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A Novel 2019 Severe Acute Respiratory Syndrome Coronavirus 2 (COVID-19) as Global Pandemic

Sharma S[1], Swapnil P[2] and Meena M[3]*

[1]School of Biotechnology, Jawaharlal Nehru University, India
[2]Department of Botany, Acharya Narendra Dev College, University of Delhi, India
[3]Department of Botany, Mohanlal Sukhadia University, India

***Corresponding author:** Mukesh Meena, Department of Botany, Mohanlal Sukhadia University, Udaipur-313001, India, E mail: mukeshmeenamlsu@gmail.com

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Abstract

A novel coronavirus disease that emerged in the 2019 end has been declared as a global health emergency by the world health organization (WHO). COVID-19 is an infectious disease caused by the severe acute respiratory syndrome (SARS) that affects the lower respiratory tract and manifests as pneumonia in the host. In response to this unprecedented outbreak, we summarise the current knowledge about the COVID-19 to spread public awareness about the disease and provide a reference for further research.

Keywords: Coronaviruses; COVID-19; Pathomechanism; Diagnosis; Prevention

Abbreviations: WHO: World Health Organization; SARS: Severe Acute Respiratory Syndrome; CoVs: Coronaviruses; RNA: Ribonucleic Acid; NSP: Non-Structural Proteins; RBD: Receptor-Binding Domain; ACE2: Angiotensin-Converting Enzyme 2; ER: Endoplasmic Reticulum; PRRs: Pattern Recognition Receptors; ARDS: Acute Respiratory Distress Syndrome; RT-PCR: Reverse Transcription-Polymerase Chain Reaction; CT: Computed Tomography.

Introduction

Coronaviruses (CoVs) belongs to the Coronaviridae family of enveloped positive-sense single-stranded RNA viruses with a diameter ranging from 60-120nm infecting humans and vertebrates [1,2]. They are widely classified into α, β, γ, and δ-coronavirus [3,4]. Human-susceptible virus among CoVs has been identified, namely 229E and NL63 which are α-CoVs, and HKU1 and OC43 which belong to β-CoVs which causes respiratory diseases similar to the common cold, thus having low pathogenicity. There are two other β-CoVs that lead to severe and potentially fatal respiratory tract infections namely SARS-CoV and MERS-CoV [5]. The novel 2019 coronavirus was officially named as "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) by The International Committee on Taxonomy of Viruses [6] the World Health Organization (WHO) named the new virus 'COVID-19'. The unknown viral pneumonia epidemic initially broke out in Wuhan, China in December 2019. SARS-CoV-2 belongs to the family of β-coronavirus as it shows approximately 79% genome sequence homology with SARS [7]. Some studies show that SARS-CoV-2 showed similarity with bat coronaviruses suggesting that maybe bat are their potential reservoir [7,8]. Covid-19 possesses a single-stranded RNA genome and has spike−like projections all over its surface, under the microscope. Many laboratories across the world have sequenced its genome which shows that it contains longs nucleotides around 29.811 bp [9]. Tang and his group have further classified the SARS-CoV-2 genome into two prevalent types, L type (~70%) and S type (~30%) after conducting 103 SARS-CoV-2 genomes population genetic study [10]. It is analysed that derivation of L type strain is from S type strain which is found more contagious and aggressive due to evolution. In January 2020, WHO declared COVID-19 as a global threat.

This article reviews available information regarding

pathogenesis, clinical characteristics, genetic structure, and route of transmission, prevention, and treatment of COVID-19. The knowledge about the SARS-CoV-2 virus is rapidly evolving, thus the latest information about the research, prevention, and treatment of this new disease is very important.

Pathomechanism

The recently discovered beta-coronavirus (2019) have the typical coronavirus structure with spike protein and possesses single-stranded, positive (+)-sense RNA as a genetic material [11]. The genomic study revealed that nucleic acid (RNA) encodes four vital structural proteins such as spike (S), glycoprotein, envelope (E), membrane (M), and nucleocapsid (N) with several accessory proteins [12]. SARS-CoV-2 genome encodes 16 non-structural proteins (NSP) and also contains the largest gene *orf1ab* which through translation gives two polyproteins (pp1a and pp1ab) [13,14]. The CoV spike (S) is the dominant surface protein and plays an essential role in viral attachment, fusion, entry, and transmission. It is composed of receptor binding N-terminal S1 subunit and C-terminal S2 subunit responsible for the virus-cell membrane fusion [15,16]. The S1 subunit contains a receptor-binding domain (RBD), which binds to the cell surface receptor angiotensin-converting enzyme 2 (ACE2) present at the surface of host epithelial cells [11]. Epithelial cells act as a primary barrier to any foreign entity entering their host via body cavities as it covers the inner and outer linings of body cavities, such as the respiratory or intestinal tract [17]. During infection, the virus attached to the host cell through S1- receptor binding domain and the ACE2 cell membrane receptor, leading to the entry inside the target cell [18,19]. Viral genomic RNA is released into the cytoplasm of the host cell and translated into polymerase and replicas polyproteins, further cleaved into small products by viral proteinases [20]. Positive-sense RNA synthesized from negative-sense genomic RNA (as a template). Afterward, in the cytoplasm replication of viral RNA and nucleocapsid takes place followed by the transcription. A structural protein such as S, M, and E transported to the Golgi after translation in the endoplasmic reticulum (ER) and further undergoes assembly of virions and transported via vesicles [21] (Figure 1). Lastly, the virion-containing vesicles fuse with the plasma membrane and released out of the host cell. CoV uses various strategies to avoid immune responses for better survival into the host cell. There are pattern recognition receptors (PRRs) that recognize microbial evolutionarily conserved structures called pathogen-associated molecular patterns (PAMPs). However, these viruses produce double-membrane vesicles which lack PRRs and replicate in viral vesicles, hence avoiding detection by host cell [22].

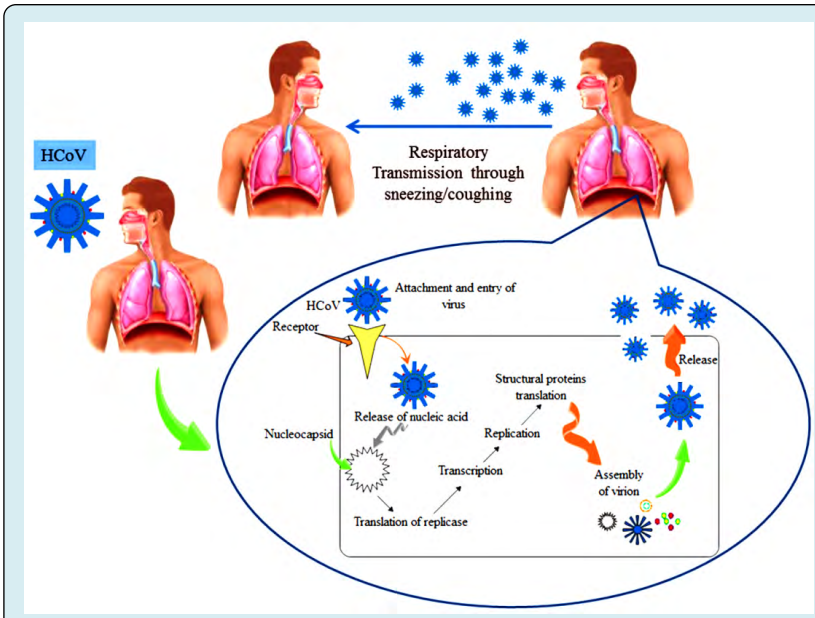

Figure 1: Pathomechanism of coronavirus in human.

Clinical Characteristics and Transmission

SARS-CoV-2 is the third zoonotic coronavirus which has created a frightening crisis around the world on human health [23,24]. All ages are susceptible to the 2019 coronaviruses disease. The virus replicates in the ciliated epithelium that causes cellular damage and contamination at infection site. Typical symptoms of infected patients are dry cough, fever, shortness of breath, fatigue, headache, pneumonia, diarrhoea, and vomiting [25,26]. COVID-19 ranges from

an asymptomatic state to severe infection leading to acute respiratory distress syndrome (ARDS) to critical condition which may lead to multiorgan dysfunction and even death. COVID-19 primarily spreads through airborne zoonotic droplets through sneezing and coughing and from infected patients or direct contact with infected persons, surfaces, or objects [23-27] and promotes community transmission. There is evidence that shows this virus remains active in aerosol for 3 hours and on stainless steel, plastic, cardboard surfaces, and copper, it survives up to 72 hours [28]. Researchers have found the presence of the virus in faces and blood, indicating the probability of multiple routes transmission [29-31]. The current epidemiological investigation reflects that the incubation period of viral particles 1-14 days and most importantly 3-7 days [32]. Clinical investigations showed aged people suffering from severe diseases like chronic obstructive pulmonary disease, hypertension, cardiovascular disease, and diabetes is more affected than adults or children. In aged people coronavirus rapidly develop respiratory failure, acute respiratory distress syndrome, septic shock, multiple organ failure, even leading to death [33].

Prevalence Rate

The virulence of coronavirus diseases in humans is affected by both viral and host factors. A case of unidentified pneumonia was reported in late December 2019 in Wuhan, China which spread rapidly by human-to-human transmission and was virulent [34]. Soon, Chinese research authorities isolated a new virus from the seafood market in Wuhan city; known as 2019-nCoV [35]. Eventually, there was exponential growth in the number of COVID-19 positive patients and the virus rapidly spread to many countries. As of 5th July 2020, 11,465,712 cases of COVID-19 have been confirmed World-wide with 532,021 deaths. Among which 2,936,890 and 675,453 cases are confined to the USA and India respectively [36]. Wu and his group calculated the basic reproduction number (R0) of SARS-CoV-2 and found that the secondary infections may cause in a completely vulnerable population without interference. His group estimated R0 to be 2.47-2.86 using the SEIR model [37]. Which was higher than the R0 value of SARS-CoV which is 2.2-3.6 [38], and MERS-CoV is 2.0-6.7 [39], indicating relatively high transmissibility that of SARS-CoV-2. The main source(s) of this new novel virus remains elusive but direct contact with infected host animals or wild animal's consumption is suspected to be the main route of SARS-CoV-2 transmission. COVID-19 positive cases are increasing continuously at an exponential rate and the doubling time of the pandemic is reported to be 1.8 days after conducting modelling studies [23]. The overall fatality rate is has been estimated 2 to 3% whereas this rate is higher ranging from 4 to 11% in hospitalized adult patients [36]. Special care is needed for neonates and the elderly since they have an immature or weak immune system.

Diagnosis, Treatment and Prevention

The emerging SARS-CoV-2 cause's global health emergency is in urgent need of interventions. Diagnosis of COVID-19 requires non-invasive detection of viral nucleic acid in patients that has high specificity, high sensitivity, low cost, eases of use, easy accessibility, and fast screening. The important methods for diagnosis of this pneumonia are nucleic acid reverse transcription-polymerase chain reaction (RT-PCR) test from the throat and nasal swab samples, chest computed tomography (CT) scan [40,41], next-generation sequencing. Serological tests such as ELISA tests, rapid chromatographic tests, and others are also used for the detection of immunoglobulin M (IgM) which rises after 1 week of initial infection and immunoglobulin G (IgG) appears about 14 days after infection [42]. Preliminary identification of the SARS-CoV-2 was conducted at the viral research institution, China through electron microscopy for observing its morphology and the classical Koch's postulates [43]. The virus infected cases could be suspected with the appearance of any of the clinical characteristics such as fever, sore throat, cough, and difficulty in breathing or travel history [32]. However, asymptomatic cases and symptomatic cases both require confirmation with a positive molecular test. Elevated levels of C-reactive protein, lactate dehydrogenase, erythrocyte sedimentation rate, creatinine, low white blood cell count, and prolonged prothrombin time are usually associated with disease condition [26-44]. No confirmed treatment or effective antiviral therapy is approved until now against COVID-19. Available treatments are focused mainly on symptomatic and respiratory support. Therefore, community transmission should be prevented via adequate isolation from an infected person, maintaining nutrition, and managing mild illness at home. Drugs including Remdesivir, Chloroquine, Lopinavir, Ritonavir, Ribavirin, Oseltamivir, penciclovir, acyclovir, or their combination are investigated to use in clinical practice as a potential cure to COVID-19. Remdesivir shows broad-spectrum antiviral activity against several RNA viruses has been reported to treat the first US case of COVID-19 successfully [45,46]. Another anti-malaria drug, chloroquine shows with great potential to treat COVID-19 infection [47], with the specific mechanism of action that is not well understood. *In-vitro* analysis of remdesivir and chloroquine combination has also proven to effectively inhibit the recently emerged CoV. Study of SARS and MERS-CoV antibodies might provide important guidelines for designing and development of SARS-CoV-2-specific antibody as this new virus is closely related to SARS-CoV and has a high sequence identity in their S proteins [34,48]. Prevention is the best way because currently there is no approved treatment knows yet against this pandemic infection. The virus incubation period before the onset of

symptoms and contact with asymptomatic positive patients are several factors leading to uncontrolled transmission of this new infection. Wearing masks, following proper cough hygiene, home isolation in case of mild illness, washing hands with soap, maintaining a healthy routine, and decontaminating the surroundings preferably with sodium hypochlorite are some of the infection control measures recommended. An adequate supply of medical essentials is very to protect healthcare workers who are taking care of patients and to prevent transmission of infection to other patients as well.

Conclusion and Future Prospective

SARS-CoV-2 continues to spread globally with an urgency to develop effective therapeutics. Further research to understand the novel coronavirus transmission and pathogenicity mechanism is required to facilitate the development of a virus-specific vaccine and drugs. More so, this new virus outbreak has challenged the medical, economic, and public health infrastructure across the world. Evidently, the pandemic potential of COVID-19 demands rigorous efforts to control this outbreak and efficient measures to monitor future outbreaks of zoonotic origin.

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