

SARS-CoV-2 causing pneumonia-associated respiratory disorder (COVID-19): diagnostic and proposed therapeutic options

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Abstract. SARS-CoV-2 is responsible for the outbreak of severe respiratory illness (COVID-19) in Wuhan City, China and is now spreading rapidly throughout the world. The prompt outbreak of COVID-19 and its quick spread without any controllable measure defines the severity of the situation. In this crisis, a collective pool of knowledge about the advancement of clinical diagnostic and management for COVID-19 is a prerequisite. Here, we summarize all the available updates on the multidisciplinary approaches for the advancement of diagnosis and proposed therapeutic strategies for COVID-19. Moreover, the review discusses different aspects of the COVID-19, including its epidemiology; incubation period; the general clinical features of patients; the clinical features of intensive care unit (ICU) patients; SARS-CoV-2 infection in the presence of co-morbid diseases and the clinical features of pediatric patients infected with the SARS-CoV-2. Advances in various diagnostic approaches, such as the use of real-time polymerase chain reaction (RT-PCR), chest radiography, and computed tomography (CT) imaging; and other modern diagnostic methods, for this infection have been highlighted. However, due to the unavailability of adequate evidence, presently there are no officially approved drugs or vaccines available against SARS-CoV-2. Additionally, we have discussed various therapeutic strategies for COVID-19 under different categories, like the possible treatment plans with drug (antiviral drugs and anti-cytokines) therapy for disease prevention. Lastly, potential candidates for the vaccines against SARS-CoV-2 infection have been described. Collectively, the review provides an overview of the SARS-CoV-2 infection outbreak along with the recent advancements and strategies for diagnosis and therapy of COVID-19.

Key Words:

COVID-19, SARS-CoV-2, Diagnosis, Proposed therapy.

Introduction

At the end of 2019, an outbreak of severe respiratory illness occurred in Wuhan City, China. The World Health Organization (WHO) and China were alerted by a rise in the number of patients with pneumonia of unknown etiology and an unidentified causative agent. On January 9, 2020, the Chinese Center for Disease Control and Prevention (Chinese CDC) declared the identification of a novel Coronavirus¹. A few days later, it was reported that this novel type of coronavirus, termed by the WHO as “novel coronavirus-2019” (SARS-CoV-2), was responsible for the outbreak². It was noted that some parts of the genome sequence of SARS-CoV-2 were identical to those of two other coronavirus strains, namely, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) (approximately 79% homology) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) (approximately 50% homology)^{3,4}. The current outbreak occurred after two outbreaks of SARS-CoV and one outbreak of MERS-CoV. The first two outbreaks occurred in 2002 and 2003 in the Guangdong region of China and were caused by the viral pathogen SARS-CoV^{5,6}. The third outbreak, which occurred in the Middle East, was caused by the microbial pathogen MERS-CoV and led to a respiratory illness epidemic (Table I)⁷.

Table I. Comparison of infection statistics COVID-19, SARS and MERS.

Disease	Year	Cases reports	Place of origin	Web reference
Severe Acute Respiratory Syndrome (SARS)	2002-2003	Total 8,098 cases, resulting in 774 deaths reported in 17 countries 5,327 cases, resulting in 349 deaths reported in China	Guangdong province of southern China	https://www.who.int/csr/sars/country/table2004_04_21/en/
Middle East Respiratory Syndrome (MERS)	2012-2019	Total 2506 cases, resulting in 862 deaths reported in 26 countries	Saudi Arabia	https://www.who.int/csr/don/31-january-2020-mers-united-arab-emirates/en/
Coronavirus Disease 2019 (COVID-19)	2019-2020	Total 462684 cases, 20834 deaths from 198 Countries and Territories	Wuhan City, China	https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200326-sitrep-66-covid-19.pdf?sfvrsn=9e5b8b48_2

Coronavirus is member of the family *Coronaviridae* and subfamily *Coronavirinae*, which consists of four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*⁸. These four genera were created based on genomic construction and phylogenetic relationships⁹. The SARS-CoV-2 belongs to the *Betacoronavirus* genus.

The SARS-CoV-2 outbreak has been associated with exposure to the Huanan Wholesale Seafood Market, Hubei province, Wuhan, China. This market is a trading hub for several live animals, including reptiles such as snakes, and birds and other small mammals, including marmots and bats¹⁰. This implies that the animal-to-human transmission of SARS-CoV-2 was responsible for the outbreak. Zhou et al¹¹ suggested that this viral outbreak has probably originated from bats. However, investigators have confirmed human-to-human transmission of this virus. According to recent information, SARS-CoV-2 has spread to different countries, including Thailand, Japan, Hong Kong, Singapore, South Korea, Taiwan, Macau, Malaysia, Australia, France, Italy, Vietnam, Nepal, India, Canada, and the United States. According to a recent report, as of March 26, 2020, > 462,684 cases of SARS-CoV-2 infection and > 20, 834 deaths have been reported. As such, the current outbreak of SARS-CoV-2 is considered a medical crisis and has been declared as a pandemic by the WHO.

This study describes several aspects of the virus, including its epidemiology and incubation period; the general clinical features of patients; the clinical features of intensive care unit (ICU) patients; SARS-CoV-2 infection in the presence of co-morbid diseases; and the clinical features of

paediatric patients infected with the virus. Moreover, we highlighted diagnostic strategies, such as sample collection methods; the use of real-time polymerase chain reaction (RT-PCR) techniques, chest radiography, and computed tomography (CT) imaging; and other modern diagnostic methods, for this infection. Treatment strategies for SARS-CoV-2 infection are also discussed under different categories, such as an outline of the treatment plan and drug treatment (antiviral and cytokine treatment and disease prevention). Finally, we discuss potential candidate vaccines for the SARS-CoV-2 infection.

Patients and Methods

A PubMed search of the English-language literature about the coronavirus infection published from year 2001 to the present was performed. For the SARS-CoV-2 literature, the PubMed search focused on the publications from 12th December, 2019 onwards. The Embase library was also searched. Recommendations were derived from clinical experts. Recommendations from two websites, including the Centers for Disease Control and Prevention (Atlanta, GA, USA) (<https://www.cdc.gov/>) and the WHO (<https://www.who.int/>) websites, were also consulted.

Epidemiology

Since December 12, 2019, SARS-CoV-2 has been spreading very rapidly. Initially, it was announced that 27 patients had been afflicted with an unexplained disease of unknown origin. As

of January 26, 2020, there were 2050 laboratory-confirmed infections caused by the virus, with 56 fatalities¹¹. Shen et al¹² reported 9692 confirmed cases up to January 30, 2020. The report stated that there were 15,238 suspected cases among 31 provinces and different municipalities in China. By that time, 1527 severe cases had been recorded, among which 171 patients recovered and were discharged home and 213 died. In total, twenty-eight paediatric cases have been reported¹². In a recent report by Jiang et al¹³ on February 1, 2020, 12,024 confirmed cases involving pneumonia were reported, and there were 259 deaths. There were 11,860 cases reported from mainland China and 164 from 26 countries and territories outside China. Researchers have reported a mortality rate of approximately 2%, lower than the mortality rate of approximately 9.6% for SARS. The transmission rate of SARS-CoV-2 is reported to be 2-3%¹³. McCloskey et al¹⁴ stated that approximately 50 million individuals in Wuhan and neighbouring cities had effectively been placed in quarantine by January 26, 2020. The same report also cited 461 cases of severe illness and 80 deaths. On February 3, 2020, researchers reported that >17,496 patients had been infected, with 362 deaths in >25 countries¹⁵. The transmission dynamics of SARS-CoV-2 were calculated by Li et al¹⁶ who estimated an epidemic growth rate of 0.10 per day, a doubling time of 7.4 days, and a basic reproductive number (R0) of 2.2. According to the recent situation report-65 (reported on 26th March, 2020) by WHO, globally 462,684 confirmed cases were reported, of which 20,834 cases were with deaths. (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200326-sitrep-66-covid-19.pdf?sfvrsn=9e5b8b48_2).

Incubation Period of the Virus

It is essential to understand the incubation period of a viral pathogen. In general, human coronavirus has an incubation period of approximately 4 days (range, 2-4 days). This incubation period was noted for the human coronavirus that can cause SARS¹⁷. The incubation period calculated for SARS-CoV was 4-6 days¹⁸. It has been noted that the incubation period of SARS-CoV-2 is 3-6 days, with the maximum being 14 days¹⁹⁻²¹.

Clinical Features

On infection with human coronavirus, patients may exhibit signs and symptoms of upper respira-

tory tract infection, such as sore throat and rhinorrhea²². However, clinical signs of SARS-CoV-2 infection include low-to-high fever, non-productive cough, myalgia, dyspnea, fatigue, standard or decreased leukocyte counts, and confirmed evidence of pneumonia on chest radiography (Figure 1). Among 138 hospitalized patients, the most common general symptoms at disease onset included fever (98.6%), dry cough (59.4%), fatigue (69.6%), dyspnea (31.2%), and myalgia (34.8%). Less common symptoms of SARS-CoV-2 infection include headache, abdominal pain, dizziness, nausea, vomiting, and diarrhea²³. In another study of 41 cases, Hui et al¹⁰ reported several symptoms, including fever (> 90%), dry cough (80%), shortness of breath (20%), respiratory distress (15%), and fatigue. The researchers found that the hallmark signs and symptoms of this disease were stable in the majority of cases. However, investigators detected lymphopenia and leukopenia in these patients. Among the 41 patients, 6 were discharged from the hospital, 7 were transferred to critical care, and 1 died (a 61-year-old man with respiratory failure and severe pneumonia, who also had an abdominal tumour)¹⁰. Wang et al¹ reported symptoms including fever (98%), dry cough (76%), dyspnea (55%), and diarrhea (3%). Among a cohort of 99 patients, Chen et al²⁰ reported clinical symptoms including fever (83%), shortness of breath (31%), confusion (9%), cough (82%), muscle ache (11%), headache (8%), sore throat (5%), rhinorrhea (4%), chest pain (2%), nausea and vomiting (1%), and diarrhea (2%). Chen et al²⁰ described some critical conditions, such as pneumothorax (1%) and acute respiratory distress syndrome (17%). The different symptoms appear of COVID-19 as different days passes (Figure 2). It has been reported that in severe cases, pneumonia and kidney failure can occur, ultimately lead to death. Huang et al²⁴ reported that SARS-CoV-2 infection may cause acute respiratory distress syndrome and may require admission to an ICU, with death being a possibility.

Infected patients must undergo laboratory investigations. For example, the laboratory test results for one patient revealed hypoproteinemia. The laboratory test results revealed reduced albumin (35.70 g/L) and total protein (62.20 g/L) levels; irregular liver function (augmented aspartate aminotransferase [72 U/L]); augmented alanine aminotransferase (79 U/L), C-reactive protein (CRP, 53 mg/L), and procalcitonin (PCT, 0.10 ng/ml) levels; reduced lymphocyte ($0.9 \times 10^9/L$) and white blood cell (WBC) ($3.72 \times 10^9/L$) counts; reduced hemoglobin (131.10 g/L) levels; mild anemia

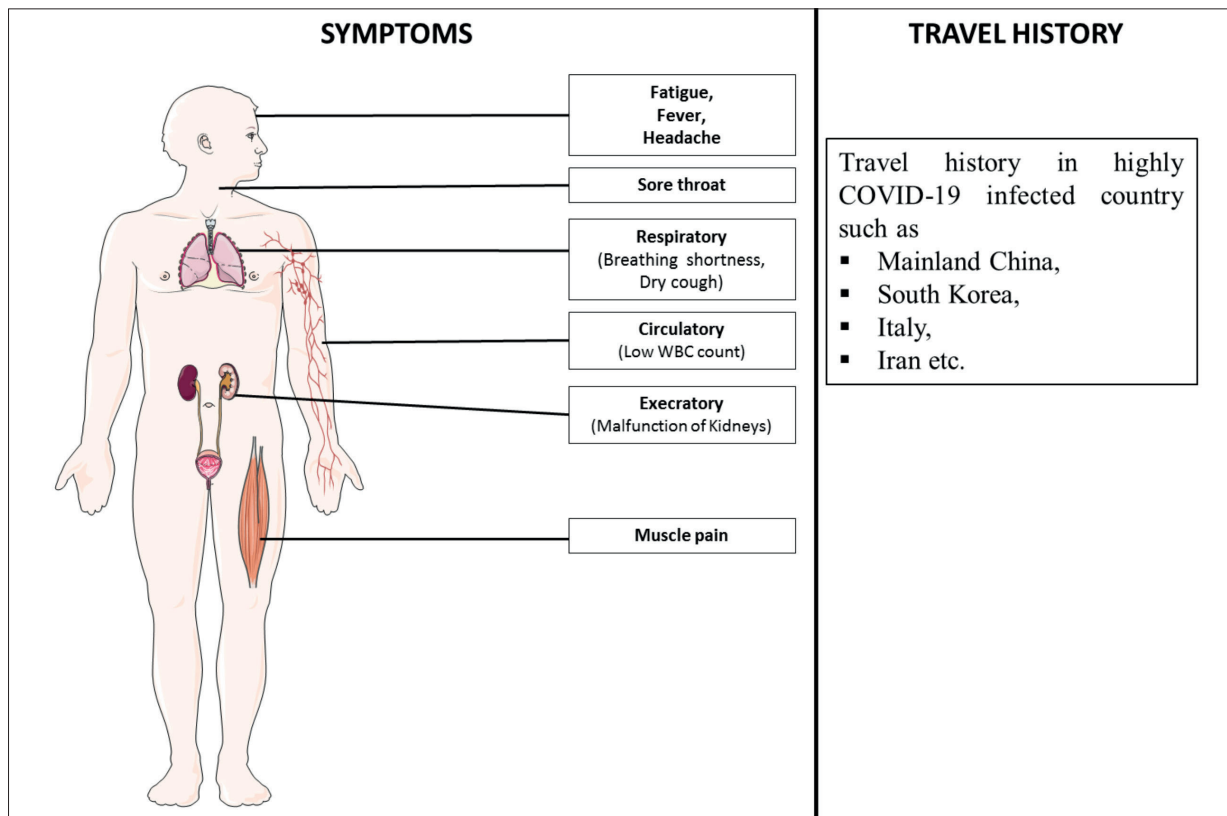


Figure 1. Diagnostic strategy of COVID-19 (different symptoms and travel history).

with a reduced red blood cell count ($4.10 \times 10^{12}/L$); and decreased hematocrit levels (39.0%)²¹.

Clinical Features of ICU Patients

Several significant findings have been observed among patients infected with SARS-CoV-2 and admitted to the ICU. ICU patients exhibit higher neutrophil and WBC counts, in addition to higher levels of D-dimer, creatine, and creatine kinase. The median time from symptom onset to ICU admission has been reported to be 10 days. The median Glasgow Coma Scale (GCS), Acute Physiology and Chronic Health Evaluation (APACHE) II, and Sequential Organ Failure Assessment (SOFA) scores on the day of ICU admission have been calculated by investigators. It appears that the median GCS score is 15 (IQR, 9-15), SOFA score is 5 (IQR, 3-6), and APACHE II is 17 (IQR, 10-22). Other factors, such as the median partial pressure of oxygen and the median of the ratio of the partial pressure of oxygen to the fraction of inspired oxygen, have also been evaluated (68 mmHg [IQR, 56-89] and 136 mmHg [IQR, 103-234], respectively)²³. Chen et al²⁰ reported that ventilator-assisted breathing was administered to ICU patients. They

provided extracorporeal membrane oxygenation and anti-infection treatment after admission to the ICU²⁰. Huang et al²⁴ reported that patients admitted to the ICU exhibited high mortality rates. They noted that ICU cases had higher plasma levels of granulocyte-colony stimulating factor, interferon gamma-inducible protein 10, interleukin (IL)-10, IL-7, IL-2, tumour necrosis factor-alpha, monocyte chemoattractant protein-1(MCP1), and macrophage inflammatory protein (MIP) 1A than non-ICU cases. They also determined the D-dimer levels and prothrombin time during admission. The median D-dimer level and median prothrombin time were 2.4 mg/L (IQR, 0.6-14.4) and 12.2s (IQR 11.2-13.4), respectively. They also described secondary infections that developed in ICU patients²⁴. Increased levels of some cytokines were noted by several clinicians.

SARS-CoV-2 in the Presence of Co-Morbid Diseases

Patients with SARS-CoV-2 infection and other disorders such as diabetes, hypertension, or other cardiovascular diseases (CVD), are at a greater risk because these diseases may damage the im-

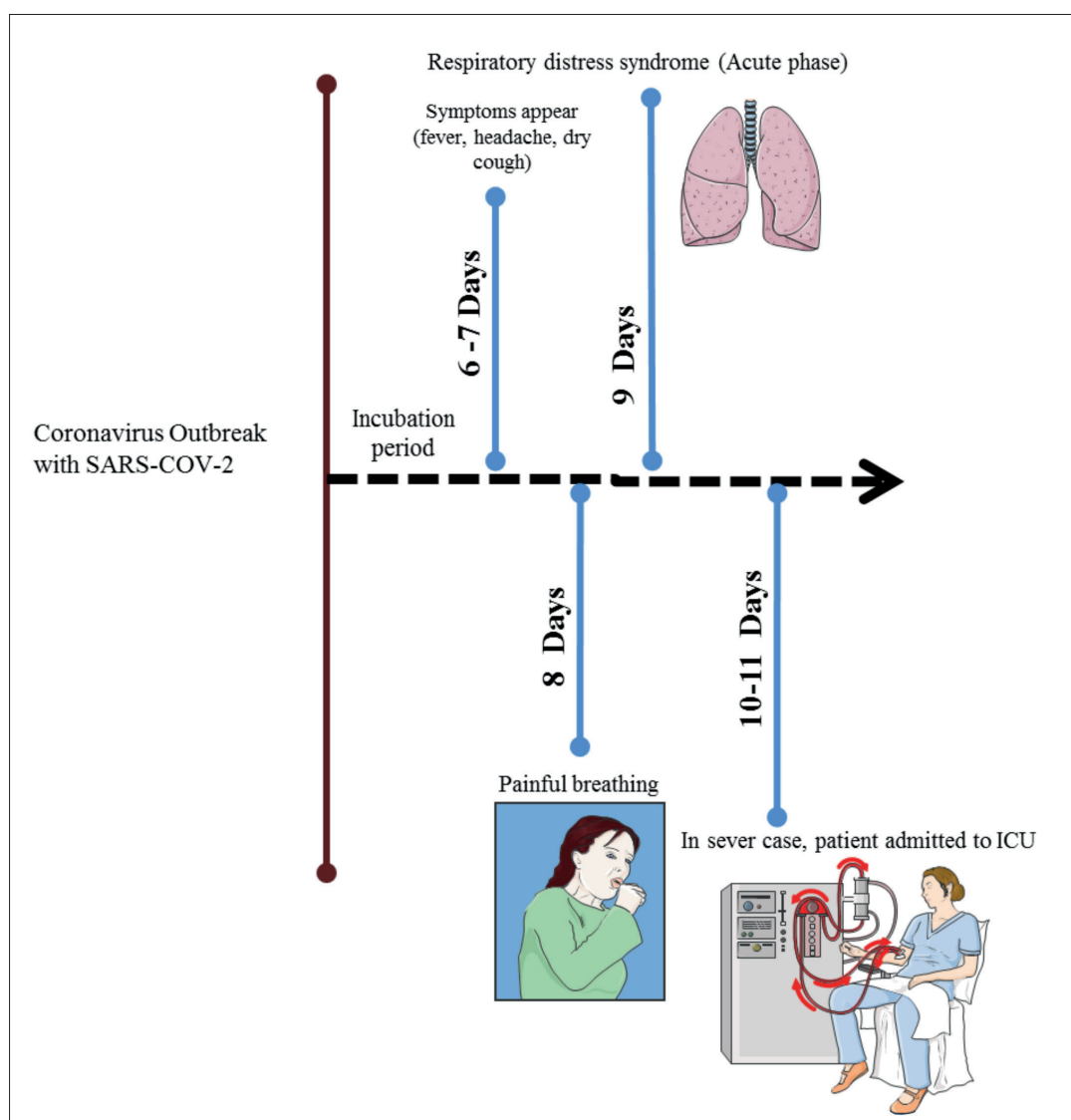


Figure 2. The appearance of symptoms of COVID-19 in respect of days.

immune system²⁵. Wang et al²³ encountered patients with SARS-CoV-2 infection combined with other diseases such as hypertension, diabetes, and CVD. Huang et al²⁴ noted that less than one-half of patients (30 cases total [all male]) had underlying diseases (n=13 [32%]), which included hypertension (n=6 [15%]), diabetes (n=8 [20%]), and CVD⁶ (n=6 [15%]).

Clinical Features of Pediatric Patients

Shen and Yang¹² described the clinical features in 28 pediatric patients (1 month to 17 years of age) with confirmed infection, including dry cough, fever, and fatigue, together with other upper respiratory symptoms, including a runny nose and nasal congestion. Pediatric patients also ex-

hibited some gastrointestinal symptoms such as vomiting, nausea, and diarrhea. On biochemical examination, CRP levels were normal or temporarily elevated; however, routine blood culture results were often normal. They found that most paediatric patients experienced mild symptoms, without fever or pneumonia¹².

Specimen Collection Methods for Diagnosis

A rapid collection of specimens (blood, swab, or sputum) is important. For nucleic acid amplification testing, the sample should be collected from respiratory regions such as the oropharynx and/or nasopharynx. Sputum and/or endotracheal aspirates or bronchoalveolar lavage fluid samples

can be retrieved from patients in a more critical condition^{26,27}.

Diagnosis Using Real-Time PCR Techniques

The SARS-CoV-2 can be detected using RT-PCR techniques²⁸. Huang et al²⁴ used RT-PCR methods to detect SARS-CoV-2 infection. Forward and reverse primers targeting SARS-CoV-2 envelope genome were used. The forward primer used was 5'-TCAGAATGCCAATCTC-CCCAAC-3', and the reverse primer used was 5'-AAAGGTCCACCCGATACATTGA-3'. However, for the diagnosis of SARS-CoV-2, the WHO published a protocol describing diagnostic testing using RT-PCR³⁰. For suspected cases, rapid sample collection and nucleic acid amplification using appropriate respiratory samples are currently recommended by the WHO²⁹. For the detection of SARS-CoV-2, two different RT-PCR protocols have been developed, one from Charité University (Berlin, Germany) and the other from Hong Kong University (Hong Kong).

Diagnosis Using Chest Radiography and CT Imaging

Chest radiography and chest CT of infected patients reveal bilateral lung involvement; the findings may differ according to disease stage, patient age, and immune status at the time of imaging²¹. With CT scanning using thinner layers, the thickening of the interlobular septa is revealed. High-resolution CT (HRCT) revealed small, honeycomb-like condensation of the interlobular septa in a study of 45 cases²¹. The resolution of the radiographic examination was not as good as that of CT imaging, which revealed ground-glass opacities (GGOs) with fuzzy edges in 9 cases. Song et al³⁰ described the chest CT observations in 51 patients infected with 2019-nCoV, including pure GGOs in 77%, GGOs with interstitial and/or interlobular septal thickening in 75%, and GGOs with consolidation in 59% of cases. More consolidated lung lesions were found in patients aged ≥ 50 years compared with younger patients³⁰. Kanne et al³¹ concluded that chest CT imaging findings are the key focus points for radiologists in patients with SARS-CoV-2 infection. Chung et al³² described typical CT imaging findings, which incorporated consolidative pulmonary opacities and bilateral pulmonary parenchymal GGOs. However, CT imaging also depicts peripheral lung distribution and, occasionally, rounded morphology³². On the basis of CT imaging, Jin et al²¹ described 5 stages according to body condition during viral infection and time of

disease onset. The ultra-early stage has no clinical manifestations and negative laboratory investigation results, but positive results for 2019-nCoV is observed when throat swabs are examined. Chest CT imaging features include dotted focal GGOs or single or double focal GGOs, patchy consolidation, and nodules positioned in the central lobule area enclosed by patchy GGOs. The early stage, which refers to the phases at 1-3 days after the emergence of clinical signs and symptoms, is characterized by fever and dry cough, among other symptoms. Chest CT imaging features include single or numerous agglomerated or scattered patchy GGOs segregated by grid-like condensed or honeycomb-like interlobular septa. The rapid progression stage occurs approximately 3-7 days after the emergence of clinical signs and symptoms. Pathological signs and symptoms include fibrous exudation attached to every alveolus throughout the inter-alveolar space, creating a fusion situation. Chest CT imaging features include pulmonary consolidation with air bronchogram. The consolidation stage occurs approximately 6-15 days after the appearance of clinical signs and symptoms. Chest CT imaging reveals numerous patchypulmonary consolidations of lower density and the range is then observed in the rapid progression stage. Finally, the dissipation stage occurs at approximately 14-21 days. This stage is observed after the onset of clinical signs and symptoms, and chest CT imaging features include strip-like opacity and patchy consolidation²¹.

Modern Diagnosis Methods

Electron microscopy and next-generation sequencing (NGS) technology can also be applied for the detection of SARS-CoV-2²¹. With these techniques, the mutation of the virus can also be assessed, although these methods are expensive and often cost-prohibitive. As such, low-cost and rapid diagnostic methods are urgently needed for the detection of SARS-CoV-2.

Treatment

Patients with suspected SARS-CoV-2 infection and/or confirmed disease must be treated in specialized hospitals with protective isolation facilities. For confirmed cases, bed rest is recommended. It is necessary to monitor parameters such as heart rate, blood pressure, pulse oxygen saturation, and respiratory rate.

Outline of the Treatment Plan

Patients should consume adequate amounts of liquids, including energy drinks and electrolytes,

to balance the body's electrolyte, water, and acid-base levels. The hospital should perform routine checks of different organ systems and function (myocardial and liver enzymes, bilirubin, blood urea nitrogen, creatinine, and urine volume, among others). Besides, assessment of PCT and CRP levels and coagulation function, routine blood work-up, and chest imaging should be performed. If necessary, patients should be provided with appropriate oxygen treatment or therapy through mask oxygen, a nasal cannula, or high-flow nasal oxygen therapy. Similarly, if necessary, patients should be provided with non-invasive ventilation or invasive mechanical ventilation. It has been recommended that patients with respiratory distress, severe respiratory infections, shock, or hypoxemia undergo oxygen therapy as first-line treatment. The preliminary flow rate should be 5 L/min. The titration flow rate according to target oxygen saturation levels should be adjusted as follows: for children and adults with symptoms, the oxygen saturation (SpO_2) should be $\geq 94\%$. For pregnant patients, SpO_2 should be $\geq 92-95\%$, and for non-pregnant patients, $\geq 90\%$. In patients with acute respiratory distress syndrome and/or hypoxic respiratory failure, respiratory support should be provided.

Proposed Therapy

Propose antiviral and cytokine therapy

No specific therapy is currently available for the SARS-CoV-2 strain. Patients infected with SARS-CoV-2 who exhibit mild signs and symptoms can, however, be treated with antibacterial drugs for pneumonia including azithromycin, fluoroquinolones, and amoxicillin. However, researchers have tested some therapeutic agents against MERS-CoV in animal models. These therapeutic molecules are broad-spectrum antiviral drugs, such as viralmethyltransferase inhibitor³³, nitazoxanide³⁴, and the nucleotide prodrug GS-5734³⁵. It was observed that GS-5734 hindered both MERS-CoV and SARS-CoV replication *in vitro*. This molecule improved clinical signs by considerably reducing the viral load in the lung³⁵. Investigators tested the effectiveness of ribavirin in combination with lopinavir and suggested lopinavir as a therapeutic agent against SARS-CoV³⁶. Interferon therapy was tested as one of several possible treatments for SARS-CoV and MERS-CoV in animal models³⁷. Sheahan et al³⁸ tested a combination therapy consisting of lopina-

vir, ritonavir, and interferon- β (LPV/RTV-IFN β) against MERS-CoV. This combination showed potential for the treatment of MERS-CoV infections. Lu et al³⁹ reported that antiviral molecules, nucleoside analogues, neuraminidase inhibitors, therapeutic peptide, RNA synthesis inhibitors, anti-inflammatory drugs, and Chinese traditional medicine could be therapeutic options for SARS-CoV-2. Among the therapeutic options for SARS-CoV-2, Lu et al³⁹ described antiviral molecules including lopinavir/ritonavir (400 mg/100 mg), a therapeutic peptide comprising EK1, RNA synthesis inhibitor molecules consisting of TDF and 3TC, and anti-inflammatory drugs containing hormones and other proteins³⁹. Some researchers have recommended alpha-interferon treatment for SARS-CoV-2 infection. The dose can be administered as an injection of 5 million IU (International Unit) twice per day in adults²¹.

Recently, it was noted that Chloroquine phosphate, a drug for the treatment of malaria, has shown its efficacy against COVID-19. The clinical trial of this drug and its derivative (chloroquine or hydroxychloroquine) is being conducted in 10 hospitals in China to test the efficacy and safety for the treatment of COVID-19 associated pneumonia⁴⁰.

Holshue et al⁴¹ reported an improvement in the condition of a patient having contracted SARS-CoV during his visit to Wuhan, China and was regarded as the first patient in the USA for COVID-19, after administration of remdesivir (a novel nucleotide prodrug under clinical trial). Patients showed a decrease in the severity of the symptoms after its administration⁴¹. Lim et al⁴² reported that a patient (54-year old male) with COVID-19 infection in South Korea when was administered lopinavir/ritonavir the SARS-CoV-2 load in the patient decreased significantly. Moreover, no or little coronavirus titers were identified in the patient after this drug administration⁴².

Recently, remdesivir (GS-5734) is being used for the treatment of MERS-CoV infection in the rhesus macaque model and it has been suggested to be a potential cure for COVID-19⁴³. Liu et al⁴⁴ suggested four potential drug candidates for the treatment of COVID-19, which are remdesivir, novel vinylsulfone protease inhibitor, an ACE2-based peptide, and 3CLpro-I⁴⁴. Recently chloroquine and hydroxychloroquine seem to be promising therapeutic agents to fight against COVID-19⁴⁵. Hydroxychloroquine is a less toxic derivative than chloroquine, which can be effective for inhibiting SARS-CoV-2 infection⁴⁶. In a non-randomized clinical trial Gautret et al⁴⁷ pro-

posed azithromycin and hydroxychloroquine as a better therapeutic molecule against COVID-19. Nevertheless, therapeutic molecules used for SARS-CoV and MERS-CoV should be tested against SARS-CoV-2 as early as possible.

Prevention using Chinese traditional medicine

Chinese traditional medicine options include *Lianhuaqingwen* and *ShuFengJieDu* capsules³⁹. Chinese medicinal tea may also be administered (agastache leaf [6 g]; perilla leaf [6 g]; stewedamomumsao-ko [6 g], dehydrated tangerine or orange peel [9 g]; and 3 slices of ginger). *HuoxiangZhengqi* capsule or *HuoxiangZhengqiShui* can be used to prevent SARS-CoV-2 infection (at half dose)²¹.

Angiotensin-converting enzyme 2 (ACE2) receptor and therapeutic possibility

Lim et al⁴² demonstrated that SARS-CoV-2 may bind to the human angiotensin-converting enzyme 2 receptor (ACE2) to enter the body. The study reported that several important residues are responsible for this binding. Significant residues of the receptor-binding domain for the ACE2 receptor vary between SARS-CoV-2 and SARS-CoV. The residues include Asn439, Gly485, Phe486, Gln493, and Asn501⁴. Several potential strategies for blocking the ACE2 receptor have been considered and have been shown to be capable of preventing SARS-CoV-2 infection. On the basis of the existing literature, several possible strategies to block the ACE2 receptor have been developed and have been shown to be effective in preventing illness due to SARS-CoV infection⁴⁸.

Propose Vaccine Candidates

To date, no specific vaccines have been developed for SARS-CoV-2. However, there may be possible subunit vaccines for this virus. Spike protein antigens of SARS-CoV-2, which bind to the receptor of the virus, are being tested as candidate vaccines⁴⁹. It has also been suggested that the receptor-binding domain of SARS-CoV-2 may be a target for the development of SARS-CoV-2 vaccines⁵⁰. Recently, through the immunoinformatics approach, we have identified 13 Major Histocompatibility Complex (MHC)-I and 3 MHC-II epitopes of B-cells having antigenicity within the spike glycoprotein of SARS-CoV-2. These epitopes could be considered for the formulation of a multi-epitopic peptide vaccine against SARS-CoV-2⁵¹.

Using genomic sequence information, a DNA vaccine has been developed for SARS-CoV. It is

currently undergoing a phase 1 clinical trial⁵², and its efficacy for preventing SARS-CoV-2 could also be tested. However, Paules et al⁵³ proposed a messenger RNA (mRNA)-based vaccine for SARS-CoV-2. The use of mRNA-based vaccine technology may accelerate the development of an effective vaccine.

Presently, several research groups, including the China CDC, are trying to develop a vaccine for this virus. Other organizations around the world are also in the process of designing and developing a vaccine.

Conclusions

Currently, SARS-CoV-2, which causes the pneumonia-associated respiratory disorder, is presenting numerous diagnostic and therapeutic challenges that require urgent consideration. Therefore, it is vital to continue investigating the mutational landscape of the SARS-CoV-2 causing pneumonia and the possible therapeutic interventions. Recent advances in understanding the molecular mechanisms of infection and transmission may help to detect the virus quickly and facilitate a more rapid diagnosis of SARS-CoV-2 related diseases. This, in turn, would be required to accelerate the treatment. Nevertheless, the present article provides information regarding advances in the diagnosis and treatment of SARS-CoV-2 infection and the current outbreak of disease. However, we should aim to better understand the clinicopathological features of SARS-CoV-2 infection to design treatment strategies leading to favourable outcomes in patients infected with the virus as early as possible. In this regard, governments should provide more funds and resources to investigators in efforts to gain a deeper understanding of the disease and develop therapeutic agents and vaccines.

Author contributions

Conceptualization: CC. Writing-original draft preparation: CC and ARS. Writing-review, and editing: GS and MB. Supervision and funding acquisition: SSL.

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Conflict of Interests

The authors declare that they have no conflict of interests.

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