Acta Scientific Pharmacology

Volume 1 Issue 7 July 2020

Review Article

CoVID-19: An Overview of the Characteristics, Diagnosis and Prevention of the Deadly Pandemic Disease

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Received: May 06, 2020

Published: June 12, 2020

Abstract

Coronavirus which causes severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) are highly infectious viral strains that belong to the group β - coronavirus family. Bats are believed to be the common origin-host of these viruses. The current pandemic caused by a similar coronavirus (SARS-CoVID-19) is also suspected to have originated from bats. However, there are different unresolved theories which are out of the scope of this review. With currently no vaccines or treatments available, except for the use of the drug Remdesivir, the world struggles to contain the virus. The only possible means to curb its spread is through proper detection, personal isolation and hygiene. Detection of this novel coronavirus is carried out using molecular biology techniques like- RT-PCR, ELISA and CRISPR based testing kits. CoVID-19 strain belongs to single-stranded positive-sense RNA viruses. Interestingly these viruses are capable of adapting and mutating to the new environment. The rapid transmission of the novel coronavirus around the world causing a severe mortality rate depends on this mutation or not is yet to be identified.

Keywords: *CoVID-19; Novel Coronavirus; Pandemic; Diagnosis; Molecular Techniques*

Introduction

SARS-CoV-2 is one of the recently known viruses which belong to the Coronaviridae family [1], commonly called "Coronavirus or CoVID-19". This group of viruses usually has RNA as its genetic material which causes severe diseases in birds as well as mammals. The virus is constituted by enveloped positive single-stranded RNA genome where capsids are helically symmetrical [2]. The term coronavirus was coined by June Almeida and David Tyrrell who was a pioneer in coronavirus studies. The term derived from Latin "Corona" meaning crown [3]. Some strains of these coronaviruses are known to cause various common cold outbreaks among humans. The samples isolated from such patients showed common morphological similarity with avian infectious bronchitis virus (IBV) hence they are also called IVB-like viruses [4]. Mouse hepatitis virus (MHV) and Transmissible gastroenteritis virus (TGEV) are other strains of animal coronaviruses that were isolated in the early 1940s. Coronavirus widely infects pigs, chickens, humans and rats which can cause a wide range of disorders including various organ systems failures [5]. The history of infection of coronavirus was found in the mid-1960s obtained from the respiratory tract of an adult with a common cold and the virus was named B814 by Tyrrell and Bynoe. They further conducted studies using human embryonic tracheal organ cultures by inoculating the medium from cultures obtained from human volunteers. Since 2003 five new human coronaviruses strains are identified including newly found group I coronaviruses NL63, NL, SARS, MERS, and New Haven coronavirus around the world which cause severe illness affecting both upper and lower reparatory tracts. These strains of viruses have a high rate of mortality hence they are grouped in highly infectious viruses affecting mammals including humans [6]. The novel virus strain 229E was inoculated which caused common cold and inactivated by ether [7]. A large number of different strains of corona-

viruses affecting animals were discovered since the 1930s. Among these strains, those predominantly infecting humans were 229E, OC43, SARS-CoV, NL63, HKU1, and MERS-CoV. Severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) are two strains of viruses that can cause severe fatal respiratory diseases in humans when compared to other strains. Recent studies showed that camels in Saudi Arabia bear three different species of HCoV including MERS HCoV which were responsible for the outbreak in the Middle East as well in South Korea during 2015 [8]. Coronaviruses that affect humans are single-stranded, enveloped, contains positive-sense RNA genome up to 26-32 kilobases in size and to date, this is the largest known genome among the RNA viruses [9]. Different viruses infecting animals during the 1960s-1970s shows pathological conditions similar to that of CoV infections excluding IBV and virus causing bronchial infections in chickens. Coronaviruses studied extensively during 1970s were found in the faeces of sheep, cattle, deer, and horses [10]. The recently evolved novel coronavirus SARS-Cov-2 is believed to have originated from bats and spread to humans from the "wet-market" in Wuhan, China in late 2019. What has left the world more puzzling is that though the virus has emerged from an animal, the effects of this SARS-CoV-2 is more pronounced in humans than in animals.

Figure 1: A 3D model of the novel coronavirus showing the RNA genetic material, envelope and the spikes made of glycoproteins found on the surface of the virus. The image has been adapted from Wikipedia.

Classification of coronavirus

Scientifically, coronaviruses have been christened Orthocoronavirinae or coronavirinae. Coronavirus belongs to the large family of Coronaviridae, order - Nidovirales, Domain - Riboviria. Further, they are divided into 4 major groups namely: - Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Among these four types, alpha and beta are known to affect animals whereas gamma and delta are known to infect birds [11]. The coronaviruses are classified based on the presence of the crown or halo-like appearance made up of glycoprotein-embedded envelope observed under the electron microscope [12].

Figure 2: Classification of coronavirus [13].

Characteristics of coronaviruses

Severe acute respiratory syndrome coronavirus has known to be originated by the recombination of bat SARS - related coronaviruses [14,15]. In four major group of coronavirus alpha and beta coronavirus are two groups which infect mainly mammals. SARS-Cov and MERS-CoV are two highly infectious viruses causing severe respiratory and gastroenteritis in animals including humans, these two groups can cause disease and death of livestock and humans, recent studies shown that all the human infectious coronavirus have animal origins. These viruses have shown rapid activity in immune-compromised hosts, it also causes severe infections in infants, young children, and elderly individuals [16]. Analysis of molecular clock showed that the most recent common ancestor of all

coronavirus was estimated at approximately 8100 BC, from studies conducted by Patrick., *et al.* reported that the bats and birds are the most suitable hosts for coronaviruses. Whereas alpha and beta coronaviruses are photogenic to bats, gamma and delta coronaviruses are pathogenic to birds [17].

SARS-CoV	MERS-CoV
The genome has 29,727 nucleotides	The genome has 30,199 nucleotides
Includes 11 openings read frames which encodes two polyproteins encoded by ORF1a and ORF1b, Structural proteins - 4, accessory proteins - 8	Includes 11 openings read frames, Contains Four structural proteins (S, E, M, and N) and five accessory proteins (ORF3, ORF4a, ORF4b, ORF5, and ORF8
Gene present to Encodes glycoprotein hemagglutinin-esterase	Does not Encode hemagglutinin-esterase
Spike proteins are 1,255	Spike proteins are 1,353

Table 1: Genomic characterization of SARS-CoV and MERS-CoV [24,25].

MERS-CoV and SARS-CoV possess five and eight accessory proteins, respectively, which might help the viruses, evade the immune system by being harmful to the innate immune response. These differences might lead to greater sensitivity to the effects of induction and signaling of type1 interferons (IFNs) in MERS-CoV than SARS-CoV [26].

In animals, coronaviruses emerged from the first outbreak of the SARS epidemic and were identified as SARS-CoV. Later in 2005 human coronaviruses or SARS-like coronavirus were found in horseshoe bats suggesting that the natural hosts were bats whereas intermediate hosts were civets [18]. Coronaviruses have spherical to pleomorphic enveloped particles which are covered by spike-like projection containing glycoproteins, and core covered by matrix protein enclosed within single-stranded positive-sense RNA genome connected by nucleoprotein. SARS-CoV was known to cause mild effects in humans causing cold and non-communicable respiratory infections until 2003 when they became fatal. During the 2003 outbreak of the SARS-CoV, new strains of viral strains were identified namely HCov-NL63 and HCoV-HKU1 [19,20]. The serologically analyzed coronavirus species shows four different antigenic groups. The recent pandemic and high mortality due to CoVID-19 (Coronavirus diseases-19) is caused by severe acute respiratory syndrome which is highly infectious, pathogenic and communicable [14]. This outbreak was declared as Public health emergency of international concern on 30 January 2020 by the World Health Organization.

Initially, the CoVID-19 outbreak was rapidly spreading in the region of Wuhan, China where patients infected by this virus showed various degrees of different clinical symptoms including fever, cough, and diarrhoea [21]. The virus is mostly spherical in shape containing a lipid bilayer envelope. The viral envelope consists of membrane (M), envelope (E) and spike proteins (S) in the ratio 1:20:300 respectively. Spike proteins on coronavirus are 74 in number. It also contains proteins called hemagglutinin esterase (HE) on the shorter spike [22]. The genomic characterization of coronavirus revealed a non-segmented positive-sense RNA genome of approximately 30kb. The translation of replicase polyproteins is done by mRNA containing 5'cap structure along with a 3' poly (A) tail. Non-structural proteins 20kb of the viral genome, untranslated region (UTR) present on the 5' end of the genome contains multiple stem-loop structures required for RNA replication and transcription [23].

Epidemiology and transmission of novel coronavirus

CoVID-19 was first observed in late December 2019, causing acute respiratory syndrome in Wuhan, Hubei province, China. The first four cases were linked to the wet market of China [27]. On 2nd January 2020, 41 confirmed cases were identified having CoVID-19 infections and half of these patients were also known to be already suffering from diabetes, hypertension, and cardiovascular disease. During this time the rapid spread of the virus within the hospital was seen during the initial spread [28]. As of 30th January 2020, 7,734 cases were confirmed in China and 90 other cases were reported in the other part of the world including Taiwan, Thailand, Vietnam, Malaysia, Nepal, Sri Lanka, Cambodia, Japan Singapore, Korea, UAE, USA, Philippines, India, Australia, Canada, Finland, France and Germany [29]. Human coronavirus can be identified by using the enzyme-linked immune-sorbent assay [30]. The infection of the virus is by the entry of the virus into the host cell by a process called endocytosis/direct membrane fusion of the envelope with the host membrane. Once the process of entering the viral genome into the host cell takes place the virus released uncoated viral par-

ticles into the host cytoplasm. The 5' cap and 3' polyadenylated tail allows RNA to attach host cell ribosome and starts translation [31].

In later cases individuals are infected without even contact with the virus origin place, this concludes CoVID-19 transmitted from human-to-human in early January. Some studies reported that patients with asymptomatic could transmit the virus to others (Table 2). Hence, self-isolation is the best way to contain the CoVID-19 virus.

Usual transmission of common reparatory infectious viruses was spread through air-droplets from coughing, sneezing. The incubation period of present highly infectious coronavirus was said to be 7 days to 2 weeks [33].

The virus can be transmitted by droplets with a size of > 5 - 10 μm in diameter. Air born transmission occurs in the form of droplets, can remain in the air for a longer period-and the droplet transmission occurs with a person with the proximity of less than 1m. If a person having respiratory infections like coughing or sneezing there is a high risk of getting novel coronavirus through mouth, nose, eyes ears, or any other exposed area of healthy individuals. Transmission may be direct or indirect through already infected patients or by touching the surfaces of the objects used by the infected person. Some transmission in recent days was reported to be carried out through the faeces, but more research in this area needs to be done to understand the proper transmission mechanism of the human novel coronavirus [34].

Diagnosis and treatment of coronavirus

According to the information published on the CDC and WHO websites, the diagnosis of novel coronavirus is done assessing the symptoms of a patient suffering from viral infections. Currently, tests for CoVID-19 are done by obtaining nose and throat swabs containing the viral genetic material.

One of the efficient diagnostic methods is using reverse transcription-polymerase chain reaction (RT-PCR) but, it can only detect viruses while present in a person. It also reported that sometimes it gives false positive if the sample is contaminated during the preparation of lab reagents. Currently, PCR based tests are widely in use but some of the tests have shown rapid accurate results includes serological tests and CRISPR-based tests which are on the horizon to give quick and accurate results of CoVID-19 within 15 - 20 minutes [35].

Antigens or antibodies could be the target molecules and appropriate immunoassays have been developed for rapidly detecting the SARS-CoV-2. These rapid point-of-care assays are generally lateral flow assays. Such assays have been developed for detecting antibodies, particularly IgM and IgG and antigens such as the SARS-Co-2 virus against COVID-19 infections.

These rapid antigen lateral flow assays theoretically would provide the advantage of having a faster result and importantly cost-effective in detecting SARS-CoV-2 but at the same time, are likely to suffer from poor sensitivity. Monoclonal antibodies specifically against SARS-CoV-2 have also been under preparation. However, since there might be the variability of viral loads in patients, there are always possibilities of low or no detection in some of the causes leading to a false negative.

Next-Generation Sequencing (NGS) can also be an optional method of detecting the infection but currently is impractical due to the high cost and non-availability of the facility in most of the laboratories. Most of the molecular diagnostics that are currently being developed for the diagnosis of COVID -19 infections involve real-time Reverse Transcriptase-PCR.

Reverse transcriptase-PCR

PCR amplification and the analysis can be performed simultaneously in a closed system that avoids or minimizes false-positive results which might arise due to contamination during amplification. This is considered to be one of the major advantages as far as a real-time RT-PCR technique is concerned. As mentioned above, the coronaviruses have an envelope (E), transmembrane (M), helicase (Hel), nucleocapsid (N) and glycoproteins spike (S). Any of these can serve as a target for the PCR assay. Some species-specific accessory genes which might play a vital role in viral replication can also be targeted for the assay [36].

Currently (as of, 03-05-2020) no treatments are specifically available for CoVID-19. Some drug therapies are carried out to decrease the symptoms of the viral infection by using antiviral or retroviral medications, breathing support- ventilation, steroids to reduce lung swelling, blood plasma transfusions therapy and anti-malarial drug (hydroxychloroquine) are currently being used to prevent CoVID-19.

Discussion

Coronavirus characterized by severe acute respiratory syndrome (SARS-CoVID-2) is a novel infectious disease that was first discovered and diagnosed in China in late December 2019 and later all around the world. Studies showed that patients suffering from

SARS-CoVID had a triphasic pattern of disease. Initially infected persons show persistent cough, fever sore throat, and myalgia with dyspnea often not becoming major feature until day 14th of the illness. In the second stage of the disease dyspnea and hypoxia with continued fever, sometimes diarrhea becomes more prominent. In some cases, respiratory tract infection occurs which requires the need for ventilation to respiration by the third week of the infection of the virus. If the condition goes to critical death may also occur as early as 4th day or as late as 108 days after onset [37]. To study the pathological nature of the virus various animal and rodent models are used, where the animals are infected with SARS-CoVID but negligible pathogenic activity was developed but virus replicated in the respiratory tract reaching lungs [38]. Some studies show that 12 - 14 months old mice compared to that of 4 - 6 week old have more number of IFN-α, IFN-γ and TNF-α concluding high level of proinflammatory cytokines observed with increased age [39]. Currently, there are no known specific treatments available to cure coronavirus diseases but certain precautionary measures can be taken by us to contain the spread of the novel coronavirus-2019 by self-isolating from the rest of the world, washing hands for 20 minutes, avoid direct contact of hands with mouth, nose, eyes, and ears, wearing a mask when going outside of the house, these are some of the guidelines given by the WHO to avoid the spread of the CoVID-19. Antiviral drugs, pain relievers, cough medications etc., are some of the remedial measures currently available.

Conclusion

SARS-CoVID-19 belongs to one of the large family of viruses (coronaviridae), have the high infectious capability in infecting the host cell, it causes various disorders including fever, cough, sneezing, difficulty in breathing, diarrhoea, upper and lower respiratory tract infections are commonly seen if the virus is infected. Various studies have shown that the viral diagnosis is carried out by the traditional molecular biology methods like- RT-PCR tests. These tests are done based on the viral particles obtained by the nose, mouth, and throat swabs of the patients by using suitable reagents and primers. Due to the high increasing rate of CoVID-19 researchers are trying to find a rapid test kit that can easily detect the virus within a short period and proceeding for further treatment without any delay. A better understanding of the genome of the virus might open up possibilities to target the structural and membrane proteins to diagnose the infection through real-time RT-PCR techniques. Due to its highly infectious nature, CDC-USA and WHO keep releasing guidelines promptly to help out the people and at present, maintaining proper hygiene, washing hands every other hour or after touching the surface of the outside objects, wearing masks and self-isolating from the outside world are the best effective methods to reduce the risk of infection of the deadly SARS-CoVID-19.

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