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**Title: 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 knowledge", and "Google Scholar" 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 attained 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 othercoronavirus 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 a underlying chronic medical condition like hypertension, diabetes, 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.

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## 1. 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 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 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 includes pangolins and snakes. The series of events for progression of COVID-19 to become a pandemic[3] are shown in Figure 1.

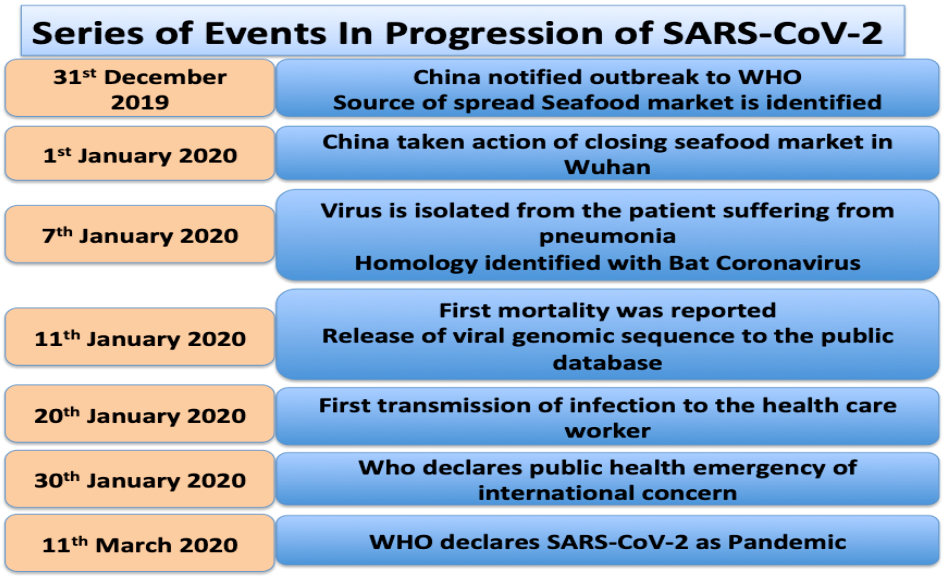


**Figure 1: - Series of events in the progression of COVID-19**

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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. Modeling 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).

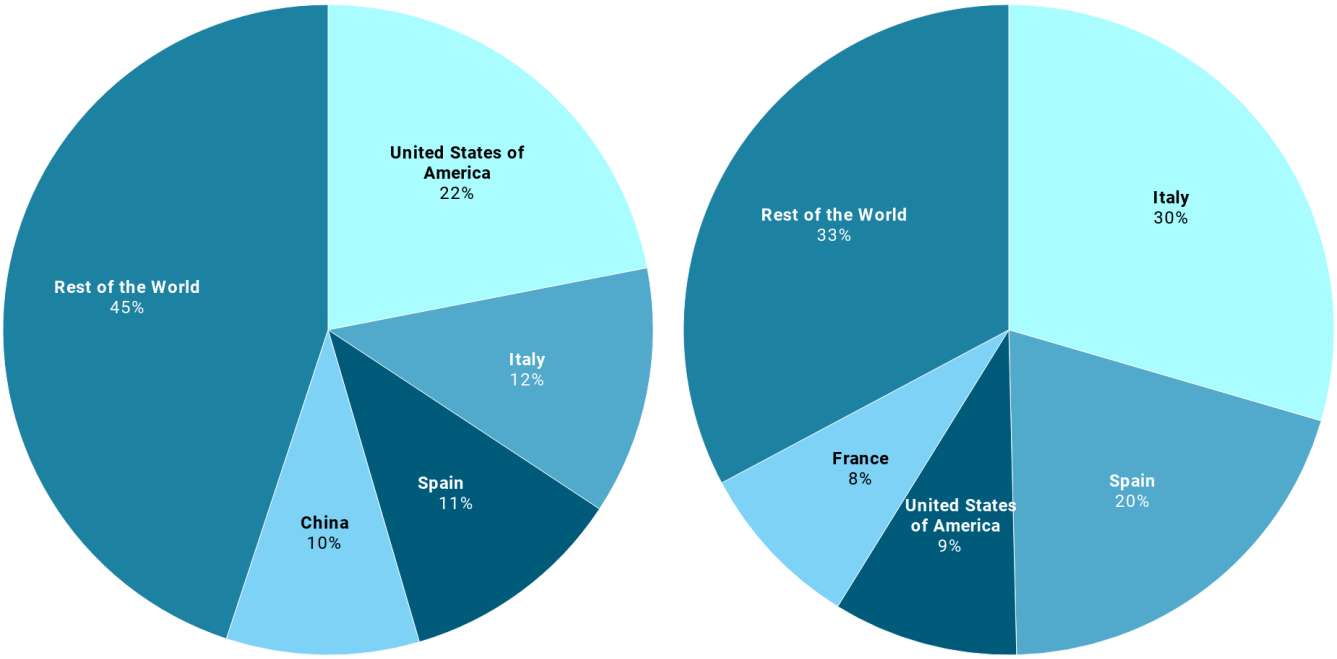


**Figure 2: - Global distribution of Positive cases and death due to COVID-19.**

## 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

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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).

**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 |

## 3. 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 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].

### 3.1 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 60nm to 140nm 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 entery into the host cell. This spike glycoprotein is a key target for vaccine, therapeutics and diagnostics.

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### 3.2 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 and functional mediator [15]. After a decade in 2012, another outbreak of corona virus 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).

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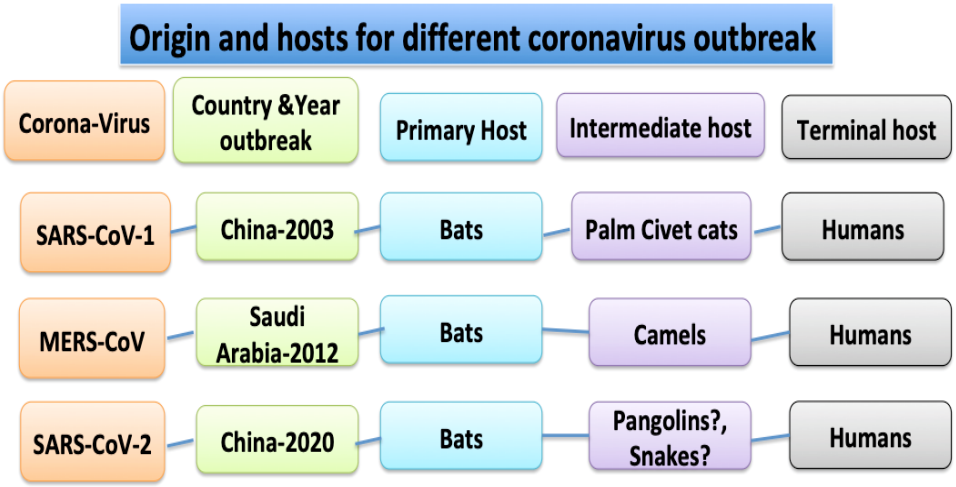


**Figure 3: - Origin and hosts of various Corona-viruses.**

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 5-10um, they are referred to as respiratory droplets and if the size is less than 5um, they are termed as droplet nuclei[19]. According to current evidence, the COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes[20]. 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 5um) 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 3hours. 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].

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

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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.

## 4. 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 tens to be more up t 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 presets 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.

## 5. 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

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suspected cases, confirmative diagnosis is only possible using specific molecular tests perfomed 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 $4^0$C - in viral transport medium in 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 $4^0$C
- Tracheal aspirate, nasal wash, nasopharyngeal aspirate- collection in sterile container- transported to the laboratory at $4^0$C
- Sputum - collection in a sterile container- transported to the laboratory at $4^0$C
- Tissue/biopsy- sterile container with saline- transported to the laboratory at $4^0$C
- Two serum samples- 3 to 5 ml- transported to the laboratory at $4^0$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].

## 6. 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 further transmission of this disease. Many asymptomatic patients still can transmit SARS-CoV-2 and later become symptomatic for COVID-19 infection[31].

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Currently, a major challenge with COVID-19 infection is the treatment of a patient with the weak or compromised immune system or that are also suffering from a chronic medical condition like cancer, respiratory illness or cardiovascular diseases.

### 6.1 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 and cardiovascular diseases[32-34]. He XW 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 from China employing a larger cohort consisting 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%)[34]. A third study related to the morbidity examined 140 cases of COVID-19 in the context of underling 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..

A study by 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 in those treated with angiotensin II type-I receptor blockers. Several pharmaco-epidemiological studies have evaluated the cardiovascular risk associated with nonsteroidal anti-inflammatory drugs (NSAIDs) in coronary disease[36] or heart failure[37]. NSAIDs can antagonize the effects of anti-hypertensive drugs by inhibiting cyclo-oxygenase and prostaglandin secretion[36]. 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 one of the studies done by Pope et al[39] 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.

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### 6.2 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]. A report suggests that vertical transmission can be prevented by felivery via cesarean section in a negative-pressure operating room[42]. Another study on 13 SARS-CoV-2 infected pregnant women showed that delivery in 38% of the women delivery was by emergency cesarean section due to pregnancy complications. These complications includes fetal distress, premature rupture of the membrane or stillbirth. In addition, 46% of the women experienced preterm labor[42]. An analysis 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[43].

In a recent study, key recommendations were provided for the management of COVID-19 infections at the time of delivery[44]. These recommendations were based on the optimal delivery timing and the safety of vaginal/cesarean 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 measure 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].

### 6.3 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 disease, however both patients survived after infection[46]. It is now evident that immunosuppressed patients may have a higher risk

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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 are 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].

**6.4 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%), diarrhea (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, in rare cases patients can even present with digestive symptoms in the absence of respiratory symptoms[48]. Mild to moderate liver dysfunction as evidenced by elevated aminotransferases, hypoproteinemia 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].

**6.5 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. An epidemiological study conducted in China during the COVID-19 outbreak indicates a higher incidence in individuals with cancer history compared to the healthy Chinese population[50]. 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 revealed that two patients who underwent lung lobectomies for adenocarcinoma, also showed an early phase of the

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lung pathology of COVID-19 pneumonia[54]. Another report suggests continuing use of treatment for lung cancer patients with SARS-CoV-2 infection[55]. 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, gynecological and breast malignancies during the outbreak of COVID19, 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.

**6.6 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]. Another study suggests a strong interaction between SARS-CoV-2 spike protein and the human ACE2 molecule[65], 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 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[67-70](Table II). A randomized trial 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[67]. Clinical trials in China has been initiated based on *in vitro* studies which revealed that the anti-

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malarial drug, chloroquine can significantly reduce the viral replication of coronaviruses[68,70]. However, the safety and efficacy of this drug to COVID19 treatment is still under investigation[69].

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 $P_H$ |
| 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 |

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 (**Table III**). In these clinical trials various drugs and their combinations like Bromhexine Hydrochloride, Arbidol Hydrochloride, recombinant human Interferon 1b & 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.

### 6.7 Precautions to be taken 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

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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; most straightforward prevention measure is to avoidance of 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 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 of 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 door knobs, doors, handrails and other contact surfaces should be implemented to avoid transmission of infection.

## Conclusion

COVID-19 is a life-threatening disease supportive care as the current primary treatment options due to the lack of a vaccine or effective anti-viral therapy. It poses a higher risk to the aged and immune-compromised individuals and mortality is accordingly disproportionate within these population. 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 .

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## Conflict of Interest

The authors declare that they have no conflict of interests.

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Table II: Ongoing clinical trials for the treatment of COVID-19 patient (Clinicaltrials.gov)

**ClinicalTrials.gov (Search Results 03/24/2020)**

| | NCT Number | Title | Status | Conditions | Interventions | Study type/ Phase | Population | Sponsor/ Collaborators | Funder Type | Dates | Location |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | **NCT 04273763** | Evaluating the Efficacy and Safety of Bromhexine Hydrochloride Tablets Combined with Standard Treatment/ Standard Treatment in Patients with Suspected and Mild Novel Coronavirus Pneumonia (COVID-19) | Enrolling by invitation | •Novel Coronavirus Pneumonia 2019-nCoV | •Drug: Bromhexine Hydrochloride Tablets<br>•Drug: Arbidol Hydrochloride Granules<br>•Drug: Recombinant Human Interferon #2b Spray | Study Type: Interventional<br>Phase: Not Applicable | Enrollment: 60<br>Age: 18 Years to 80 Years (Adult, _Older Adult)<br>Sex: All | •Second Affiliated Hospital of Wenzhou Medical University<br>•WanBangDe Pharmaceutical Group Co.,Ltd. | •Other | Study Start: February 16, 2020.<br>Study Completion: April 30, 2020<br>Results Posted: No Results | China |

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| 2 | **NCT 04252118** | Mesenchymal Stem Cell Treatment for Pneumonia Patients Infected With 2 019 Novel Coronavirus | Recruiting | 2019 Novel Coronavirus Pneumonia | •Biological: MSCs | Study Type: Interventional Phase: Phase 1 | Enrollment: 20 Age: 18 Years to 70 Years (Adult, Older Adult) Sex: All | •Beijing 302 Hospital. •Wuhan Huoshenshan Hospital, Wuhan, China. •Innovative Precision Medicine Group (IPM), Hangzhou, China. •Tianjin Haihe Hospital. •Shenzhen Third People's Hospital. •Fifth Affiliated Hospital, Sun Yat-Sen University | •Other | Study Start: January 27, 2020. Study Completion : December 2021 Results Posted: No Results | Beijing, China |
| 3 | **NCT 04273321** | Efficacy and Safety of Corticosteroids in COV ID-19 | Recruiting | •COVID-19 •Novel Coronavirus Pneumonia | •Drug: Methylpredniso lone | Study Type: Interventional Phase: Not Applicable | Enrollment: 400 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Beijing Chao Yang Hospital | •Other | Study Start: February 14, 2020. Study Completion : May 30, 2020 Results Posted: No Results | Wuhan, Hubei, China. |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 4 | **NCT 04313127** | A Phase I Clinical Trial in 18-60 Adults | Recruiting | •COVID-19 | •Biological: Recombinant Novel Coronavirus Vaccine (Adenovirus Type 5 Vector) | Study Type: Interventional<br><br>Phase: Phase 1 | Enrollment: 108<br><br>Age: 18 Years to 60 Years (Adult)<br><br>Sex: All | •CanSino Biologics Inc. •Institute of Biotechnology, Academy of Military Medical Sciences. PLA of China. •Jiangsu Province Centers for Disease Control and Prevention •Hubei Provincial Center for Disease Control and Prevention. •Tongji Hospital | Industry •Other | Study Start: March 16, 2020. Study Completion : December 20, 2022 Results Posted: No Results | Wuhan, Hubei, China |
| 5 | **NCT 04320238** | Experimental Trial of rhIFN# Nasal Drops to Prevent 2019 nCOV in Medical Staff | Recruiting | 2019 Novel Coronavirus Infection | •Drug: recombinant human interferon Alpha-1b. •Drug: thymosin alpha 1 | Study Type: Interventional<br><br>Phase: Phase 3 | Enrollment: 2944 Age: 18 Years to 65 Years (Adult, Older Adult) Sex: All | •Shanghai Jiao Tong University School of Medicine | •Other | Study Start: January 21, 2020 Study Completion : June 2020 Results Posted: No Results | Hubei, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 6 | **NCT 04269525** | Umbilical Cord (UC)-Derived Mesenchymal Stem Cells (MSCs) Treatment for the 2019-novel Coronavirus (nCOV) Pneumonia | Recruiting | •Pneumonia, Viral •Pneumonia, Ventilator-Associated | •Biological: UC- MSCs | Study Type: Interventional Phase: Phase 2 | Enrollment: 10 Age: 18 Years to 75 Years (Adult, Older Adult) Sex: All | •ZhiYong Peng •Tuohua Biological Technology Co. Ltd. •Zhongnan Hospital | •Other | Study Start: February 6, 2020. Study Completion :September 30, 2020 Results Posted: No Results | Wuhan, Hubei, China |
| 7 | **NCT 04305106** | Bevacizumab in Severe or Critically Severe Patients With COVID-19 Pneumonia-RCT | Recruiting | •COVID-19 Pneumonia | •Drug: Bevacizumab | Study Type: Interventional Phase: Not Applicable | Enrollment: 118 Age: 18 Years to 80 Years (Adult, Older Adult) Sex: All | •Qilu Hospital of Shandong University •Renmin Hospital of Wuhan University •Italy Moriggia Pelascini Gravedona Hospital S.p.A. •Wuhan University. •Jiangbei Union Hospital of Huazhong University of science and technology •Shandong Provincial Chest Hospital | •Other | Study Start: March 17, 2020. Study Completion : July 31, 2020 Results Posted: No Results | Jinan, Shandong, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 8 | **NCT 04280588** | Fingolimod in COVID-19 | Recruiting | •Coronavirus Disease (COVID-19) | •Drug: Fingolimod 0.5 mg | Study Type: Interventional Phase: Phase 2 | Enrollment: 30 Age: 18 Years to 80 Years (Adult, Older Adult) Sex: All | •First Affiliated Hospital of Fujian Medical University | •Other | Study Start: February 22, 2020 Study Completion: July 1, 2020 Results Posted: No Results | Fuzhou, China |
| 9 | **NCT 04252664** | Mild/Moderate 2019-nCoV Remdesivir RCT | Recruiting | • 2019-nCoV | •Drug: Remdesivir •Drug: Remdesivir placebo | Study Type: Interventional Phase: Phase 3 | Enrollment: 308 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Capital Medical University •Chinese Academy of Medical Sciences | •Other | Study Start: February 12, 2020 Study Completion: April 27, 2020 Results Posted: No Results | Wu Han, Hubei, China |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | **NCT 04283461** | Safety and Immunogenicity Study of 2019-nCoV Vaccine (mRNA-1273) to Prevent SARS-CoV-2 Infection | Recruiting | •Corona Virus Infection | •Biological: mRNA-1273 | Study Type: Interventional Phase: Phase 1 | Enrollment: 45 Age: 18 Years to 55 Years (Adult) Sex: All | •National Institute of Allergy and Infectious Diseases (NIAID) | •NIH | Study Start: March 3, 2020. Study Completion: June 1, 2021 Results Posted: No Results | Georgia, United States. Seattle, Washington, United States |
| 11 | **NCT 04252274** | Efficacy and Safety of Darunavir and Cobicistat for Treatment of Pneumonia Caused by 2019- nCoV | Recruiting | •Pneumonia, Pneumocystis •Coronavirus | •Drug: Darunavir and Cobicistat | Study Type: Interventional Phase: Phase 3 | Enrollment: 30 Age: Child, Adult, Older Adult Sex: All | •Shanghai Public Health Clinical Center | •Other | Study Start: January 30, 2020. Study Completion: December 31, 2020 Results Posted: No Results | Shanghai, China |
| 12 | **NCT 04257656** | Severe 2019-nCoV Remdesivir RCT | Recruiting | • 2019-nCov •Remdesivir | •Drug: Remdesivir •Drug: Remdesivir placebo | Study Type: Interventional Phase: Phase 3 | Enrollment: 453 Age: 18 Years and older (Adult, | •Capital Medical University | •Other | Study Start: February 6, 2020 Study Completion: May 1, | Beijing, China |

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| | | | | | | | Older Adult) Sex: All | | | 2020 Results Posted: No Results | |
| 13 | **NCT 04280224** | NK Cells Treatment for Novel Coronavirus Pneumonia | Recruiting | •Novel Coronavirus Pneumonia | •Biological: NK Cells | Study Type: Interventional Phase: Phase 1 | Enrollment: 30 Age: 18 Years to 65 Years (Adult, Older Adult) Sex: All | •Xinxiang medical university. •First Affiliated Hospital of Xinjiang Medical University | •Other | Study Start: February 20, 2020. Study Completion : December 30, 2020 Results Posted: No Results | Henan, China |
| 14 | **NCT 04305457** | Nitric Oxide Gas Inhalation Therapy for Mild/Moderate COVID-19 | Recruiting | •Coronavirus Infections •Pneumonia, Viral •Acute Respiratory Distress Syndrome | •Drug: Nitric Oxide | Study Type: Interventional Phase: Phase 2 | Enrollment: 240 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Massachusetts General Hospital •Xijing Hospital •Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico | •Other | Study Start: March 21, 2020. Study Completion : April 1, 2022 Results Posted: No Results | Boston, Massachusetts, United States |

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| 15 | **NCT 04264533** | Vitamin C Infusion for the Treatment of Severe 20 19-nCoV Infected Pneumonia | Recruiting | •Vitamin C •Pneumonia, Viral •Pneumonia, Ventilator-Associated | •Drug: VC •Drug: Sterile Water for Injection | Study Type: Interventional Phase: Phase 2 | Enrollment: 140 Age: 18 Years and older (Adult, Older Adult) Sex: All | •ZhiYong Peng •Zhongnan Hospital | •Other | Study Start: February 14, 2020. Study Completion :September 30, 2020 Results Posted: No Results | Wuhan, Hubei, China |
| 16 | **NCT 04306393** | Nitric Oxide Gas Inhalation in Severe Acute Respiratory Syndrome in COVID-19 | Recruiting | •SARS (Severe Acute Respiratory Syndrome) •Coronavirus | •Drug: Nitric Oxide Gas | Study Type: Interventional Phase: Phase 2 | Enrollment: 200 Age: 18 Years to 99 Years (Adult, Older Adult) Sex: All | •Massachusetts General Hospital •Xijing Hospital •Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico •Niguarda Hospital | •Other | Study Start: March 21, 2020. Study Completion : March 21, 2022 Results Posted: No Results | Boston, Massachus etts, United States |

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| 17 | **NCT04310228** | Favipiravir Combined with Tocilizumab in the Treatment of Corona Virus Disease 2019 | Recruiting | •COVID-19 | •Drug: Favipiravir Combined with Tocilizumab •Drug: Favipiravir •Drug: Tocilizumab | Study Type: Interventional Phase: Not Applicable | Enrollment: 150 Age: 18 Years to 65 Years (Adult, Older Adult) Sex: All | •Peking University First Hospital | •Other | Study Start: March 8, 2020. Study Completion: May 2020 Results Posted: No Results | Hefei, Anhui, China. Beijing, China. Wuhan, Hubei, China. |
| 18 | **NCT04244591** | Glucocorticoid Therapy for Novel Coronavirus Critically Ill Patients with Severe Acute Respiratory Failure | Recruiting | •Coronavirus Infections •Respiratory Infection Virus | •Drug: methylprednisolone therapy. •Other: Standard care | Study Type: Interventional Phase: •Phase 2 •Phase 3 | Enrollment: 80 Age: 18 Years and older (Adult, Older Adult) Sex: All | •Peking Union Medical College Hospital. •Zhongda Hospital. •Zhongnan Hospital. •Renmin Hospital of Wuhan University. | •Other | Study Start: January 26, 2020. Study Completion: December 25, 2020 Results Posted: No Results | Beijing, China |

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| 19 | **NCT 04276688** | Lopinavir/ Ritonavir, Ribavirin and IFN-beta Combination for nCoV Treatment | Recruiting | •Novel Coronavirus Infection | •Drug: Lopinavir/ ritonavir •Drug: Ribavirin •Drug: Interferon Beta-1B | Study Type: Interventional Phase: Phase 2 | Enrollment: 70 Age: 18 Years and older (Adult, Older Adult) Sex: All | •The University of Hong Kong •Hospital Authority, Hong Kong | •Other | Study Start: February 10, 2020. Study Completion : July 31, 2022 Results Posted: No Results | Hong Kong |
| 20 | **NCT 04280705** | Adaptive COVID-19 Treatment Trial (ACTT) | Recruiting | •Corona Virus Infection | •Other: Placebo •Drug: Remdesivir | Study Type: Interventional Phase: Phase 3 | Enrollment: 440 Age: 18 Years to 99 Years (Adult, Older Adult) Sex: All | •National Institute of Allergy and Infectious Diseases (NIAID) | •NIH | Study Start: February 21, 2020 Study Completion : April 1, 2023 Results Posted: No Results | Alabama, United States. California, United States. Denver, Colorado, United States. •and 27 more |