

Coronavirus: A Review

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ABSTRACT

Coronavirus is the emerging mutagenic pathogenic microorganism that is affecting the human beings in a larger extent. The name is given after its crown shaped like structure. In this review, structure and history of coronavirus is explained in detail. The history depicts the similarity and dissimilarity of novel coronavirus with preexisting SARS virus. Apart from that review also concludes about the mechanism of action of virus, how it spreads and transfer in human system. The symptoms and preventive measures are also discussed in the review.

Keywords: *Coronavirus, SARS, Symptoms and Prevention*

1. INTRODUCTION

There are different types of microorganisms [1]. These can be harmless, harmful or beneficial to their host. Harmful ones are called pathogenic microorganisms. These microorganisms may cause kinds of communicable diseases by competing metabolic resources, destroying cells or tissues, or secreting toxins. Pathogenic microorganisms may be viruses, bacteria, mycobacteria, fungi, protozoa and so on and infects people or animals in direct or indirect ways. Virus often results in serious diseases. Recent years, humans have been challenged by several diseases caused by virus, such as SARS, Ebola virus, hepatitis B, HIV etc. Once an infectious pathogen microorganism has transmitted to a new host, it may cause disease directly or after a prolonged period of time. Acute infections like influenza, rhinovirus and bacillus anthracis lead to the rapid progression of symptoms usually within a few days. [2] The capacity of a microorganism to cause disease is called pathogenicity. A microorganism that has the ability to cause disease is called pathogen. There are wide ranges of microorganisms that can cause severe harm to the body and become lethal. In spite of the remarkable research and development in the treatment and prevention procedure, infectious diseases still remain the topmost cause of death in world, particularly in the developing countries; more virulent pathogens are continuously emerging. Virulence is the harm caused to the host by the pathogen. It varies from species to species ranging from negligible to immediate death. Classic theory of virulence evolution is mainly based on a trade-off between the pathogen growth-transmission and the host survival. This indicates that higher the growth within the host, higher is the transmission and virulence. [3] The range of infectious diseases is evolving quickly. Evolving infectious microbes display an interesting group of nosocomial infection. [4] Pathogens which are already present in the environment causes most of the emerging infections, brought out either unknowingly or by selectively taking opportunity of changing conditions and infecting new host population. [5] Specificity of a pathogen towards its host is defined as the ability of the pathogen to colonize or infect the host. Specificity of pathogens towards its host is determined by determining the molecular interactions between the host and the pathogen. Due to relative simplicity of viral genomes and their structure, their host

specificity is easy to determine. Viral specificity is predominantly defined by the interactions between the viral proteins and their cognate cellular receptors.

[6] A virus is a set of genes, composed of either DNA or RNA, packaged in a protein-containing coat called a CAPSID. Some viruses also have an outer lipid bilayer membrane external to the coat called an ENVELOPE. The resulting complete virus particle is called as VIRION. Viruses have an obligate requirement for intracellular growth and a heavy dependence on the host cell structural and metabolic components. Therefore, viruses are also referred to as obligate intracellular parasites. Viruses do not have a nucleus, cytoplasm, mitochondria, or other cell organelles. Viruses that infect humans are called human viruses, but as considered along with the general class of animal viruses; viruses that infect bacteria are referred to as bacteriophages (phages for short), and viruses that infect plants are called plant viruses [7]. Pathogenic viruses are the microorganism that has the capacity/ability to infect and replicate within the human system. There is continuous emergence and re-emergence of pathogenic viruses that cannot be controlled and become a major threat to public health. The sudden emergence of pathogenic viruses made impossible to detect them rapidly. Due to which it becomes difficult to imply certain specific control measures to lemmatize the virus spread. Furthermore, to understand the viral behavior it is required to study the molecular characterization so that we can develop the diagnostic tests and countermeasures. Advancement in molecular biology techniques has made easy to detect and characterize pathogenic viruses timely and accurately. In this case, PCR merged with DNA sequencing is one of the emerging techniques that provide the highly sensitive and specific methods to determine virus circulation [8]. Of the known viruses that infect humans, about 80% perpetuate naturally in non-human "reservoirs," largely farm mammals and poultry and, to a lesser extent, in wild animals and arthropods.[9,10,11] It is estimated that zoonotic infectious agents constitute about 60% of the known human pathogens and up to 75% of "emerging" human pathogen.[12] It is assumed that there is a pool of human virus species still to be discovered. The composition of such a viral pool is dynamic, changing over time, i.e., while some virus species tend to become extinct, others continue to evolve in their natural host. More commonly, new species arise as a result of jumps from one another, thus crossing the species barrier.[13,14] Humans are therefore, no more than "incidental" or "spillover" hosts for pathogens. However, only a minority of such viruses are capable of persisting in certain human populations (endemics) or spreading across populations (epidemics) in the absence of a reservoir. Differential host factors like age, health, physiology, nutritional status, exposure history, simultaneous infection with >1 pathogen, immune-competence, and genetics are determinants to human susceptibility to an infection. The field of phylodynamics, combining a modeling framework for host, epidemiological, and molecular data, especially for RNA viruses, shows particular promise for understanding the patterns of viral evolution during epidemics.

Coronavirus belongs to a family of single-stranded RNA Viruses known as coronaviridae. It can cause a range of illness in humans including common cold and more severe forms like SARS and MER's which are life threatening. It can cause disease in mammals, birds and reptiles. The virus is named after its shape which takes the form of a crown with protrusions around it and hence is known as corona virus. COVID-19 is a new strain of coronavirus that has not been previously identified in humans. Although the incubation period of this strain is unknown but symptoms may appear in as few as 2 days or as long as 14 days after exposure. In humans, several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). Coronaviruses have extraordinarily large single-stranded RNA genomes- approximately 26,000 to 32,000 bases or RNA "letters" in length. Coronavirus particles are surrounded by a fatty outer layer called an envelope and

usually appear spherical, as seen under an electron microscope, with a crown or “corona” of club shaped spikes on their surface. Coronaviruses replicate their RNA genomes using enzymes called RNA-dependent RNA polymerases, which are prone to errors, but genomic analysis so far suggests that COVID-19 is mutating slowly. The researchers proposed bats as the most likely reservoir for COVID-19. There are no documented cases of direct bat-human transmission, however, suggesting that an intermediate host was likely involved between bats and humans.

STRUCTURE

Corona virus virions are spherical to pleomorphic enveloped particles as shown in figure1 [15]. The envelope is studded with projecting glycoprotein's, and surrounds a core consisting of matrix protein enclosed within which a single strand of positive- sense RNA is associated with nucleoprotein. The envelope glycoprotein's are responsible for attachment to the host cell and also carry the main antigenic, particularly the epitopes recognized by neutralizing antibodies. OC43 also possesses a haemagglutinin.

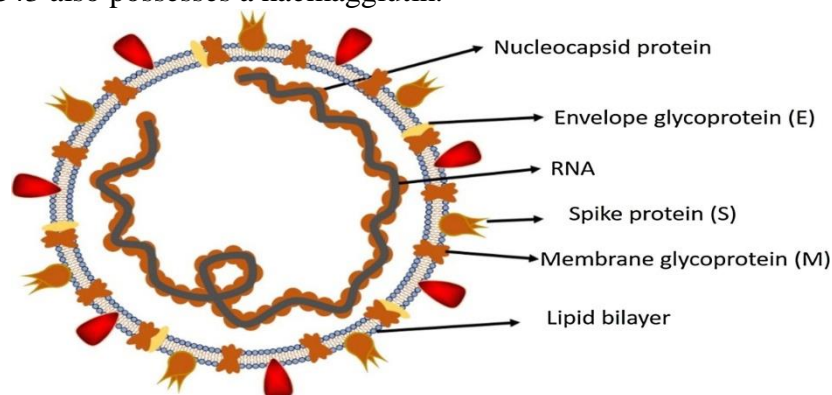


Figure1: Spherical shape of coronavirus [15]

[16] The study was founded in part by NIH's National Institute of Allergy and Infectious Diseases (NIAID). Results were published on February 19, 2020, in science. The researchers used a technique called cryo-electron microscopy to take detailed pictures of the structure of the spike proteins. This involves freezing virus particles and firing a stream of high-energy electrons through the sample to create tens of thousands of images. These images are then combined to yield a detailed 3D view of the virus. The researchers found that the SARS-CoV-2 spikes were 10 to 20 times more likely to bind ACE2 on human cells than the spike from the SARS virus from 2002. This may enable SARS-Cov-2 to spread more easily from person to person than the earlier virus.

HISTORY

The clinical spectrum of COVID-19 varies from asymptomatic or paucisymptomatic forms. The clinical symptoms related to this disease are characterized by respiratory failure. This is the reason that the person suffering from the disease requires ventilation facility and support in an intensive care unit (ICU). ICU is required to take care of other organs of human system and its manifestations including sepsis, septic shock, and multiorgan dysfunction syndromes (MODS) [17]. Huang et al. while studying on the first case suffered from coronavirus reported that the patient experienced the syndromes such as fever, malaise, dry cough, and dyspnea. CT scan of numerous patients' chest showed the pneumonia also. Out of the total patients, 13.32% are severe cases that require ICU care and 6% cases are fatal [18-19]. In 2003, the Chinese population was infected with a virus causing severe acute respiratory syndrome (SARS) in Guangdong province and then spread rapidly around globe with more than 8000 infected persons and 776 death cases. The virus was confirmed as specie belongs

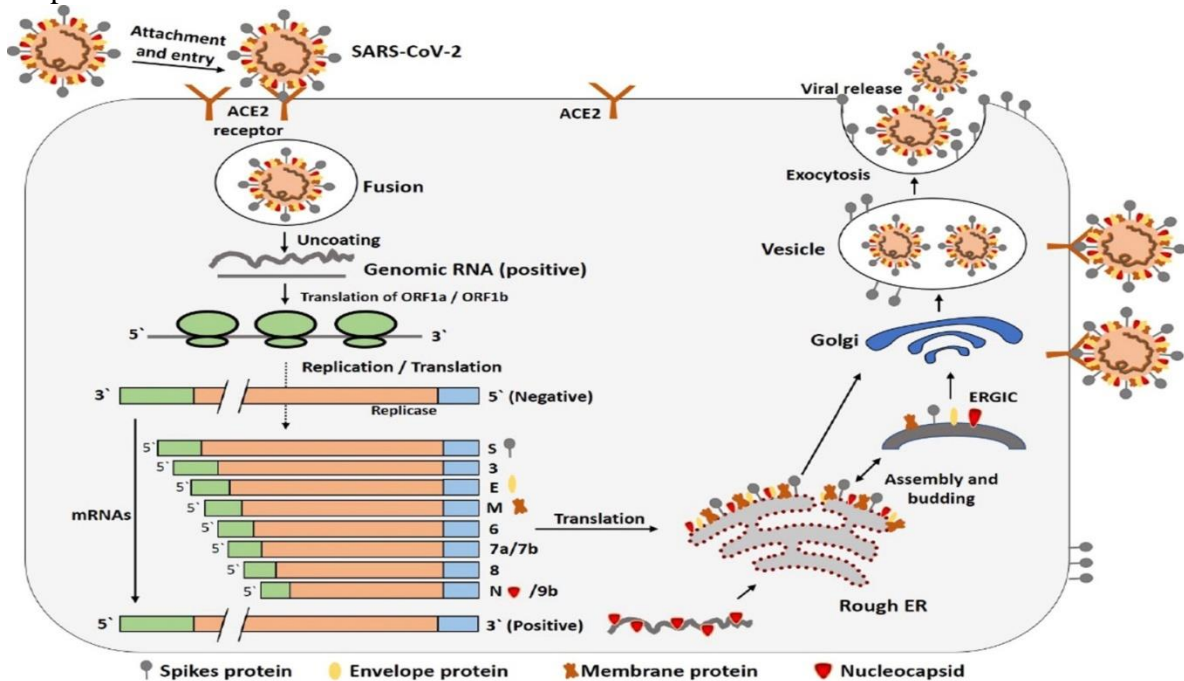
to the β -coronavirus subgroup and was named SARS-CoV[20]. The people infected with the SARS experienced pneumonia symptoms with an injury in alveoli are which lead to acute respiratory distress syndrome (ARDS). In 2012, a couple of Saudi Arabia was diagnosed to be infected with another coronavirus. The detected virus was confirmed as a member of coronaviruses and named as the Middle East Respiratory Syndrome (MERS-CoV). According to the WHO report it was found that MERS-coronavirus infected more than 2428 individuals and 838 deaths [21]. MERS-CoV is also a member β -coronavirus subgroup but it is phylogenetically different from the other human-Cov. The person infected from MERS-CoV suffered from the mild upper respiratory injury which further leads to severe respiratory disease. There was one similarity between the SARS and MERS-coronavirus infected patients that they all suffer from pneumonia, followed by ARDS and renal failure[21]. Recently, by the end of 2019, WHO was informed about several cases of pneumonia with unfamiliar etiology by the Chinese Government. It was found that the outbreak of new infection was initiated from the Hunan seafood market in Wuhan city of China. When report was submitted to WHO the virus had infected almost fifty people already [22]. The National Health Commission of China on 12 January 2020 released further details about the epidemic and viral pneumonia. [23-26]. Further studies was started to find the consequences from the sequence-based analysis of patients sample. It was found that the reason behind the infection is virus that belongs to same family of coronavirus and named as a novel coronavirus. Moreover, the genetic sequence was also provided for the diagnosis of viral infection. Initially, it was believed that the patients those who are infected with Wuhan coronavirus are experiencing induced pneumonia may had visited seafood market and may have used infected animals or birds as a source of food. However, further investigation revealed that some individuals contracted the infection even with no record of visiting the seafood market. These observations indicated a human to human spreading capability of this virus, which was subsequently reported in more than 100 countries in the world. The human to the human spreading of the virus occurs due to close contact with an infected person, exposed to coughing, sneezing, respiratory droplets or aerosols. These aerosols can penetrate the human body(lungs) via inhalation through the nose or mouth

ENTRY MECHANISM OF HUMAN CORONAVIRUSES

All the members of coronavirus family contain specific genes in ORF1 downstream regions. This gene encodes the protein that helps in viral replication, capsid and spikes formation [27]. The spikes are glycoprotein in nature present on the outer surface of coronaviruses that are responsible for the attachment and entry of the virus to the host cells [28-29]. The virus is capable of binding to multiple hosts because the receptor binding domain (RBD) is attached loosely among virus[30]. MERS-coronavirus employs dipeptidyl peptidase 4 (DPP4), while HCoV-NL63 and SARS-coronavirus require angiotensin- converting enzyme 2 (ACE2) as a key receptor [31-32]. SARS-CoV-2 possesses the typical coronavirus structure with spike protein and also expressed other polyproteins, nucleoproteins, and membrane proteins, such as RNA polymerase, 3-chymotrypsin-like protease, papain-like protease, helicase, glycoprotein, and accessory proteins. [33] The spike protein of SARS-CoV-2 contains a 3-D structure in the RBD region to maintain the van der Waals forces. The 394 glutamine residue in the RBD region of SARS-CoV-2 is recognized by the critical lysine 31 residue on the human ACE2 receptor [34].

The cycle of SARS-CoV-2 in host cells; begins its cycle when S protein binds to the cellular receptor ACE2 shown in figure 3. After binding to receptor, the S protein changes its conformation that facilitates fusion of viral envelope with the cell membrane through the endosomal pathway. Then SARS-CoV-2 release RNA into the host cell. After entering into host cell, genomic RNA translates into viral replicase polyproteins pp1a and 1ab, which are

than cleaved into small products by viral proteinases. The polymerase produces a series of sub-genomic mRNAs by discontinuous transcription and finally translated into relevant viral proteins. Viral proteins and genome RNA are subsequently assembled into virions in the ER and Golgi and then transported via vesicles and released out of the cell. ACE2, angiotensin-converting enzyme 2; ER, endoplasmic reticulum; ERGIC, ER-Golgi are intermediate compartment.



MULTIPLICATION

It is thought that human coronaviruses enter cells, predominantly, by specific receptors. Aminopeptidase-N and a sialic acid-containing receptor have been identified to act in such a role for 229E and OC43 respectively. After the virus enters the host cell and uncoats, the genome is transcribed and then translated. A unique feature of replication is that all the mRNA from a “nested set” with common 3’ ends; only the unique portions of the 5’ ends are translated. There are 7 mRNA produced. The shortest mRNA codes for the nucleoprotein and the others each direct the synthesis of a further segment of the genome. The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particle forms by budding from internal cell membranes.

OUTBREAK OF COVID-19

The situation with the ongoing epidemic of coronavirus disease 2019 (COVID-19) that started in Wuhan, China, continued to rapidly evolve. As of 9 February 2020, China had confirmed 37 251 cases of COVID-19, an increase of 2657 since the previous day. 6188 of these cases were severe and there had been 812 deaths. Every region of the country has been affected. 24 other nations have reported 307 cases and one death. On January 30, 2020, WHO declared the outbreak of COVID-19 a public health emergency of international concern (PHEIC). The virus has now spread to over 150 countries across the globe, and was characterized as a pandemic by the World Health Organization (WHO) on March 2020. As of 30 March 2020, there were 752,189 laboratory-confirmed cases of coronavirus disease 2019 (COVID-19) infection, with 37,883 reported deaths. The number of cases and death outside of china overtook those within the country on 16 March 2020. As of 9am on March 30, 2020,

there were 1251 confirmed cases of virus in INDIA and 32 deaths. As of 9am on March 30, 2020, there were 164,359 confirmed cases of virus in the USA and, as of 5pm on 30 March 2020, there were 3173 deaths. This virus has infected mostly USA, ITALY, SPAIN, IRAQ with the high number of confirmed cases and the high number of deaths.

SYMPTOMS

COVID-19 symptoms range from mild to severe [35]. It takes 2-14 days after exposure for symptoms to develop. Symptoms may include: fever, cough, shortness of breath. Those with weakened immune systems may develop more serious symptoms, like pneumonia or bronchitis. Coronavirus infects the lungs. The symptoms start with a fever followed by a dry cough, which can lead to breathing problems. This is a new, continuous cough and means coughing a lot for more than an hour, or having three or more coughing episodes in 24 hours. It takes five days on average to start showing the symptoms, scientists have said, but some people will get symptoms much later than this. In fact the World Health Organization (WHO) says the incubation period lasts up to 14 days.

PREVENTION

Till certain vaccines are not developed, preventive measures are the only solution to limit the spread of the virus. The major preventive measure is to isolate the patient, adapt careful diagnosis and the provision of clinical care to an infected patient. The WHO and other organizations have issued the following general recommendations which include to maintain distance from the person suffering from acute respiratory infections, to wash hands on frequent basis, cover mouth while coughing or sneezing, avoid unprotective contact from farm or wild animals, to follow strict hygiene measures for prevention and control of infections and avoid mass gathering especially those people who are immune-compromised. The most important strategy for the populous to undertake is to frequently wash their hands and use portable sanitizer and avoid touching their face and mouth after interacting with a possibly contaminated environment.

Various studies on corona viruses have been undertaken along with pandemic virus like zika viruses and substantial informations have been gathered for human benefits and to tackle the pandemic condition [36-45].

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