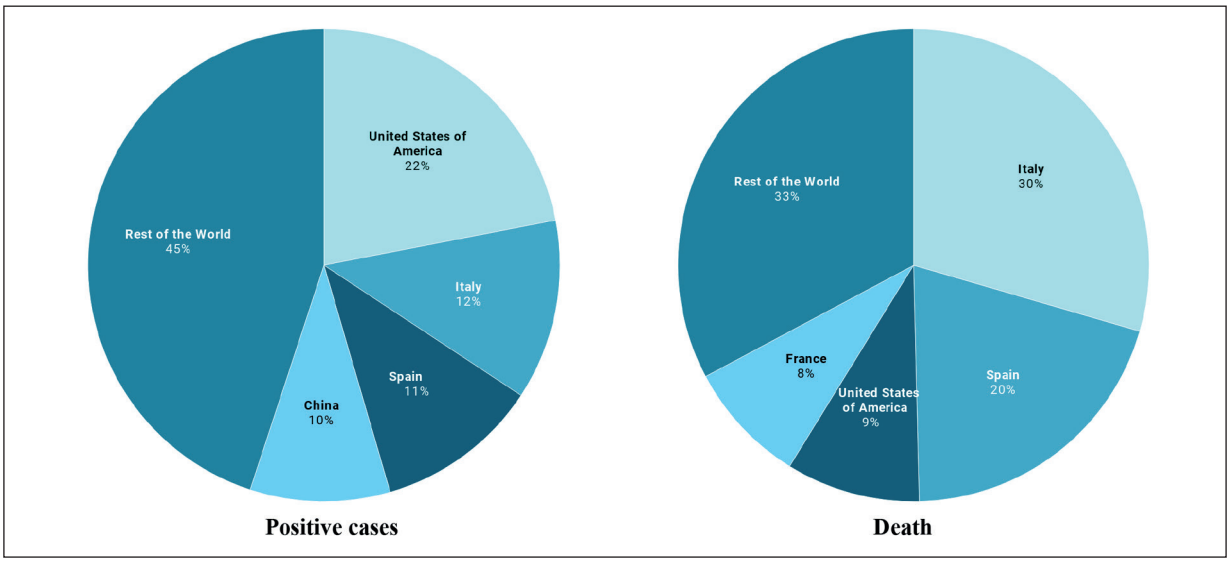

Figure 2. Global distribution of positive cases and death due to COVID-19.

transmission. SARS-CoV-1 MERS-CoV, SARS-CoV-2 can cause severe respiratory diseases in humans while others, such as HKU1, NL63, OC43, 229E were associated with mild symptoms[12].

Structure

The coronavirus family was initially discovered in the 1960s and classified under the family Coronaviridae, which is the largest family within the order Nidovirales. Family coronaviridae includes two subfamilies: Orthocoronavirinae and Torovirinae. Orthocoronavirinae encompasses four genera; alpha, beta, gamma and delta coronavirus[1]. Coronaviruses are spherical, enveloped (lipid bilayer derived from the host cell membrane) positive-sense single-stranded RNA viruses ranging from 60 nm to 140 nm in diameter. It resembles a crown-like appearance with spike-like projections radiating from the surface during the electron-microscopic examination[13]. Spikes on the coronavirus surface contains glycoprotein, which attaches to the host cell membrane, and is hypothesized to play a major role in facilitating virus entry into the host cell. This spike glycoprotein is a key target for vaccine, therapeutics and diagnostics.

Mode of Transmission

The spread of coronavirus infection to humans is mainly achieved by the domestic animals with modified genomic recombination. Previous to the onset of SARS-CoV-2, two previous incidences were reported where the transmission of the animal coronaviruses to the human-caused severe disease and mortality. The first instance was in 2002-2003 when the beta-coronavirus, which was originated from bats, crossed over to humans *via* the palm civet cats in the Guangdong province of China. It was designated as SARS-Co-V-1 and was widely transmitted with a mortality rate of around 11% before being contained[14]. SARC-CoV-1 has been found to infect the type 2 pneumocytes and non-ciliated bronchial epithelial cells and to exploit angiotensin-converting enzyme 2 (ACE2) as a receptor

Table I. Basic reproductive number for various viruses.

Sr No	Disease	Year	Ro
1	Smallpox[6]	1968-1973	3.5-6
2	SARS[7]	2002-2003	2-5
3	H1N1[8]	2009	1.3-1.7
4	MERS[9]	2012	2.7- 3.9
5	Ebola haemorrhagic fever[10]	2014	1.5-2.5
6	Novel Coronavirus[11]	2019-2020	2.4-3.58

and functional mediator[15]. After a decade in 2012, another outbreak of coronavirus with bat origin (MERS-CoV) emerged in the Middle East and affected more than 200 peoples with an approximately 34% of mortality rate[16]. The identified receptor for the MERS-CoV is dipeptidyl peptidase 4 (DPP4), a transmembrane glycoprotein also expressed type 2 pneumocytes and non-ciliated bronchial epithelial cells[17].

It has been found that human infection from coronaviruses is transmitted through bats, which acts as a primary host for the virus. The intermediate hosts in the SARS-CoV-1 were identified as civets and raccoon dogs[18]. MERS-CoV has a similar primary host as SARS-CoV-1 but the intermediate hosts were identified as camels in the Middle East part of the world[17]. The current SARS-CoV-2, not surprisingly is also thought to act probably on the ACE2 receptors causing severe respiratory distress and pneumonia and binds to the ACE2 receptors with higher affinity as compared to the SARS-CoV-1. With humans as a terminal host, the primary host for SARS-CoV-2 again was identified as a bat and suspected intermediate hosts incudes pangolins and snakes[2] (Figure 3).

Human to human transmission of viral respiratory infections occurs through the droplets of varying sizes generated during coughing and sneezing. If the droplets are more than 5-10 um, they are referred to as respiratory droplets and if the size is less than 5 um, they are termed as droplet nuclei[19]. According to current evidence[20], the COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes. The droplets can spread up to 7-8 meters under favorable environmental conditions, such as humidity and temperature, the gas cloud and its payload of pathogen[21]. Transmission may also occur through fomites in the immediate environment around the infected person[22]. Therefore, the transmission of the COVID-19 virus can occur by direct contact with infected people and indirect contact with surfaces in the immediate environment or with objects used on the infected person.

One of the studies evaluated the stability of SARS-CoV-1 and SARS-CoV-2 in aerosols (less than 5 um) and on various surfaces using a Bayesian regression model under the controlled condition. SARS-CoV-1 and SARS-CoV-2 remains in the aerosol form for up to 3 hours. SARS-CoV-2 is more stable on stainless steel and plastic surfaces for 48 hours and 72 hours respectively. On the copper surface, the stability of SARS-CoV-2 is 4 hours as compared to SARS-CoV-1, which is 8 hours. On cardboard surface SARS-CoV-2 will remain stable till 24 hours as compared to SARS-CoV-1, which is 8 hours[23].

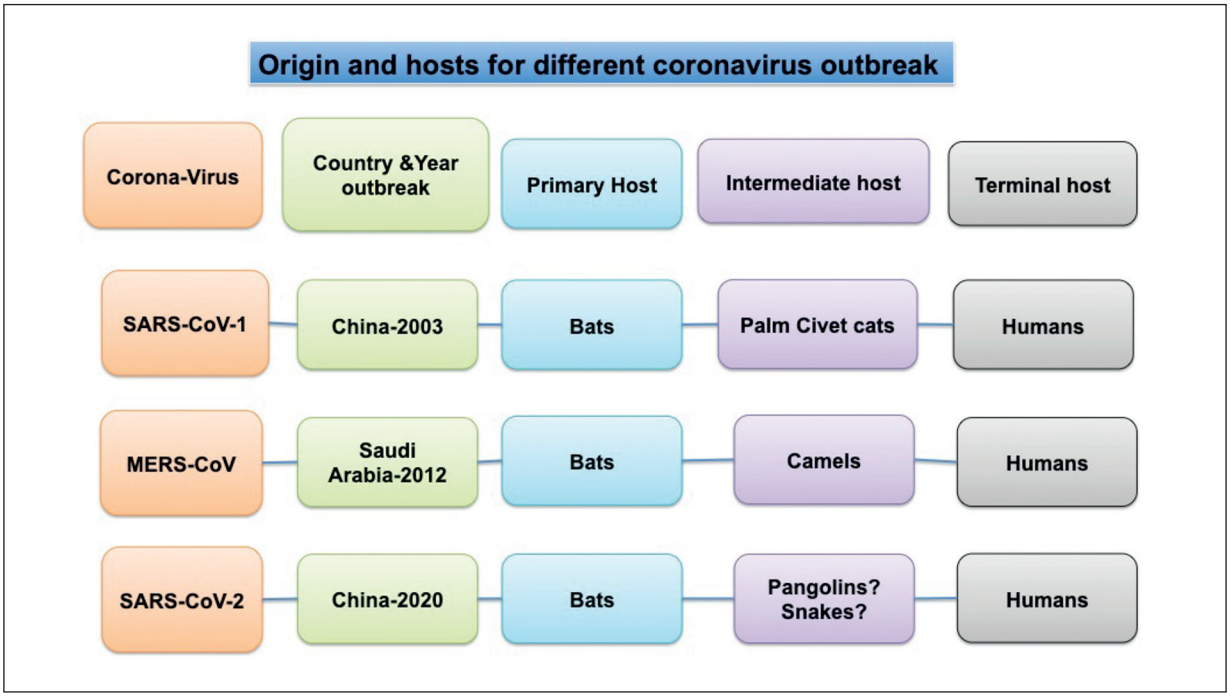

Figure 3. Origin and hosts of various Corona-viruses.

The incubation period identified for the entire human infection-causing viral group has been identified as between 2-14 days. Therefore, at least 14 days of quarantine is mandatory for avoiding the transmission. But the fatality rate for the current SARS-CoV-2 (3-4%) is, fortunately, less as compared to SARS-CoV-1 (10%) and MERS-CoV (approx. 35%)[24]. However, the ultimate fatality rate will not be accurately known until the containment of the disease is attained.

Presenting Features of COVID-19 Patients

Individuals of all ages are susceptible to SARS-CoV-2 infection. Diseases in neonates, infants and children have also been reported but the disease is significantly milder as compared to adult counterparts. The infection and symptoms were significantly less in children below 12 years of age. It is possible that in children more than 12 years of age, the overall immune status is stronger than adults[25]. Vaccinations may also play an important role in the case of children, as they tend to be more up to date with the vaccines, which may prevent them from other secondary infections often triggered by the primary infection[26].

Varied signs and symptoms were observed in patients infected with SARS-CoV-2. The presentation ranges from asymptomatic stages to severe lower respiratory infection in the form of pneumonia. Most patients initially present with fever, cough, sore throat, headache, fatigue, myalgia and breathlessness[27]. Observations indicate that patients with severe disease progress to pneumonia at the end of the first week followed by respiratory failure and possible death. For the majority of patients, recovery starts in the second or third week of infection. Individuals suspected or confirmed positive SARS-CoV-2, but with mild disease can be discharged from the hospital or discontinued from the quarantine based on the following criteria:

- Normal body temperature lasting longer than 3 days;
- Resolved respiratory symptoms;
- Substantially improved acute exudative lesion on chest CT images;
- Two consecutive negative RT-PCR test results separated by at least 1 day.

Negative patients should be correlated with the history of contact, clinical observation and epidemiological information.

Primary Diagnosis for SARS-CoV-2

Patient diagnosis is based upon the clinical presentation of features, such as fever, sore throat, headache, fatigue, myalgia, respiratory distress and breathlessness. In suspected cases, confirmative diagnosis is only possible using specific molecular tests performed on the respiratory samples collected from the throat, nasopharynx, sputum, endotracheal aspirates or bronchoalveolar lavage in more critical patients[28]. The definitive diagnosis is based on the PCR analysis[29] of various type of samples from symptomatic patient, such as:

- Throat swab, nasal swab-dacron or polyester swab transported to laboratory 4°C – in viral transport medium in the cold chain, swabs should be placed in the same tube to increase viral load;
- Bronchoalveolar lavage – collection in a sterile container – transported to the laboratory at 4°C;
- Tracheal aspirate, nasal wash, nasopharyngeal aspirate – collection in a sterile container – transported to the laboratory at 4°C;
- Sputum – collection in a sterile container – transported to the laboratory at 4°C;
- Tissue/biopsy – sterile container with saline – transported to the laboratory at 4°C;
- Two serum samples – 3 to 5 ml – transported to the laboratory at 4°C – paired samples collection – acute – first week of illness, convalescent – 2 to 3 weeks later.

Chest X-rays usually show bilateral infiltrates, but findings may not be present in the early stages of the infection. CT is a more reliable, sensitive and specific investigation. CT images generally show infiltrates, ground-glass opacities and subsegmental opacities. The recommended current scenario is to perform the CT investigation for the diagnosis of COVID-19 in suspected cases with negative molecular results[30].

Emerging Challenges and Treatment Strategies for the Treatment of COVID-19 Infection

The exponential increase in cases of COVID-19 from SARS-CoV-2 infection and resulting respiratory illness poses a global public health threat that is currently challenging medical and research communities. In response to the outbreak, many affected countries have enforced travel restrictions and lockdown in attempts to attenuate fur-

ther transmission of this disease. Many asymptomatic patients still can transmit SARS-CoV-2 and later become symptomatic for COVID-19 infection[31]. Currently, a major challenge with COVID-19 infection is the treatment of a patient with a weak or compromised immune system or that is also suffering from a chronic medical condition, like cancer, respiratory illness or cardiovascular diseases.

SARS-CoV-2 Infection in Hypertensive, Diabetic and Cardiovascular Disease Patients

Recent reports suggest a higher risk of SARS-CoV-2 infection-related mortality in patients with hypertension, diabetes mellitus, and cardiovascular diseases[32-34]. He et al[32] conducted a study in 54 patients and reported the highest mortality in patients with hypertension (44.4%), diabetes (24.1%) and coronary heart disease (14.8%). Another study[34] from China employing a larger cohort consisting of 191 patients yielded similar findings and established that the risk factor for mortality was highest in the patients with hypertension (30%), followed by diabetes (19%) and coronary heart disease (8%). A third study related to the morbidity examined 140 cases of COVID-19 in the context of underlying medical conditions: 30% had hypertension and 12% had diabetes[33]. These reports indicate that severe or critically ill COVID-19 patients with concurrent hypertension, diabetes and cardiovascular disease have a significantly higher risk of mortality and require special attention during their hospitalization.

Fournier et al[35] suggested that patients treated with ACE inhibitors are more likely to receive treatment intensification when exposed to NSAIDs. This study also suggested that ACE2 expression is increased through the use of ibuprofen, in diabetic patients and those treated with angiotensin II type-I receptor blockers. NSAIDs can antagonize the effects of anti-hypertensive drugs by inhibiting cyclo-oxygenase and prostaglandin secretion[36]. Several pharmaco-epidemiological studies have evaluated the cardiovascular risk associated with nonsteroidal anti-inflammatory drugs (NSAIDs) in coronary disease[36] or heart failure[37]. Johnson et al[38] performed a meta-analysis and found that NSAID exposure increases the blood pressure by 5.4 mm of Hg in previously controlled hypertensive subjects. In Pope et al[39] the range of increase of blood pressure was found to be 3.5-6.2 mm of Hg for Indomethacin, naproxen and piroxicam. Consequently, it was suggested that increased expression of ACE2 in these co-morbid patients could facilitate infection with COVID-19[40]. Hence, the patients who require the NSAIDS will preferentially require an anti-hypertensive drug not interfering with the renin-angiotensin pathway.

SARS-CoV-2 Infection and Pregnancy

Pregnant women are susceptible to severe illness after SARS-CoV-2 infection because of perinatal physiological changes in their immune and cardiopulmonary systems[41]. Li et al[42] suggest that vertical transmission can be prevented by delivery *via* caesarean section in a negative-pressure operating room. SARS-CoV-2 infected pregnant women showed that delivery in 38% of the women delivery was by emergency caesarean section due to pregnancy complications. These complications include fetal distress, premature rupture of the membrane or stillbirth. Also, 46% of the women experienced preterm labor[42]. An analysis[43] of 38 pregnant women with COVID-19 showed that unlike in SARS and MERS infections, COVID-19 did not lead to maternal deaths and no evidence of intrauterine transmission of SARS-CoV-2 was found.

In a recent study[44], key recommendations were provided for the management of COVID-19 infections at the time of delivery. These recommendations were based on the optimal delivery timing and the safety of vaginal/caesarean delivery to prevent vertical transmission. As an initial management, it is recommended that women with confirmed SARS-CoV-2 infection should be admitted and isolated in an intensive care unit with negative pressure rooms. When possible, uteroplacental oxygenation is improved while lying in a lateral-decubitus position, regardless of the mother's respiratory status. Additional prudent measures include managing perinatal care by electronic fetal heart rate monitoring, lowering the delivery timing and delivery in a negative pressure isolation ward. Placenta from infected women should be considered as biohazardous waste. A rapid cord clamping and cleaning of the neonate is recommended. To avoid further transmission of the virus, women should use personal protection and should be in isolation until the recovery from delivery[44]. Overall, the perinatal and neonatal management plans for prevention and control of COVID-19 needs special consideration[45].

SARS-CoV-2 Infection in Patients Undergoing Transplantation

Li et al[46] reported two microbiologically confirmed COVID-19 cases in heart transplantation patients detected in the Hubei province in China. These two patients presented with variable severity of the disease, however, both patients survived after infection[46]. It is now evident that immunosuppressed patients may have a higher risk of COVID-19 complications, a credible concern for patients undergoing organ transplantation. However, the role of transplantation related immunosuppression effects on predisposition to acquire SARS-CoV-2 infections is not known. Therefore, the American Society of Transplantation and the Transplantation Society have updated their factual information to provide specific clinical guidelines on COVID-19 and transplantation[47].

SARS-CoV-2 Infection in Patients with Digestive Disorders

A descriptive, cross-sectional, multi-centric study on 204 patients with COVID-19 infection revealed that digestive disorder symptoms are common in admitted patients[48]. The most common symptoms in these cases were lack of appetite (78.6%), diarrhoea (34%), vomiting (3.9%), and abdominal pain (1.9%). However, the lack of appetite was excluded from this study for further analysis. These patients also had evidence of longer coagulation and higher liver enzyme levels. According to this report[48], in rare cases patients can even present with digestive symptoms in the absence of respiratory symptoms. Mild to moderate liver dysfunction as evidenced by elevated aminotransferases, hypoproteinaemia and prothrombin time prolongation has been reported in clinical investigations of COVID-19. However, there is no clear indication of specific SARS-CoV-2 infection in the liver[49].

SARS-CoV-2 Infection in Cancer Patients

Cancer patients are more susceptible to infection because of their immune suppression caused by malignancy and anti-cancer treatment. Liang et al[50] conducted a study in China during the COVID-19 outbreak which indicated a higher incidence in individuals with cancer history compared to the healthy Chinese population. Among the cancer patients, lung cancer was the most frequent cancer type to be associated with COVID-19[50]. Strict protection to lung cancer patients is required because of difficulties in differentiating clinical symptoms of lung cancer from COVID-19. This necessitates the development of the individual clinical management strategies for these cancer patients during the current COVID-19 outbreak[51,52]. It is recommended that immunotherapy treatment for lung cancer patients should be carefully weighed, given the potential pulmonary toxicity and adverse effects of lung injury from immunotherapy[53]. A recent report[54] revealed that two patients who underwent lung lobectomies for adenocarcinoma also showed an early phase of the lung pathology of COVID-19 pneumonia. Zhang et al[55] suggest continuing use of treatment for lung cancer patients with SARS-CoV-2 infection. As clinical management, intensive care and CT scans should be performed in the case of pneumonia exacerbation and cancer progression[55].

To date, there is no original research published showing specific treatment strategies for hepatobiliary, gastrointestinal, colorectal, gynaecological and breast malignancies during the outbreak of COVID-19, but rather discussion and suggestions for general clinical management of cancer patients in the current context [56-62].

Overall standard care should be pursued to integrate social distancing concepts as possible during diagnosis, treatment and follow-up treatment to avoid and minimize the SARS-CoV-2 infection to cancer patients. Alternative treatment strategies may also be required during the current COVID-19 pandemic to appropriately manage clinical cancer practice.

Treatment Strategies for COVID-19

ACE2 has been identified as the most likely cell receptor for SARS-CoV2, the same as found for SARS-CoV and HCoV-NL637[63,64]. Xu et al[65] suggest a strong interaction between SARS-CoV-2 spike protein and the human ACE2 molecule, which plays an important role in cellular entry within ACE2 expressing cells. Zou et al[66] identified the various organs and located specific cell types that are vulnerable to SARS-CoV-2 infection. The ACE inhibitor has been shown to prompt increased expression of ACE2 receptors, however, there is no current evidence related to the worsening of SARS-CoV-2 infection in humans treated with ACE inhibitor. More detailed studies are required to assess the effect of the ACE inhibitor on SARS-CoV-2 infection in humans exhibiting COVID-19.

The researchers are currently underway to develop the various vaccine candidates for clinical trials, as well as therapeutics for lethal COVID-19. However, to date no effective vaccine or therapeutics have been approved for clinical use. Recent reports[67-70] suggest that many healthcare professionals have tried various combinations of previously approved antibiotics, anti-viral, anti-malarial and anti-HIV drugs to treat the COVID-19 affected patients (Table II). A randomized trial[67] of HIV anti-viral drug lopinavir-ritonavir combination on 199 patients with laboratory-confirmed SARS-CoV-2 infection showed no benefits beyond the standard care. Clinical trials in China have been initiated based on *in vitro* studies[68,70] which revealed that the anti-malarial drug, chloroquine can significantly reduce the viral replication of coronaviruses. However, the safety and efficacy of this drug to COVID19 treatment is still under investigation[69].

Currently, 20 active clinical trials have been registered for potential COVID-19 treatments to study the safety and efficacy of various drug and antibody combinations (**Supplementary Table I**). In these clinical trials various drugs and their combinations like Bromhexine Hydrochloride, Arbidol Hydrochloride, recombinant human Interferon 1b and 2b, Methylprednisolone, thymosin alpha 1, Bevacizumab, Fingolimod (0.5 mg), Remdesivir, Darunavir and Cobicistat, Nitric Oxide, Favipiravir combined with Tocilizumab, methylprednisolone, Lopinavir/ritonavir and Ribavirin as well as many biological agents like Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector), mesenchymal stem cells, mRNA-1273, NK Cells, are being tested in COVID-19 patients.

Precautions to Prevent the Spread of COVID-19

Indeed, "prevention is always better than cure" and current prevention strategies are aimed at minimizing social interaction and attenuating transmission of SARS-CoV-2. To prevent the spread of the coronavirus international travel should be limited or avoided if needed. The virus can remain viable on the surface for days but can be easily destroyed by the alcohol-based hand sanitizers, sodium hypochlorite and hydrogen peroxide[71].

Prevention strategies for COVID-19 are very much similar to those for other respiratory infections; the most straightforward prevention measure is to avoid contact with those afflicted. The efficacy of N95 or surgical masks for preventing SARS-CoV-2 infection is indeterminate, and a current global shortage has prompted recommendations against their use by the general public so that existing stocks may be reserved for use by medical staff. It is worth noting that use of masks has not been associated with a lower risk of laboratory-confirmed influenza[72].

To be effective, N95 and surgical masks must fit properly to seal against entry of airborne droplets. Also, as SARS-CoV-2 is encapsulated, washing the hands for more than 30 seconds with soap and hot water is a facile means for avoiding the transmission of the virus. Lastly, frequent cleaning of doorknobs, doors, handrails and other contact surfaces should be implemented to avoid transmission of infection.

Conclusions

COVID-19 is a life-threatening disease supportive care as the current primary treatment option

Table II. A brief list of drugs under clinical trials for COVID-19 patients.

Sr. No.	Drugs under clinical trial	Mechanism of action
1.	Chloroquine Phosphate	9-aminoquinolone Inhibit the viral replication by increasing endosomal PH
2.	Ritonavir	Protease inhibitor
3.	Lopinavir	Protease inhibitor
4.	Oseltamivir	Neuraminidase inhibitor
5.	Favipiravir	Inhibits RNA-dependent-RNA-polymerase
6.	Fingolimod	Sphingosine 1-phosphate receptor modulator
7.	Remdesivir	Adenosine nucleotide analogue
8.	Bevacizumab	Inhibitor of VEGF-A
9.	Lironlimab	Anti-CCR-5 receptor antibody
10.	Methylprednisolone	Decrease the inflammatory cytokine cascade, inhibiting the activation of T cells
11.	Darunavir	Protease Inhibitor
12.	Tocilizumab	Anti-human IL6-receptor antibody

due to the lack of a vaccine or effective antiviral therapy. It poses a higher risk to the aged and immune-compromised individuals and mortality is accordingly disproportionate within these populations. It is essential to learn and incorporate the recent scientific knowledge into the current practice and clinical management of this disease to minimize the spread of SARS-CoV-2. Also, as future outbreaks of viruses and pathogens are inevitable, we need to devise comprehensive measures to prevent and manage such public health emergencies resulting from infectious disease.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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