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Review Article

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-Cov-2): A Review of the Basics

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Abstract

The recent outbreak of an unusual viral pneumonia in Wuhan, China, and then a pandemic has created a panic world over. Genetic and Phylogenetic studies revealed that the causative virus is SARC-CoV-2 and the disease it caused is given the name COVID-19. It (Coronavirus) is a member of the family Coronaviridae and subfamily Coronavirinae and belongs to the order Nidovirales. The Coronavirus Study Group of the International Committee on Taxonomy of Viruses termed the virus as SARS-CoV-2. The virus enters into the cell through ACE2 receptors. It is important to understand the basics of genetic and Phylogenetic properties of the virus. This knowledge will ultimately help in the development of vaccines and drug treatment. In this article, an effort is made to explain the basics of coronavirus and its transmission, to the host cell.

Keywords: SARS-CoV-2, COVID-19, Coronavirus, RNA virus, Spike glycoprotein, ACE2.

INTRODUCTION

The Coronavirus is an RNA virus. It is known to cause disease in mammals and birds. Coronaviruses are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. [1]These viruses primarily cause respiratory tract infection which may range from mild to lethal. The mild form is like any other common cold infection while the lethal form of the disease is SARS, MERS, and COVID-19. The genome size of coronaviruses is largest among RNA viruses and it ranges from approximately 26 to 32 kilobases [2]. The outer surface of virus has characteristic club-shaped projections or spikes. Because of this typical look; they are given the name coronavirus. These club-like projections create an image like solar corona, from which its name is derived [3].

The name corona means “crown” or “wreath” and is a Latin word. (This itself is borrowed from the Greek word for garland, wreath). This name was coined by June Almeida and David Tyrell, who first observed and studied human coronaviruses. An Informal group of virologists designates the new family of the virus in 1868, as was published in journal Nature. The name refers to the characteristic appearance of virion i.e. infective form of the virus by the electron microscope. These viruses have large bulbous projections on the surface that looks like solar corona under an electron microscope. The morphology is created by the viral spike peplomers, which are proteins on the surface of the virus [4].

HISTORY AND ETYMOLOGY

It was the British Medical Journal (BMJ) who, first published about this emerging infection on 8th January 2020. The article reported as; “outbreak of pneumonia of unknown cause in Wuhan, China, has prompted authorities in neighboring Hong Kong, Macau, and Taiwan to step up border surveillance, amid fears that it could signal the emergence of a new and serious threat to public health". [5] The very next day i.e. on 9 January 2020, the World Health Organization (WHO) confirmed that SARS-CoV-2 was the cause of the new disease [6, 7]. On 16th January the World Health Organization (WHO) published the first scientific article, in the Journal of Medical Virology, about this new disease. They initially termed the disease as the 2019-New Coronavirus (2019-nCoV) [8]. On 13 January 2020, the first confirmed case was found in a Chinese tourist in Thailand [9]. On 30th January 2020, the WHO declared this infection as a Public Health Emergency Concern (PHEIC). [10]On 28 February 2020, the global risk assessment of COVID-19 was raised as ‘very high” by WHO, which is considered as the highest level of global risk. On 11 March 2020, COVID-19 was declared a pandemic by the WHO. [11]On 27th March, The USA surpassed China as the country with the most confirmed cases. This assessment was as per the Johns Hopkins CSSE case dashboard.

On 3rd April, the number of confirmed cases globally exceeded the one million mark. It became two million on 15th April. On the 10th of April, the number of global deaths surpassed the 100,000 marks.

The nomenclature

The WHO originally called this illness "novel coronavirus-infected pneumonia (NCIP)" and the virus itself had been named "2019 novel coronavirus (2019-nCov)" [12]. The WHO officially renamed the clinical condition as COVID-19 (a shortening of COronaVIrus Disease-19) on 11th February 2020 [13]. The Coronavirus Study Group of the International Committee on Taxonomy of Viruses renamed the virus "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) on the same day. [14-16]. The infectious disease COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is a strain of coronavirus which was previously known as 2019 novel coronavirus (2019-nCoV). In late December 2019, the first case was seen in Wuhan, China and then it spread globally [17-19]. On 11th March 2020, the current outbreak was officially recognized as a pandemic [20].

The morphology of coronavirus

It is a single-stranded and a positive-sense RNA virus. It belongs to the genus Coronavirus and Coronaviridae family. Its genome size is ~30kb. The genus Coronavirus has been further classified in the subfamily Coronaviridae that contains four genera viz. alpha coronavirus (αCoV), Beta Coronavirus (βCoV), Gamma Coronavirus (γCoV) and Delta Coronavirus (δCoV)· [21] The study of the evolutionary trends of Coronavirus has revealed that αCoV and βCoV are originated from bats and rodents, while γCoV and δCoV were found to have been originated from avian species [22]. It has caused disease in human beings due to its ability to cross the species barrier. The disease may cause moderate respiratory infection to severe acute respiratory syndrome-CoV (SARS-CoV) and Middle East Respiratory Syndrome (MARS-CoV) [23].

SARS-CoV-2 has been declared as a pandemic, with 1,844,683 confirmed cases and 117,021 deaths globally by 14th April 2020 (World Health Organization 2020). Phylogenetic analysis has revealed that bats might be at the source of SARS-CoV-2 [24]. Additionally, some studies have suggested that the origin of SARS-CoV-2 is associated with pangolins [25].

The Coronavirus is having helical nucleocapsid comprising viral RNA; it is enveloped in the host membrane-derived lipid bilayer. The surface is having spikes made up of viral proteins; due to its typical look this virus is given the name coronavirus. (fig-1), [26] *Yen et al.* in 2020 resolved the misery behind the structure of spikes and that of the protease of SARS-CoV-2 by *Zhang et al* in the same year. This study provides an opportunity to develop a new class of drug for the treatment of COVID-19. It has a virion size ranging from 70 to 90nm which is similar to SARS-CoV. Its genome comprises of 6-11 open reading frames (ORFs) with 50 and 30 flanking untranslated regions (UTRs). The nonstructural proteins (nsps) are involved in the transcription and replication of SARS-CoV-2. They consist of two viral cysteine proteases, including papain-like protease (nsp3), chymotrypsin-like, 3C-like, or main protease (nsp5), RNA-dependent, RNA polymerase (nsp12), helicase (nsp13) and others. The SARS-CoV-2 uses ACE receptors for internalization. For the priming, it uses TMPRSS2 and serine protease. There are four major structural proteins i.e. glycoprotein (S) membrane, nucleocapsid protein (N), envelope (E), and accessory proteins encoded by ORFs. At N-terminal end of M protein, there is the presence of N-terminal glycosylated ectodomain. It comprises of a long C-terminal CT domain and three transmembrane domains (TM) for the virus morphogenesis, assembly and budding, M and E proteins are required. The S glycoprotein is a fusion viral protein and it comprises of two subunits S1 and S2. The S1 subunit consists of a signal peptide, N-terminal domain (NTD), and receptor-binding domain (RBD) [27].

The spike glycoprotein binds to the cellular receptors for entry into the target cells. During the process the host cell proteases prime the S protein. The ACE2 receptors are used by the virus for internalization and for the S protein priming TMPRSS2 serine proteases are utilized [28].

The ACE2 receptors have wide tissue expression which explains the extra-pulmonary spread of SARS-CoV-2. It has also been documented that the spike protein of this virus exhibits 10-20 times more affinity as compared to that of SARS-CoV [29].

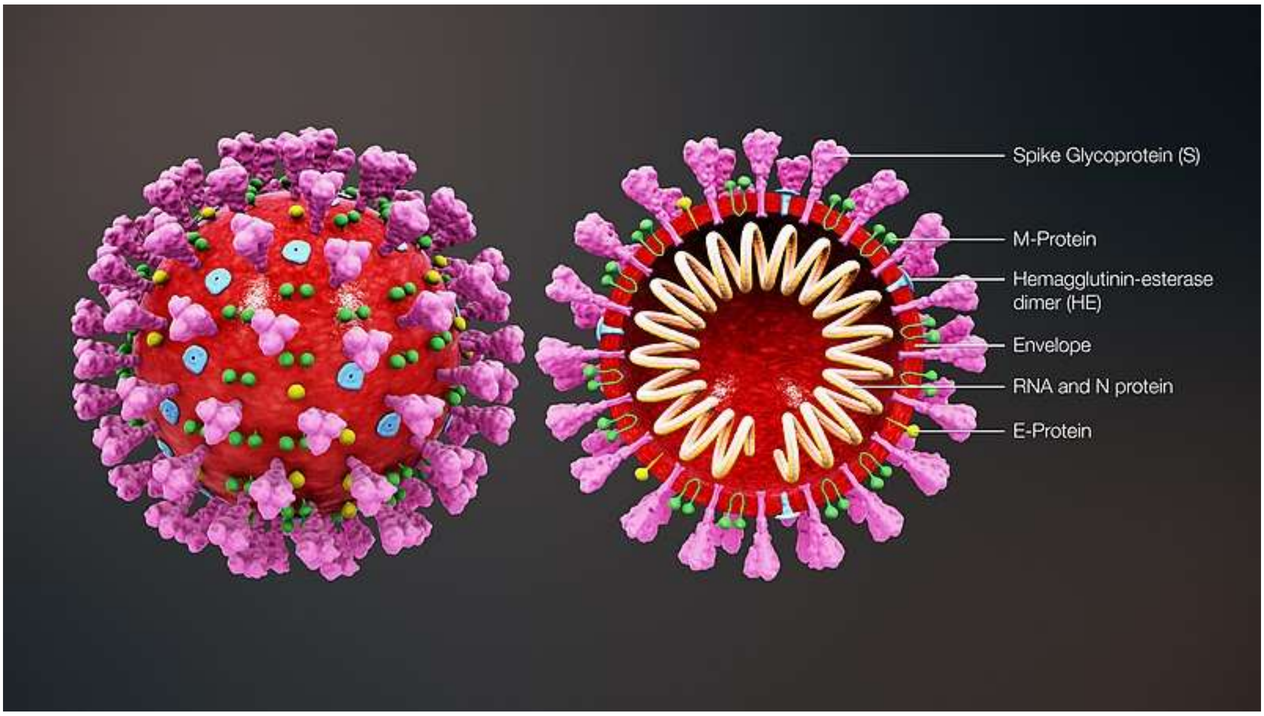

Fig-1: The Structure of Coronavirus [30]

The conformational changes occur in spike protein after its binding with ACE2 receptors. This event leads to the fusion of viral envelope protein to the host cell membrane [31]. After the entry through the endosomal route, there is a release of viral RNA into the host cytoplasm. This undergoes translation and generates replicase polyproteins pp1 and pp1b. This is further cleaved by the virus-encoded proteinases in small proteins. During the translational process, there is ribosomal frame-shifting and replication of coronavirus. This process generates multiple copies of subgenomic RNA species. The viral RNA and protein interactions at the endoplasmic reticulum (ER) and Golgi complex and help in the assembly of the virion. This virion is subsequently released out of the cell via vesicles.

The modes of transmission of coronavirus

The infection with coronavirus may be transmitted through the droplets coughed out from the infected patients. Scientifically speaking the droplets may be of different sizes: When the droplet particles are >5-10µm in size they are labeled as respiratory droplets, and when they are <5µm in diameter they are referred to as droplet nuclei [32]. The current evidence supports the primary transmission of the COVID-19 virus through respiratory droplets and contact routes [33-35]. The infection occurs from an infected person to another when they are within one-meter distance from each other by droplet transmission. Transmission may also occur through fomites in the immediate environment around the infected person [36]. Thus the infection can occur by direct contact with an infected person & it can also occur indirectly by contact with surfaces, in the immediate environment. The transmission is also possible with the objects used by the infected person like a thermometer, stethoscope, etc. airborne transmission is possible in certain circumstances. The airborne transmission is said to occur through droplet nuclei. These are particles less than 5µm diameter and can remain in the air for a long time; they are known to travel distance more than 1 meter. As far as COVID-19 is concerned this mode of transmission is possible in specific circumstances that generate aerosols. They are endotracheal intubation, bronchoscopy, open suction, manual ventilation, etc.

Based on available pieces of evidence, the WHO recommends droplet and contact precautions for those persons caring for COVID-19 patients. It also recommends airborne precautions during aerosol generation procedures and support treatment [37-39]. The World Health Organization continues to emphasize the utmost importance of frequent hand hygiene, respiratory etiquette, environmental cleaning, and disinfection. It also recommends maintaining the physical distance and avoidance of close, unprotected contact with a person having fever or respiratory symptoms.

DISCUSSION

SARS-CoV-2 is the cause of COVID-19 as was confirmed by the World Health Organization (WHO) on 9th January 2020. At that time the name of the virus was 2019-nCoV). The virus belongs to the genus Betacoronavirus. It is a single-stranded RNA virus. It is a zoonotic disease. The bat coronavirus is the closest animal coronavirus as far as the genetic sequence is concerned, and is the likely ultimate origin of this virus. Six coronaviruses are known to cause human disease. The Severe Acute Respiratory

Syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome coronavirus (MERS-CoV) are zoonotic in origin. The remaining four viruses cause the common cold.

The SARS-CoV virus affects its entry via attachment of its virion spike protein (a.k.a. S protein) to the angiotensin-converting enzyme2 (ACE2) receptor. Although it is a zoonotic disease originally, characteristically now its transmission is human-to-human. It is transmitted in a similar way to the common cold, via contact with droplets of infected individual's upper respiratory tract secretions e.g. from sneezing or coughing and also from fomites and aerosols. The recognition of the receptor is of utmost importance to understand the viral infection and a key determinant of the host cell and tissue tropism. Enhanced binding affinity between SARS-CoV and ACE2 was proposed to correlate with increased virus transmissibility and disease severity in humans [40].

As cited by the *Millet and Whittaker* in 2015 the priming of the S glycoprotein by host protease through cleavage at the S1/S2 and the S'2 is another crucial factor that modulates the tropism and pathogenicity [41].

There is more than 95% genomic similarity between SARS-CoV-2 and bat coronavirus. It thus indicates that the bats are the most probable host of the former [42-44], besides bat, several other animal hosts are reported as the reservoir of the virus; like, snake, pangolins, etc. The bats are known to contain a wide variety of coronaviruses, and this is considered to be the main culprit for SARS-CoV and SARS-CoV-2 in humans. The mechanism of virus zoonotic spillover is still not clear and ill-understood. This is most likely that the outbreak and emergence of SARC-CoV-2 are due to the disruption of the host immune system. In the infected person there is disturbance in immune system. It erodes the immune response. Novel coronavirus disease (COVID-19) presents as a mild illness in the majority of cases with less than 5% developing the life-threatening critical illness. A detailed history of exposure and prompt symptom recognition leads to early diagnosis of the cases. It also helps in better contact tracing and early isolation of suspects. All these measures and prompt action brings down the spread of the disease and also reduces the mortality related to COVID-10.

As our understanding of the virus, its origin, spread, and pathogenicity is limited, every care must be taken to reduce human to human transfer of the virus by following the guidelines issued by administrative authorities. The future lies in complete genome analysis to understand the similarities and differences of SARS-CoV-2 with previously reported viruses. The complete genome analysis will help in the development of vaccines and medications against the virus.

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