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A REVIEW ON GLOBAL PANDEMIC COVID-19

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ABSTRACT

SARS-CoV2 is a new virus responsible for an outbreak of respiratory illness known as COVID-19, which has spread to several countries around the world. It is single stranded positive sense RNA a capsid enveloped with a nucleoprotein comprised of matrix protein. Before developing in humans, it is first developed in animals. The virus transmitted when a person comes in contact with an animal that carries the infection and this likely occurred in the open food market in Wuhan, China in December, 2019. China quickly informed to the World Health Organisation (WHO) about the outbreak and shared the sequence information with the International Community after discovering the causative agent. There are six types of coronavirus which is known to infect human. Among those, Severe Acute Respiratory Syndrome Coronavirus (SARs-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) are zoonotic and highly pathogenic coronavirus that have resulted in Regional and Global Pandemic.

KEYWORDS: Virus, Coronavirus, COVID-19,SARs-CoV,WHO,RNA,MERs CoV.

INTRODUCTION

SARS-CoV-2 is a new virus responsible for an outbreak of respiratory illness known as COVID-19, which has spread to several countries around the world. The word corona means “crown” and, the round virus has a “crown” of proteins called peplomers jutting out from its centre in every direction.

Corona virus is a single stranded positive sense enveloped RNA virus with a nucleoprotein within a capsid comprised of matrix protein belonging to the family Coronaviridae. It is a respiratory illness, most people infected with the COVID-19 virus will experience mild to moderate respiratory illness. This virus spreads primarily through droplets of saliva or discharge from the nose, when an infected person coughs or sneezes. Infants, children, older people and people with medical conditions may be more vulnerable to becoming severely ill. Corona viruses are zoonotic. It first develops in animals before developing in humans. From animal to human, the virus pass when a person come into close contact with an animal that carries the infection. This transmission likely occurred in the open food market in Wuhan, China.[1,2]

MATERIALS AND METHODS

A novel corornavirus also known as Covid-19 is a large family of Single stranded RNA virus. It is the largest known RNA viruses, CoVs are further divided into four genera alpha coronavirus, beta coronavirus, gamma coronavirus and delta coronavirus. It is found that there are six human coronavirus (HCoVs) identified, including the alpha CoVs HCoVs-NL63 and HCoVs-229E and the beta CoVs HCoVs-OC43,HCoVs-HKU1,severe acute respiratory syndrome-CoV (SARs-CoV) and Middle East respiratory syndrome-CoV (MERs-CoV).Among all these SARs-CoV which is occurred in Dec 2019 in Wuhan, China is a new strain that has not been previously identified in human. The Outbreak was declared as a public health emergency of International concern on 30th Jan 2020 by WHO and announced as Global Pandemic on 11th Mar 2020.

This virus is mainly transmitted through respiratory droplets generated when an infected person coughs, sneezes, or exhales.[1,2,4]

As of 10 june 2020 number of people infected is approximately 7.4 million all across the World in which approximately 4,14,476 recorded deaths and 3.6 million recovered.[3]

This virus can transmit from person to person in following ways

1) By respiratory droplets like coughing and sneezing without covering the mouth can disperse droplets into the air.
2) Touching or shaking hand with the infected person.
3) Touching the surface or objects which came in contact with the infected person and the touching nose, eyes or mouth.[1,2,5]

The National Institute of Health suggest that several groups of people have the highest risk of developing complications due to covid-19. This groups include-

1) Young children
2) People age 65 years or older
3) Women who are pregnant
4) People with pre-existing medical conditions (such as asthma, diabetes, heart disease).[1]

Classification &Virion Structure

Corona viruses and toto-viruses are classified together on the basis of the crown or halo-like appearance of the envelope glycoproteins. The envelope glycoproteins are responsible for attachment to the host cell and also carry the main antigenic epitopes, particularly the epitopes recognized by neutralizing antibodies. There are one of two serotypes, in which most of human coronaviruses classified, these are OC43- like and 229E- like. OC43-like possesses a haemagglutin. Viruses can be isolated or adapted to growth; 229E-like coronaviruses can usually be isolated in human embryonic fibroblast culture.[6,9]

Corona viruses particles contain four main structural protein in coronaviruses particle all of which are encoded with 3' end of the viral genome and these are spike (S), membrane (M), envelope (E) and nucleocapsid (N) and one more structural protein, i.e. the fifth protein hemagglutinin esterase (HE) present in subset of β-coronaviruses. The S protein (~ 150 k Da), utilizes an N-terminal signal sequence to gain access to the ER, and is heavily N-linked glycosylated. Homotrimers of the virus encoded S protein makeup the distinctive spike structure on the surface of the virus. The trimeric S glycoprotein is a close I fusion protein and mediates attachment to the host receptor. The m protein is the most abundant structural protein in the virion. It is a small (~ 25- 30 k Da) protein with S transmembrane domains and is thought to give the virion its shape. The E protein (~8 - 12 k Da) is found in small quantities within the virion. The membrane topology of E protein is not completely resolved but most data suggest that it is transmembrane protein. The N protein constitutes the only protein present in the nucleocapsid. It is composed of two separate domains, an N terminal domain (NTD) and a C-terminal domain (CTD), both capable of binding RNA in-vitro, but each domain uses different mechanisms to bind RNA.[6,7,8,9]

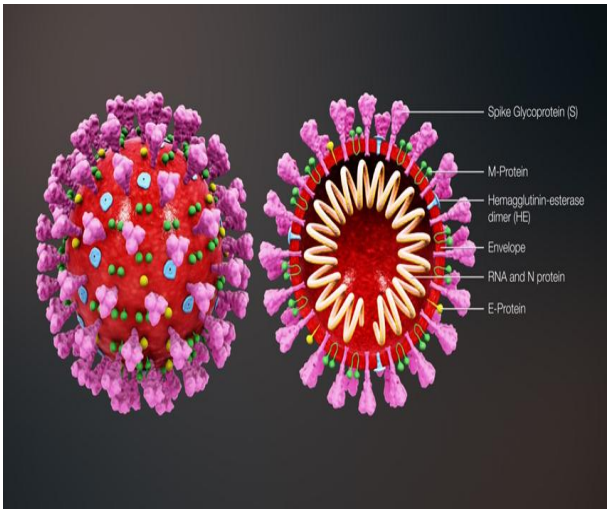

Fig. 1: Structure of Coronavirus.

Life cycle

The life cycle of coronavirus in host cells, it is thought that human coronaviruses enter cells, predominantly by specific receptors starts its life cycle when S protein binds to the other cellular receptor ACE 2.After receptor binding, the conformation change in the S protein facilates viral envelop fusion with the cell membrane through the endosomal pathway .Then SAR-CoV-2 releases RNA into the host cell. The release of the viral genome into the cytoplasm takes place which promotes the completion of virion assembly and these are released by exocytosis and these activities are thought to enhance S protein mediated cell entry and virus spreads through the mucosa, which allows the virus to spread within an infected organism without being detected or neutralized by specific antibodies.[10]

Many coronaviruses utilize peptidases as their cellular receptor. Many α- corona viruses utilize amino peptidases N (APN) as their cellular receptor; SARS-CoV and HCoV-NL63 use angiotensin-converting enzyme 2 (ACE 2); MHV enters through CEACAMS. Following receptor binding, the virus gain access to the human cell cytosol. After the virus enters the host cell and unwants the genome is transcribed and then translated. A feature of replication is all the mRNAs form a nested set with common 3' ends; only the unique portions of the 3' ends are translated. There are 7 mRNAs produced. The shortest mRNA codes for the nucleoprotein, and the others each direct the synthesis of a further segment of the genome. Viral RNA synthesis produces both genomic and sub-genomic RNAs. Sub genomic RNAs serve as mRNAs. The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particles forms by budding from internal cell membranes. However S protein that does not required for the assembly of virions transits to the cell surface where it mediates cell- cell fusion between infected and adjacent uninfected cells, which leads to the formation of giant multinucleate cells, which allows the virus to spread within an infected organism

without being detected or neutralized by virus specific antibodies.[10,11]

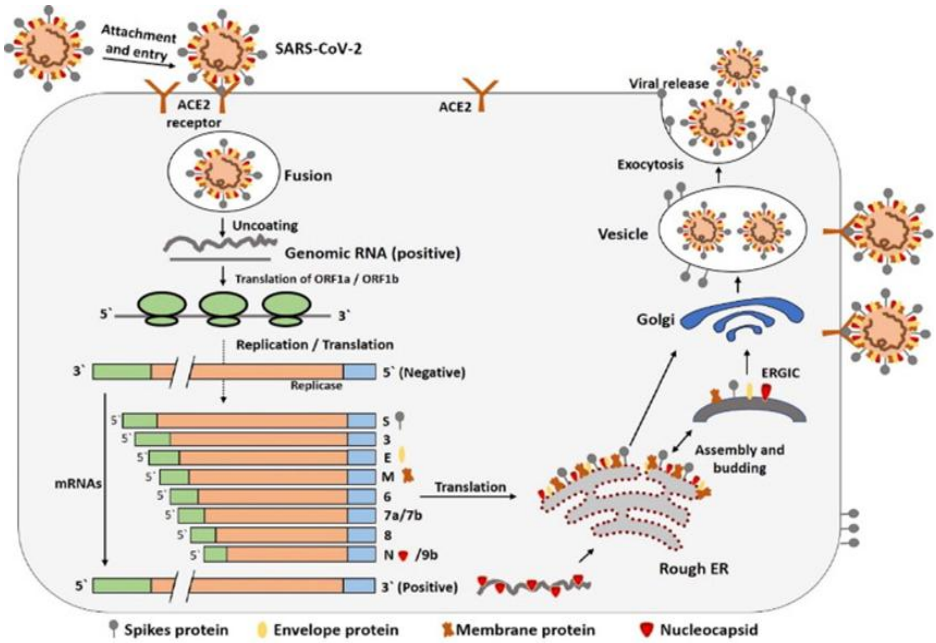

Fig. 2: Life Cycle of Corona Virus.

Signs and Symptoms[12,13]

COVID-19 symptoms range from mild to severe. It takes 2-14 days after exposure for symptoms to develop.

1) Fever,
2) Dry cough,
3) Headache,
4) Shortness of breath

Pathogenesis and Epidemiology

In both organ cultures and human volunteers show that corona viruses are extremely fastidious and grow only in differentiated respiratory epithelial cells. SARS-CoV primarily infects epithelial cells within the lungs. The macrophages and dendritic cells. Infected cells become vacuolated show damaged cilia, and may form syncytia. Cell damage triggers the production of inflammatory mediators, which increase nasal secretion and cause local inflammation and swelling. These responses in turn stimulate sneezing, obstruct the airway and raise the temperature of the mucosa. Prior to the SARS-CoV outbreak, coronaviruses were only thought to cause mild, self-limiting respiratory infections in humans. These are two human coronaviruses, there are α- coronaviruses (HCoV-229E and HCoV-NL63) while the other two are β- coronaviruses (HCoV-OC42 and HCoV-HKU1). HCoV-229E and HCoV-OC43 were isolated nearly 50years ago while HCoV- OC43 and HCoV-HKU1 were only recently identified following the SARS-CoV outbreak. SARS-CoV, a group 2b β- coronavirus, was identified as the causative agent of the Severe Acute Respiratory Syndrome outbreak that occurred in 2002-2003 in the Guangdong Province of China. During that phase, outbreak approx. 8098 cases occurred with 774 deaths. It also impact in the economic activity, as many activities in Southeast Asia and Toronto, Canada was shut down for several months. While the SARS-CoV epidemic was controlled in 2003, a novel human CoV emerged in the Middle East in 2012; named as Middle East Respiratory Syndrome (MERS-CoV) was found to be the causative agent of highly pathogenic respiratory tract infections in Saudi Arabia and other countries in the Middle East. About 50% mortality rate in the early stages of the outbreak, it was feared the virus would lead to a very serious outbreak. Although the outbreak didn't accelerate in 2013. In April 2014, a hike of over 200 cases almost 40 deaths occurred, prompting fears that the virus had mutated and was more capable of human-to-human transmission. According to the European Centre for Disease Prevention and Control, as of August 27th, 2014, there have been a total of 815 cases of MERS-CoV, with 333 deaths were recorded. After that the severe symptoms of COVID-19 are associated with an increasing numbers and rate of fatalities specially in the epidemic region of China. On January 22, 2020, the China National Health Commission reported the details of the first 17 deaths and on Jan 25, 2020 the death cases are increased to 56 deaths.[1,2,14]

Table 1: Total no. of cases reported from different continents as of 10th June 2020.

Continent	No. of cases reported
America	3,488,230
Europe	2,100,711
Asia	1,408,945
Africa	2,03,142
Oceania	8,738
Others	696

Table 2: Total no. of death reported from different continents as of 10th June 2020.

Continent	No. of cases reported
America	1,89,300
Europe	1,80,171
Asia	36,069
Africa	5,517
Oceania	131
Others	7

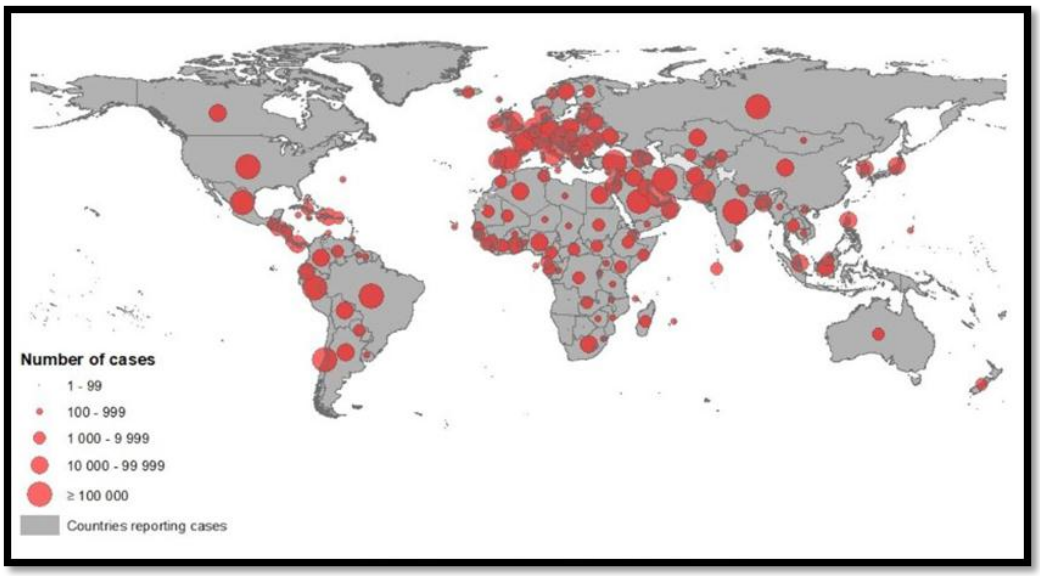

Fig. 3: Geographical distribution of COVID-19 Cases worldwide as of 10th June 2020.

Diagnosis

For research purpose virus can be cultured from nasal swabs or washing by inoculating organ cultures of human fetal or nasal tracheal epithelium. The virus in these cultures is detected by electron microscopy or other methods. It is also important to diagnose cases of severe veterinary CoV-induced disease such as PEDV and IBV to control these pathogens and protect food supplies. RT-PCR has become the method of choice for diagnoses of human CoV, as RT-PCR assays are able to detect all four respiratory HCoVs.

Several different laboratory tests are conducted to detect MERs CoV infection. These lab tests fall into two categories.

i) Molecular tests and
ii) Serology tests.

i) Molecular tests: Molecular tests are used to diagnose the presence of active infection MERS-CoV by rRT PCR (real time reverse transcription polymerase chain reaction) are used to detect viral RNA in clinical samples. For this rRT-PCR assay, collects multiple, specimens including lower (brochalveolarlavage, sputum and tracheal aspirates) and upper (nasopharyngeal and oropharyngeal swabs) respiratory samples, serum and stool specimens. If the two consecutive rRT-PCR tests on all specimens shows negative. Then the patient with known MERs consider to be negative for active MERs-CoV.

ii) Serology tests: Used to detect previous infection (antibiotics to MERs-CoV) in people who may have been exposed to the virus. There are two phase approach for this testing, two screening test and one confirmatory tests to detect antibodies to MERs-CoV. ELISA(Enzyme Linked Immunosorbant Assay) is used to detect the presence or concentration of specific antibodies. If a clinical sample is determined to be antibody positive by either ELISA. CDC then uses micronutralization test to confirm the positive result. And if a clinical sample is positive by either ELISA, and positive by micronutralization then the specimen is determined to be confirmed positive.

If a clinical sample is positive by both ELISA and negative by micronutrilization then the sample is determined to be in determinate. And if a clinical sample is positive by only one ELISA and negative by micronutralization then the sample is determined to be negative. If a clinical sample is negative by both ELISAs the sample is determined as Negative. A final determination of a confirmed positive serology result

requires a positive ELISA test and confirmation by micronutrilization assay.[16,17,18,19]

Prevention, Control and Treatment

There is no treatment or vaccine available for COVID-19 till now. Currently the treatment of COVID-19 remains symptomatic. However hydroxychloroquine is found useful in treating COVID-19 into some extent as the experimental studies have suggested that chloroquine is a proven anti-malarial drug that has the capacity of inhibiting the replication of several intracellular microorganisms including coronavirus in vitro. Since the structure and the mechanism of action of chloroquine and hydroxychloroquine (HCG) are exactly same except an additional hydroxy moiety in one terminal in HCG. It is believed that both the agents could be effective tools against SARs-CoV-1 and SARs-CoV-2.A Chinese study involving more than 100 patients of COVID-19 found chloroquine superior to the control group in reducing symptoms duration, exacerbation of pneumonia including radiological improvement and promoting virus negative seroconversion without any severe side effects. This represents the first human trial ever conducted with chloroquine against COVID-19.The second human study which is currently available conducted with HCQ. In an open label, non-randomized trial conducted in Marseilla, France, Gautretet. al. found that HCQ alone and combination of HCQ plus azithromycin was highly and significantly effective in clearing viral nasopharyngeal carriage (measured by PCR) in only 3-6 days in COVID-19 subjects, compared to control.

The likelihood of transmission can be reduced by practising hygienic measure, staying away from infected person (at least 1 metre), wearing mask and washing hands often with soap or sanitizer.[1,2,20,21]

You can protect yourself and help prevent spreading the virus to other, if you DO THE FIVE-

1. Hands- Wash them often
2. Elbow- Use it to sneeze and cough into it
3. Face- Don't touch it.
4. Social Distance- Maintain a Social Distance (at least 1 metre)
5. Home- Stay if you can

CONCLUSION

Over the past years, it was likely seem that these viruses continued to emerged and evolved and cause both human and veterinary outbreaks owing to their ability to recombine, mutate and infect multiple species and cell types. Furthermore, understanding the mechanisms of how coronavirus cause disease and understanding the host immunopathological response will significantly help to improve the ability to design vaccines and reduce disease burden. Till now no specific drugs and no vaccines are available until now hygiene measure can reduce the rate of transmission and will help to overcome this pandemic.

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