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EC MICROBIOLOGY
Review Article

COVID-19; A Narrative Review

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Received: July 04, 2020; **Published:** September 10, 2020

Abstract

The World Health Organization has declared the ongoing outbreak of a novel coronavirus as a global public health emergency. At present, the research work on the novel corona virus is still in its nascent stage. Depending on the current published research studies and other relevant sources, we have tried to systematically summarize the epidemiological features, clinical characteristics, diagnostic procedures, treatment protocols and preventive strategies regarding COVID-19. This review article will help the wider society to acknowledge and effectively tackle the 2019 novel coronavirus issues and will provide a reference for future research studies.

Keywords: *2019-nCoV; Coronavirus; Wuhan; Respiratory Tract Infection; SARS-CoV-2*

Introduction

The 2019 novel coronavirus is a new human coronavirus that has emerged in a live seafood market in the city of Wuhan, China and has crossed international borders to infect countries globally [1]. COVID-19 is the clinical syndrome associated with SARS-CoV-2 infection [2]. The SARS-CoV-2 was proclaimed by the World Health Organization [3] as a Public Health Emergency of International Concern on 30th of January 2020 [4]. This novel coronavirus results in a respiratory illness that fluctuates from mild symptomatic illness to severe pneumonia and acute respiratory distress syndrome (ARDS) distinguished by respiratory failure requiring intense care management [3,5]. More research studies are urgently needed to investigate the modes of transmission and pathogenic mechanisms of this viral illness to understand the molecular aspects of viral entry and its replication within the cell that will provide the foundation of developing a targeted antiviral drug therapy and development of vaccine to prevent billions from being infected.

Since December 8th, 2019, Chinese health authorities were able to recognize a SARS-like illness in some patients in Wuhan, China without being able to identify the etiological agent. Connecting links between the index cases and the city's South China Seafood Market (where live animals were also available for sale) were noted. Most patients who initially contracted the virus had some form of contact with this market by either working there or buying items or meeting other individuals who had been to the market recently. The pneumonia like illness precipitated by this virus resulted in acute respiratory distress and the symptoms did not resolve even after antibiotic treatment for 3 to 5 days [2,5]. Some patients abruptly developed severe complications and went into respiratory failure [6]. On January 7th 2020, after the examination of a throat swab of a patient by the Chinese CDC, the World Health Organization (WHO) put out the name for the disease; 2019-novel coronavirus (2019-nCoV), which is currently also called severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1].

SARS-CoV-2 made dramatic headlines in the international press, scientists immediately started to conduct epidemiological and etiological investigations of the outbreak and the pathogen. A research team led by Prof. Yong-Zhen Zhang [7], on January 10th, 2020, published further about the identification of the pathogen and of its genome by developing highly specific diagnostic tools within weeks of the initial case detection. The number of cases increased exponentially affecting individuals located very far from the live animal market where the virus had first originated. This observation suggested human-to-human transmission. This was further confirmed by the infection of 15 healthcare practitioners after close contact with one infected patient in a Wuhan hospital [8]. The first death from this virus was confirmed on January 11th, 2020 [2]. In mid-January 2020, China began passenger transportation during or around the Chinese New Year which fueled the epidemic [9]. On January 23rd, 2020, Wuhan city was placed under lockdown with entry and exit restrictions that extended to other cities in Hubei, China. Meanwhile cases of COVID-19 in other countries were increasing gradually, even in areas where people had no history of travel to China [8]. Later, it was confirmed that asymptomatic contacts could transmit the disease and this virus had an incubation period of around 14 days. On January 30th, 2020, WHO declared the COVID-19 as a global health emergency [10].

SARS-CoV-2 belongs to the family of coronaviruses that infects humans. Similar to MERS-CoV, first identified in Saudi Arabia in 2012 and SARS-CoV in 2002 to 2003, SARS-CoV-2 is a positive-sense single-stranded enveloped RNA virus and a zoonotic coronavirus, which can be transmitted from animal to animal, animal to human and human to human. SARS-CoV-2 transmission has been growing exponentially compared to the previous outbreaks that were confirmed to occur from human-to-human mainly through droplets infection induced by coughing, sneezing, or speaking [8,11,12]. Government authorities around the world are working to establish measures to assess the impact of the virus on the healthcare system and economy of their country along with other possible adverse effects caused by this virus. Scientists and researchers are making efforts to generate data and translate new information on this outbreak through publishing the information.

This review aims to provide evidence of current findings on 2019-nCoV by reviewing its epidemiology, clinical manifestations, diagnosis, as well as the Public Health response. This review provides meaningful information for future research related to this topic; since knowledge about this virus is rapidly evolving, the information should be updated constantly.

The studies selected for this review were identified by searching the PubMed online database, WHO and information published online by the Chinese Centre for Disease Prevention and Control. The search was restricted to human studies in the English language. We searched full texts scientific publications from December 1st, 2019 onwards. The search terms were 'n-CoV', '2019 ncov', 'SARS-CoV-2', 'novel coronavirus', and 'COVID-19'. Bibliographies of all studies were also reviewed to identify additional relevant studies. All non-scientific papers such as commentary, reports, and newspapers were excluded.

Pathophysiology

Structure

Coronaviruses are positive-stranded RNA viruses and are composed of a nucleocapsid covered by a phospholipid bilayer envelope. The envelope is studded with spikes of glycoproteins (composed of two subunits S1 and S2) that are responsible for attaching to receptors of host cells. These spikes gives the virus a crown look (coronam in Latin means crown). SARS-CoV-2 like SARS-CoV and MERS-CoV belongs to the beta-CoVs (Beta-coronavirus under the subfamily "Orthocoronavirinae") that have the ability to infect mammals. The structure of this virus is round or elliptical and usually pleomorphic, with a diameter of about 60 - 140 nm [13].

Physiologically, SARS-CoV-2 resembles other coronaviruses which cannot resist ultraviolet rays and heat. In addition to these factors, several lipid solvents can successfully eliminate the virus. Some of these solvents include 75% ethanol, disinfectant that contains chlorine, or peroxy-acetic acid and chloroform with the exception of chlorhexidine [13].

Genome and viral factors

After isolating a strain from a worker infected with the novel coronavirus at the Wuhan live animal market, it was reported that the complete viral genome is 29.9 kb organized in +ssRNA, which means it is one of the largest known RNA viruses; its genome starts with a 5′-cap and ends with a 3′-poly-A and is similar to the genome sequence of a bat CoV RaTG13 with 96.2% similarity, however, it shares only 79.5% of similarity with SARS-CoV [14,15].

The genome of SARS-CoV-2 includes a frameshift of several open reading frames (ORFs). Most of the RNA (almost 2/3rd) is located in the open reading frame ORF1a and ORF1b, which translate into two polyproteins, pp1a and pp1ab. These polyproteins in turn are cleaved into16 non-structural proteins (nsps) by protease that include chymotrypsin-like protease (3CLpro), main protease (Mpro) and papain-like proteases. The remaining ORFs translate into structural and accessory proteins like a) spike glycoprotein (S), b) envelope protein (E), c) membrane protein (M), d) nucleo-capsid protein (N) [13].

As previously mentioned, close to 80% of the genome novel coronavirus is similar to the genome of SARS-CoV but they also have some differences. One difference is the amino-acid substitution that occurs in NSP2 and NSP3; some researchers suggesting that this mutation results in differences in transmission capacity and pathogenic mechanisms between these two viruses [16]. Zhang., *et al*. in their study analyzed several coronavirus genotypes from different infected Chinese patients and concluded that 27 isolates can be divided into six genotypes indicating that the mutation of the novel coronavirus genome has occurred [17]. However, Tang., *et al*. added to Zhang's research and did further analysis of SARS-CoV genomes from 103 infected patients, and concluded the different strains of the genome: "the S type" and "the L type". The L type is the more prevalent strain with a frequency of 70% and is derived from the S type, which is hypothesized to be the more aggressive and contagious strain [18].

Coronavirus replication and pathogenesis

Angiotensin-converting enzyme 2 (ACE2) is an enzyme attached to the membranes of various cells in the lungs, heart and kidney [19]. ACE2 plays a vital role as a cellular entry receptor of coronavirus SARS-CoV, and as a regulator of its transmission [20]. A study of Zhou., *et al*. reported that the novel coronavirus 2019 shares the same enzyme entry receptor (angiotensin-converting enzyme 2) as SARS-CoV [15].

Structural glycoproteins have different functions regarding the pathogenicity; among these functions, the envelope of the virus promotes the assembly and release of the virus. SARS-CoV-2 Spike (S) glycoprotein recognizes ACE2 receptor and then forms a virus-receptor complex, which facilitates the virus entry into the cell. This step is considered crucial due to the affinity of the virus-receptor binding and is currently studied with different approaches. The membrane fusion helps to form a bridge, through which the viral genome gets released into the cytoplasm of the host cell. The translation of the two polyproteins pp1a and pp1ab, from the uncoated viral genome begins in the host cell. This helps in the production of non-structural proteins; the transcription starts with the production of a replication-transcription complex (RTC) organized in double-membrane vesicles and goes on till the formation of sub-genomic RNA (sgRNA) sequences. Termination of the RNA transcription occurs between open reading frames (ORFs). Once the sub-genomic RNAs (sgRNAs) sequences are released, the translation begins with the formation of accessory and structural protein chains [13,14,21,22]. The assembly of the nucleocapsid proteins and envelope glycoproteins forms a new viral particle. The newly formed vesicle containing the viral particle fuses with the plasma membrane of the host cell and releases the virion.

The pattern recognition receptors (PRRs) mostly Toll-like receptors (TLRs) present in the phagocytic cells detect the viral RNAs as the pathogen-associated molecular patterns (PAMPs) [23]. These complex virus-cell interactions induce an excessive immune reaction in the host cells with a diverse and invading set of immune mediators. If the innate immunity fails to eliminate the virus, it is called immunopathology. This was seen in SARS-CoV-2 where a few cases had increased plasma cytokines and chemokines called "cytokine storm",

which caused serious immunological reactions that damages the cells and tissues extensively [13,24]. The leading factor of these reactions is interleukin 6 (IL-6), which activates the other immune cells. In this way, several virus particles initially start invading the respiratory mucosa and then continue to damage other systems, with a series of immune responses [14].

Epidemiology

In the past few centuries, only a limited number of human coronaviruses that caused mild respiratory symptoms were noted [25]. The start of the 21st century has seen an increase in the outbreaks, which have emerged periodically in many countries caused by two highly pathogenic coronaviruses. In 2002, Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) [26] and then in 2012 Middle East Respiratory Syndrome coronavirus have appeared (MERS-CoV) [27]. Coronavirus "2019-nCoV" has become the third coronavirus to emerge in the human population. However, the transmissibility of 2019-nCoV with a mean R0 ranged 3.3 to 5.5, which is notably elevated compared with other epidemics [28]. The transmission of the novel coronavirus is mainly through droplets passed on when an infected person discharges respiratory secretions through coughing, sneezing, or while speaking. When these droplets fall on the floor, solid objects or surfaces, they become contaminated and pose a risk for the other humans who come in contact with these objects and surfaces. According to current research, the virus is not only airborne. A person can be infected by breathing in the droplets containing the virus if the individual is within a close distance (1 meter) of an infected person, or by touching a contaminated surface and then touching the face (eyes, nose, and/or mouth) before properly washing the hands. Research shows that a higher viral load is reported mainly in the nasal cavity as compared to the throat [14,29,30]. The virus can remain alive on surfaces for many days if there are favorable atmospheric conditions, but it can't resist common disinfectants such as sodium hypochlorite and hydrogen peroxide. The virus can also survive in the feces and contaminate water supply and subsequent transmission through aerosolization/feco-oral route [31]. All ages are susceptible; however, elderly individuals and people with comorbidities are at a much higher risk. Individuals with underlying respiratory illnesses are also at a great risk as these illnesses are the principal risk factors for the progression of the disease [32].

The novel coronavirus 2019-nCoV is still in its spreading phase with high predicted projections suggesting that thousands of people are getting infected globally every day. The CFR (case fatality rate) for the whole world as of today 4/7/2020 is 4.76% which has increase by 1.39% as the CFR value on 25th of February 2020 was 3.37%. The CFR varies from below 1% in countries like Bahrain, Belarus, Singapore to more than 15% in countries like Yemen, France and United Kingdom [33].

Current situation of the epidemic

Globally, as of 10:33am CEST, 4 July 2020, there have been 10,902,637 confirmed cases of COVID-19, including 522,446 deaths, reported to WHO. By this time, it was identified that SARS-CoV-2 has spread worldwide into most of the countries with the highest incidence in America and Europe (Figure 1). It is remarkable to note that while the number of new cases has reduced in China, they have increased exponentially in other countries including the United States, India, United Kingdom and Brazil.

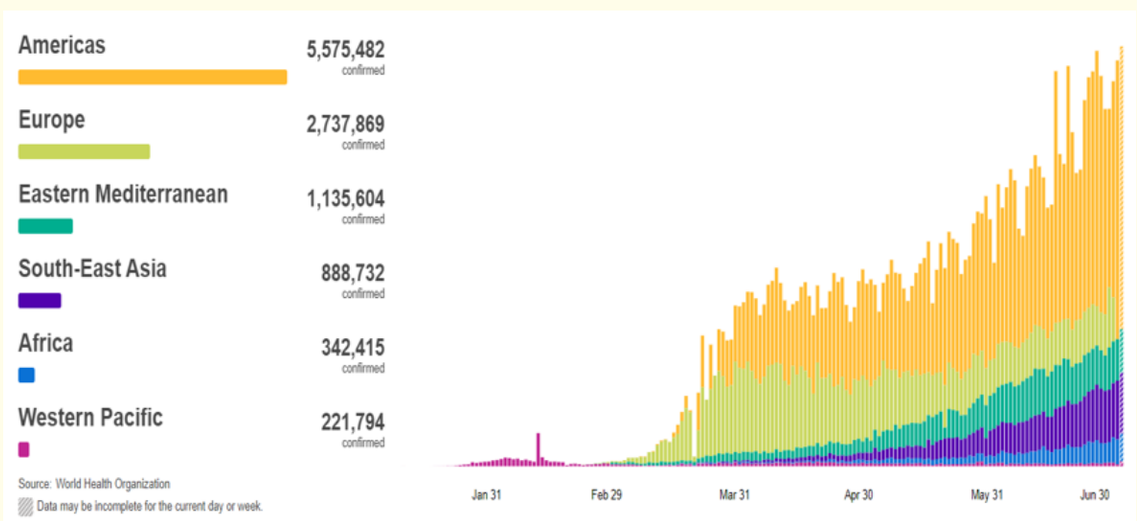

Figure 1: *Distribution of the cases worldwide (Adopted from https://covid19.who.int/).*

Clinical presentation

COVID-19 is considered as an acute infectious disease of the respiratory system, which is primarily transmitted through the respiratory tract, either by respiratory droplets, secretions, or direct contact even for a low infective dose [29,30]. The virus has been found in stool samples and blood of severely pneumonic patients, thereby implying the likelihood of feco-oral transmission as well as pointing towards multiplicity of transmission routes of the virus. Mother to child transmission has already been reported [34].

Based on a statistical analysis of publicly available case data, the incubation period of COVID 19 falls within the range of 2 - 14 days and has a mean of around 5 days [35]. This community-acquired pneumonia is highly contagious especially in the elderly and patients having chronic comorbid illnesses like hypertension, chronic obstructive pulmonary disease (COPD), diabetes and cardiovascular disease. In a study done by Zhang., *et al*. 2020, the median age of the patients was found to be 55.0 years and 48.9% were male [36].

The most common symptoms reported (Table 1) are fever (some early cases may not have fever but only respiratory symptoms), dry cough, cough with expectoration, shortness of breath, fatigue, nasal congestion, runny nose, sore throat, headache and diarrhea. All of the infected patients had at least one symptom. The dominant symptoms were fever and cough, whereas symptoms in the upper respiratory and gastrointestinal tracts were found in minority of patients [14]. Most reported cases experienced mild symptoms and may not present positive signs (have the coronavirus but are asymptomatic). The rapid spread of this virus shows why data regarding the relative frequency of these cases is likely to be skewed by detection bias; these cases may be over-represented in recent data. Most common presentation of this infection is with mild flu-like symptoms; however some patients developed serious illness in the form of acute respiratory distress syndrome (ARDS), or respiratory failure, multi-organ dysfunction syndromes (MODS), systemic manifestations (sepsis, septic shock), or multiple organ failure, and even death [13].

Clinical features	Guan., *et al*. 2020 Number of patients: 1099	Liu., *et al*. 2020 Number of patients: 137	Xu., *et al*. 2020 Number of patients: 62	Wang., *et al*. 2020 Number of patients: 138
Fever	88.7%	81.8%	77%	98.6%
Cough	67.8%	48.2%	81%	59.4%
Expectoration	33.7%	4.4%	56%	26.8%
Dyspnea	18.7%	19%	3%	31.2%
Headache	13.6%	9.5%	34%	6.8%
Sore throat	13.9%	NA	NA	17.4%
Diarrhea	3.8%	8.0%	8%	10.1%
Fatigue	38.1%	32.1%	52%	69.6%
Hemoptysis	NA	5.1%	3%	NA

Table 1: *Common symptoms of COVID-19 in infected patients.*

Laboratory features included normal range or low white blood cell count and lymphocytopenia for most of the patients along with raised lactate dehydrogenase [37]. However, most of the ICU patients at the time of admission had raised Prothrombin time and D-dimer levels. Additionally, raised cytokine levels (IL1B, IFNγ, IP10, and MCP1) were detected signifying inflammatory activity probably leading to activated T-helper-1 (Th1) cell responses [3].

The Computerized Tomography (CT scan) findings varied with the age of the patient, immune status, and the stage of the disease at the time of screening/scanning. The most common patterns seen are pure ground-glass opacity, septal thickening, consolidation, with

prominent distribution in the posterior and peripheral part of the lungs. Presence of Consolidation lesions serves as a marker of progressive disease [9].

Diagnosis

If patients satisfy the epidemiological and clinical criteria as specified, then they are classified as a presumptive case:

- Supportive epidemiological history: If the case has traveled or lived in an infected city or is in direct contact with patients having suspected respiratory symptoms within 14 days of the onset of illness.
- Clinical symptoms: Fever, laboratory and imaging findings (serum samples with a decreased level of lymphocytes and elevated C-reactive protein, CT scan findings of small patchy shadows, interstitial changes and infiltrations).
- Golden clinical diagnosis method: Nucleic acid technique (NAT) is used to detect the nucleic acids and it employs real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assay and final confirmation by next-generation sequencing. Samples used are swabs from nasal and throat areas as well as specimens like bronchial/alveolar lavage fluid and deep sputum.
- Serological testing: CDC has developed serologic test which is an ELISA-based test to detect antibodies against SARS-CoV-2 in serum or plasma. This test uses purified S protein as antigen. This test has a specificity of greater than 99% and a sensitivity of 96%; so it can be used detect past SARS-CoV-2 infection [38].

Public health response

Personal precautions

- One of the most important and effective measures for the prevention of infection is frequent and correct hand washing (especially after coughing or sneezing) with ordinary soap or alcohol-based hand sanitizer.
- Cleaning and disinfecting the frequently touched objects and surfaces and keeping the rooms ventilated.
- Maintain good respiratory hygiene and cover the mouth while coughing or sneezing with a tissue or the elbow but not with bare hands.
- Avoiding touching the face (eyes, nose or mouth) before washing the hands.
- Maintaining a strong health with a good diet, regular sleep schedule and exercising often.
- Keeping distance to people with the illness and anyone who you don't live with as they could have the virus but be asymptomatic (avoid crowded places, and take precautions in public places).
- Seeking medical help if suspected with respiratory symptoms or fever [39].

Non-pharmaceutical interventions

Non-pharmaceutical interventions remain a primary line of intervention for management of COVID-19 (e.g. face masks) especially for a first responder who is directly involved in providing healthcare during an infectious disease outbreak, which includes primary, second-

ary, and tertiary care providers [40]. The masks should be worn and taken off properly. The role of the mask is to block the carrier of the virus, so it is not transmitted. The most effective mask is N95 that can filter 95% of the particles, with 3 layers (the middle one is the filter). Beside healthcare workers, pregnant women, elderly and those with chronic diseases or critical condition as well as children should wear masks [39].

Control measures

The classical public health measures to flatten the curve of this epidemic is to prevent the person-to-person spread (community spread) of the disease by a) isolation of ill persons from non-infected individuals in the hospital settings, b) quarantine, effective during the 2003 SARS epidemic, restricting movement of persons who are exposed to the disease but aren't sick and c) physical distancing to reduce interactions in the community, in which suspected infectious individuals have not been identified and not yet isolated. If these measures aren't sufficient, "community-wide containment" needs to be implemented. It's an expansion from physical distancing to community-wide quarantine, which is applied to an entire community, city or region, with extensive movement restrictions allowing only vital supplies and basic human necessities such as access to groceries, medications, and doctors [41].

Control of hospital infection

Infection control protocols must be strictly implemented by all the medical staff by wearing personal protective equipment (preferably N95 masks or surgical or other type of masks depending on what is available, goggles, and gloves), with protection measures like hand sanitizing, disinfection; especially for those in contact with COVID-19 patients, blood or specimen, or preforming invasive and non-invasive procedures such as endoscopy [39].

Travel restrictions

National borders may be closed and entry may be banned into provinces implementing community containment. International travelers are already stuck in these areas and will be able to leave only if their governments initiate the evacuation process. Once the citizens return to their country of origin it is mandatory that they should be quarantined for minimum 14 days to prevent spread of the virus and reduce number of cases in their country. Studies have shown that travel restrictions delayed the spread of the epidemic by reducing import of infected cases [42,43].

Future of infectious diseases

Future investigation on viral transcription, replication, pathogenesis, diagnosis, treatment and other characteristics of the novel coronavirus will help to contain the spread of the virus and prevent others from contracting it. However, given the emergency of this respiratory outbreak as a new infectious disease with the interspecies transmission (animals-human and human-human), lessons have to be learned on the origin of the pathogen. To fully understand the properties of the virus, it is vital to trace the origin of the virus. Changes in the ecology and human practices such as the invasion of natural habitats of animals by humans and the consumption of some of these animals, the viruses will transfer from their natural hosts to humans and have devastating effects already being seen through the outbreaks in the last several decades [44].

The high lethality of the viruses (SARS-CoV, MERS-CoV, H5N1, H7N9, Ebola and currently SARS-CoV-2) should alarm the world to reduce the probability of their occurrence by not ingesting these animals and keeping distance from their habitat. The investigation of animal etiology should be strengthened, with identifying high-risk pathogens and maintaining the line between natural hosts/reservoirs and the human society [45].

Treatment

Currently, there are no specific antiviral treatments that have been proven effective in reducing the symptoms or curing COVID-19. Patients generally receive management as per best supportive care for any respiratory disease and mainly involves symptomatic and respiratory support like oxygen therapy (ventilator) [46]. The WHO has recommended the use of extracorporeal membrane oxygenation (ECMO) to patients with refractory hypoxemia [47].

While fighting the outbreaks of previous SARS-CoV and MERS-CoV viruses, we have gained experiences for some treatment protocols regarding coronaviruses. Some of the drugs such as remdesivir (Ebola-antiviral) and chloroquine have been found to be effective against a broad-spectrum of viruses including SARS-CoV and MERS-CoV [48,49]. These drugs have demonstrated the most successful antiviral management with the lowest cytotoxicity effect [50]. Initial reports showed that oseltamivir was also given to most of the patients (75 mg, 2 times/day) in combination with antibiotics. Researchers have even reported both prophylactic and therapeutic advantages of chloroquine CQ (used for autoimmune disease and malarial infection) for SARS-CoV infection that functions at both viral entry and post-entry stages of the SARS-CoV-2 infection, with potential broad-spectrum antiviral activities. Preliminary results showed apparent efficacy of chloroquine phosphate; however, its overdose is highly fatal without the known antidote [51]. The potential of hydroxychloroquine HCQ in the treatment of COVID-19 has been partially confirmed to improve symptoms [52]. A number of antiviral therapeutic agents have been identified in clinical trials (Table 2).

Name of drug	No. of patients	Phase	Clinicaltrail.gov identifier
Glucocorticoid	80	Phase 3 (RCT)	NCT04244591
Baricitinib	12	Phase 3 (Non-randomized clinical trial)	NCT04358614
Hydroxychloroquine	30	Phase 3 (RCT)	NCT04261517
Three therapeutic arms (Hydroxychloroquine + Lopinavir/Ritonavir + Interferon-β 1a group and Hydroxychloroquine + Lopinavir/Ritonavir + Interferon-β 1b group and the Base Therapeutic Regiment Group, i.e., Hydroxychloroquine +/Ritonavir).	60	Phase 2 (RCT)	NCT04343768
Danoprevir +ritonavir+/-Interferon nebulization	11	Phase 4 (Single group assignment)	NCT04291729
Lopinavir/ Ritonavir, Ribavirin and Interferon Beta 1b Combination Versus Lopinavir/ Ritonavir Alone	127	Phase 2 (RCT)	NCT04276688

Table 2: *Chemotherapeutic drugs under clinical trial for COVID-19.*

Vaccination

Multiple efforts are being at the international level to develop a COVID-19 vaccine. Although there has been considerable progress in the development of vaccine but as of now, no vaccine has completed clinical trials. WHO organized a telethon on 4 May 2020 for the development of COVID-19 vaccine and received US$8.1 billion from forty countries [53]. According to the WHO website, 18 vaccines are in clinical evaluation phase (Phase 1, 2 and 3) and 129 candidate vaccines are in preclinical evaluation phase. The only vaccine which has reached Phase 3 clinical trial is the ChAdOx1-S type of vaccine being developed by the University of Oxford/AstraZeneca [54].

Conclusion

COVID-19 is the clinical syndrome associated with SARS-CoV-2 infection. COVID 19 is highly contagious with a mean R0 ranged 3.3 to 5.5. SARS-CoV-2 Spike (S) glycoprotein recognizes ACE2 receptor that helps the virus entry into the host cell. The severity of the novel coronavirus ranges from mild symptoms (majority of cases) to severe respiratory tract infection and pneumonia. However, in few cases it induces "cytokine storm" that damages the cells and tissues extensively. The most susceptible population is elderly and individuals with underlying medical conditions. Golden method for diagnosing the disease is real-time reverse transcriptase polymerase chain reaction (rRT-PCR). Currently, there are no specific antiviral treatments and patients are managed with the best supportive care which may sometimes involve oxygen therapy and ventilator support. A number of antiviral therapeutic agents are under clinical trials.

More scientific research is required to understand the transmission modes and pathogenicity of this virus to help develop new targeted antiviral drugs and vaccines.

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