Coronavirus disease (COVID-19) is caused by SARS-CoV-2 and is the causative agent of a potentially lethal disease which is of great concern for global public health. It is proposed that this is possibly the zoonotic origin of COVID-19 based on the large number of infected people who were exposed to the wet animal market in Wuhan City, China. Transmission of COVID-19 infection from one person to another resulted in the isolation of patients who were subsequently given a variety of treatments. To monitor the current outbreak, robust steps have been placed in place to reduce the transmission of COVID-19 from person to person. Special attention and efforts should be given to preventing or reducing transmission in vulnerable populations, including infants, health care providers and the elderly. In this review we highlight the origin, transmission and possible treatments of this heinous infection which has become a global threat.

ABSTRACT
Coronavirus disease (COVID-19) is caused by SARS-CoV-2 infection, has spread across 31 provinces across China and more than 40 countries around the world. The transition from initial symptoms to acute respiratory distress syndrome (ARDS) is most likely due to uncontrolled release of cytokines. There is a growing need to find medications that are safe and appropriate for care. The inhibitory effect of chloroquine (CQ) is positive. Clinical use of CQ can, however, cause severe side effects. We suggest that hydroxychloroquine (HCQ), which has a highly similar antiviral effect to CQ, may serve as a better therapeutic approach.

INTRODUCTION:
A novel coronavirus disease (COVID-19), caused by SARS-CoV-2, has spread across 31 provinces across China and more than 40 countries around the world. The epidemic has spread considerably to infect 3,81,521 people with 16553 deaths around the world in 201 countries by March 24, 2020. The causative virus was initially referred to as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the resulting infectious disease was referred to by the World Health Organization as Coronavirus Virus 2019 (COVID-19). [Fig1]

Coronaviruses are a highly diverse group of enveloped, positive-sense, single-stranded RNA viruses. They cause many diseases of varying severity in humans and animals affecting respiratory, enteric, hepatic, and neurological systems. Infections with human coronavirus (CoV) have historically caused a small percentage of annual respiratory infections. HCoV-OC43, HCoV-229E, HCoV-NL63 and HCoV-HKU1 are found to cause moderate respiratory illness. Two novel coronaviruses, severe acute respiratory syndrome CoV (SARS-CoV) and Middle East respiratory syndrome CoV (MERS-CoV), have arisen over the past two decades, causing significant human diseases.

Origin of Pathogen
SARS-CoV-2 is a novel member of coronaviruses, a wide community of extremely complex, enveloped, positive-sense, single-stranded RNA viruses. Recent work has confirmed that SARS-CoV-2 possibly originated in bats, based on its genetic sequence close to that of other coronaviruses. The SARS-CoV-2 intermediate animal host between a possible pool of bats and humans is still unknown. Although this novel coronavirus has genetic characteristics that are consistent with the coronavirus family, it also has distinct gene sequences that vary substantially from previously sequenced coronaviruses.

The protein spike (S) in the envelope is important for coronavirus. The S protein mediates receptor binding and membrane fusion, and is critical to determining host tropism and capacity for transmission. The S protein is generally divided functionally into the S1 domain, which is responsible for receptor binding, and the S2 domain which is responsible for cell membrane fusion. Analysis of the structure suggested the receptor-binding domain was composed of a core and an external subdomain. The enzyme-converting angiotensin II (ACE2) was shown as a SARS-CoV cell receptor. SARS-CoV-2 similarly uses ACE2 as an input receptor in the ACE2-expressing cells, suggesting that SARS-CoV-2 may share the same lifecycle with SARS-CoV.

Biophysical and structural research showed that the SARS-CoV-2 protein binds ACE2 with around 16- to 20-fold higher affinity than the SARS-CoV protein. The high affinity of S protein to human ACE2 can facilitate SARS-CoV-2 spread among human populations. While, SARS-CoV-2 does not use other receptors of the coronavirus to enter cells, such as aminopeptidase N and dipeptidyl peptidase 4 (DPP4).

Molecular Characterization:
Within just a month of the incident case identification, several Chinese scientists isolated the virus, sequenced its full-length genome and identified its unique morphology. On 12 January 2020, the initial sequence of genomes was shared with the WHO. Several research teams have identified and characterized the viral genome separately, and the sequences have been made publicly accessible on the Global Initiative for Sharing All Influenza Data (GISAID) website (https://www.gisaid.org). Zhou et al. demonstrated that COVID-19 shared sequence identity with SARS-CoV at 79.5 per cent. It was then isolated from a critically ill patient’s bronchoalveolar lavage fluid, and from similarly contaminated patients, serafound neutralization. COVID-19 has also been reported to use the same cell entry receptor, angiotensin converting enzyme 2 (ACE2) as SARS-CoV, which highly expresses in epithelial airway cells.

Even COVID-19 was described and characterized by Zhu et al. They documented virus isolation and provided the initial summary of its basic cytopathic and morphological effects. COVID-19 appears to be the seventh member of the coronavirus family which infects humans. Notably, unlike SARS-CoV or MERS-CoV, COVID-19 has evolved more readily in primary human airway epithelial cells than normal tissue culture cells, indicating the potential for increased infectivity. Homology analysis showed that at main residues benchmarked with SARS-CoV, COVID-19 had several combinations of amino acids.

Whether these improvements contribute to the facilitation of infection with viruses is not clear.

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KEYWORDS
COVID-19, SARS-CoV-2, Chloroquine; Anti-malarial
The knowledge created by this research enables the medical and scientific community to better understand COVID-19 transmission, improve rapid diagnostic testing and efficient epidemiological control, and promote progress.

Symptoms

The signs of COVID-19 infection occur within 2-14 days of incubation. The time from the onset of COVID-19 symptoms to death ranged from 6 to 41 days, with a 14-day median. This time depends on the patient’s age and immune status. Symptoms included fever, cough, fatigue, and muscle pain. Other symptoms were headache, diarrhea, dyspnea, and lymphopenia.

However, there were pathological symptoms such as RNAemia, acute respiratory distress syndrome, acute heart injury, and the occurrence of ground-glass opacity that resulted in death. In certain cases, several peripheral ground-glass opacities have been identified in both lung subpleural areas, which are likely to cause both systemic and localized immune response, leading to increased inflammation. Regrettably, treatment with interferon inhalation in some cases had little therapeutic benefit, and only tended to exacerbate the condition by advancing pulmonary opacity. It is important to remember that the symptoms between COVID-19 and SARS-CoV-2 are similar, even though the former is milder. The major pathogenesis of COVID-19 is the occurrence of ground-glass opacity that results in death. In certain cases, several pathological symptoms such as pneumonia, acute heart injury, and the occurrence of ground-glass opacity that resulted in death. In certain cases, severe side effects are observed in patients with MERS-CoV or SARS-CoV encountered severe GI distress. Therefore, checking faecal and urine samples is necessary in order to eliminate a possible alternative route of transmission, specifically through health care staff, patients, etc.

Possible Treatment and Therapy

The transmission of COVID-19 infection from person to person has contributed to the isolation of patients despite the range of treatments. There are currently no effective antiviral medications or vaccines against infection with COVID-19 for future human therapy. The only alternative available is to use wide-spectrum antiviral drugs such as nucleoside analogs, as well as HIV-protase inhibitors that can attenuate viral infection before the actual antiviral treatment. The therapy of antivirals has shown that antiviral medications have been given to 75 patients. Treatment courses included oral administration of 75 mg oseltamivir twice a day, 500 mg lopinavir and 500 mg ritonavir.

The study showed that wide-spectrum antiviral remdesivir and chloroquine are highly effective in managing in vitro infection of 2019-nCoV. Such antiviral compounds have been used with safety in treating coronavirus human patients. Therefore, treating COVID-19 infection may be considered as such therapeutic agents. Additionally, a variety of other compounds are under development.

Pathogenesis

Patients diagnosed with COVID-19 displayed higher numbers of leukocytes, irregular breathing findings and elevated rates of pro-inflammatory cytokines in plasma. One of the COVID-19 case reports revealed that patients with COVID-19 presented insidious symptoms such as diarrhea, a low percentage of patients with MERS-CoV or SARS-CoV encountered severe GI distress. Therefore, checking faecal and urine samples is necessary in order to eliminate a possible alternative route of transmission, specifically through health care staff, patients, etc.

Several groups of scientists are currently working hard to build a non-human primate model for studying COVID-19 infection in order to create fast-track novel therapies and to evaluate new vaccines and drugs to have a deeper understanding of virus-host interactions. The fifth edition of the Guidelines recommends antivirals for the diagnosis of COVID-19 infection including IFN-α, lopinavir/ritonavir and ribavirin. The sixth edition of the Recommendations contains chloroquine phosphate and arbidol based on the results of clinical trials. For adults, the therapeutic procedure for administering IFN-α is vapor inhalation at a dosage of 5 million U (and 2 mL of 1% aqueous solution) twice a day. The lopinavir/ritonavir dosage for adults is 400 mg/100 mg, twice a day. Ribavirin should be administered in conjunction with IFN-α or lopinavir/ritonavir by intravenous infusion at a dosage of 500 mg for adults 2 to 3 times/day. For adults, chloroquine phosphate is administered orally at a dosage of 500 mg (300 mg chloroquine), twice a day. Arbidol is given orally to adults at a dosage of 200 mg, three times a day. Treatment period is no greater than 10 days.

IFN-α is a broad-spectrum antiviral widely used to treat other viral illnesses, although it is stated to inhibit in vitro reproduction of SARS-CoV. Lopinavir/ritonavir is a human immunodeficiency virus (HIV) drug used in combination with other drugs for the treatment of HIV-1-infected adults and children under 14 days of age. Oseltamivir (Tamiflu) is the antiviral of choice. Ribavirin is an equivalent nucleoside with a wide spectrum of antiviral activity.

In research compared 111 patients with severe acute respiratory syndrome (SARS) treated with ribavirin monotherapy, and 41 patients with SARS treated with lopinavir/ritonavir and ribavirin. Patients treated with combination therapy had a lower risk of acute respiratory distress syndrome (ARDS) and death. Chloroquine is a commonly used antimalarial which was reported in 2006 as a possible broad-spectrum antiviral. Chloroquine was found to prevent infection with low micromolar concentrations of SARS-CoV-2, with a half-maximum effective concentration (EC50) of 1.13 μM and a half-cytotoxic concentration (CC50) greater than 100 μM.

Control and Preventive Measures

Controlling the current outbreak requires rigorous steps to reduce the
transmission of COVID-19 from person to person. Specific attention and efforts should be given to preventing or reducing transmission in vulnerable populations, including infants, health care providers and the elderly. For medical professionals, health care practitioners, and public health individuals and researchers involved in the COVID-19 nCoVAg guidelines have been written. The early cases of COVID-19 outbreak occurred mainly in the elderly, likely due to a poor immune system that allows for faster viral infection progression. The public utilities and facilities will regularly include decontaminating handwashing reagents. When dealing with the virus, direct contact with wet and infected materials should be considered, when particular allergens such as faecal and urine show samples which may potentially serve as an alternate transmission path. China and other nations, including the US, have adopted significant prevention and control initiatives to monitor further spread of the virus, including travel screenings.

Epidemiological changes in the COVID-19 infection should be monitored taking into account potential transmission routes and subclinical infections, as well as the adaptation, evolution and dissemination of viruses among humans and possible intermediate animals and reservoirs. A large number of issues still remain to be answered. They provide information about how and how many were screened, what proportion of these turned positive and whether this rate remains constant or variable, but are not restricted to that.

There is an alarming need to work on the studies discussed above in order to bring an effective solution to stop the spread of this dangerous threat to the world.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES