

Rapid transmission of SARS-2 among Individuals – A Mini Review

Review Article

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ABSTRACT

The coronavirus disease emerged at the end of 2019 from Wuhan, China, and ultimately resulted in pandemic. It is a single positive-sense RNA virus spreading from person to person through contact in any form. Bats are the natural hosts of the SARS-CoV-2 virus. SARS-CoV-2 has the largest genome as compared to all RNA virus present so far. Spike proteins are responsible for their entrance into the human body. Social distancing and quarantine resulted in the best possible prevention for the less transmission of coronavirus. We performed a narrative review to describe its origin, transmission, pathogenesis, clinical manifestation, social implications, future possibilities, treatment, and vaccination.

Keywords: SARS-CoV-2, Transmission, Disease Outbreaks, Virus Replication, Genome, Quarantine

INTRODUCTION

Wuhan, a city in Hubei Province of China, often referred to as the “Chicago of China” was the ground zero for Novel Coronavirus, whose index patient became symptomatic on December 1, 2019.[1] On 13th January 2020, 1st case was reported outside China, in Thailand.[1]

Coronavirus is a member of the Coronaviridae family which has 124 other viruses. It is an RNA positive, enveloped with glycoprotein spikes emerging from it, giving a king's crown or halo shape, thus, named corona. Previously, coronaviruses were mainly involved in causing various respiratory and intestinal diseases among domestic animals and birds. Out of the Coronaviridae, 6 types were the culprit of human diseases, both minor and major. 4 out of those six causes of common cold, and the other 2 were involved in causing severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS-CoV). In a recent publication, it is stated that coronaviruses have the broadest and longest genetic material with a length range of 26 to 32 KB.[2] Along with transcription for the major structural protein, a large portion of the genome is

also transcribed and translated to polypeptides important for gene expression and viral multiplication. Over the past years, multiple types of research and experiments were conducted to get a better understanding of the molecular root of viral replication, virulence, and its adaptations to develop medicines and vaccines for therapeutic purposes and get a better grip on its diagnostics and evaluation procedures. Bats are the natural hosts of the SARS-CoV-2 virus. The infection began to spread to other humans via airborne respiratory droplets mainly in hospitals and clinics near the seafood market especially in those people who stayed for a long while at that place. It is a β -coronavirus that is enveloped, non-segmented positive ssRNA virus. Coronavirus is categorized into 4 genera, α - β - γ - δ -COV. Alpha and beta infect mammals whereas gamma and delta tend to affect birds. Previously 6 COV's have been identified to infect humans. Alpha-CoV HCoV-229E and HCoV-NL 63 and Beta COV HCoV-HKU1 and HCoV-OC43 have low pathogenicity and bring about slight respiratory symptoms same as the common cold. The other two beta CoV, SARS-CoV-2 and MERS-CoV lead to severe and potentially fatal respiratory tract infections. The bat COV genome (RaTG13) is 96.2% identical to SARS-CoV-2 and 79.5% to SARS-CoV-2. The genome sequencing results and analysis suspected that bat has been a natural host origin for the virus.[3, 4] Angiotensin-converting enzyme (ACE-2) is used by the SARS-CoV-2 because it has the same receptor as SARS-CoV-2 to infect the human.[5]



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SARS-CoV-2 is transmitted from bats via an unknown intermediate host to humans. Bats are the reservoirs for a wide variety of coronaviruses including severe acute respiratory syndrome COVID (SARS-COV) like viruses. SARS-CoV-2 originates in bats and can cross the species barrier into humans. SARS-CoV-2 is a non-enveloped positive ssRNA virus. 2/3rd of the viral RNA is located in the opening frame (ORF 1a/b), contains 16 non-specific proteins (NSPs). The rest of the genome has four essential structural proteins, which are. The spike (S)glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein along with some accessory proteins. S proteins of the virus bind to the host cell receptor, ACE 2 and is a critical step in the entry of the virus into the host. The mechanism of specific molecules-assisted endocytosis of the SARS-CoV-2 through membrane invagination is still not clear. Host factors such as old age also help to susceptibility to infection and disease progression.[2,3]

POSSIBLE SARS CORONAVIRUS TRANSMISSION

The respiratory droplets are thought to be the main cause for the transmission of coronavirus in the employees causing respiratory illness that is someone associated with SARS-CoV-2. Some procedures are performed on the patients having SARS that may transmit SARS-CoV-2.[5] The main routes of transmission are respiratory droplet transmission which is also known as air transmission and contact transmission. Inhalation of droplets through the respiratory tract from an ill person due to COVID-19 when the patient coughs, sneezes, or talks can cause infection in close contacts so it is advisable to maintain a 1-meter distance from the infected person or to wear the face mask.[6] Aerosol transmission has been documented with small aerosol particles. Contact transmission occurs when one touches objects like a door handle, lift switch, etc (on which virus can survive for 20-24 hours) and then touches these infected hands to their mouth, nose, or eye causing viral entry. It is advisable to do frequent hand wash. Fecal-oral transmission has also been established. Maternal-fetal transmission is being extensively studied and can't be ruled out.[7,8]

CORONAVIRUS REPLICATION

Angiotensin-converting enzyme-2 (ACE-2) is the cell receptor in the lower lungs for SARS- CoV and COVID-19 regulating both humans to human and cross-species transmission.[8, 9] A virion called S-glycoprotein on the surface of COVID-19 attaches to the ACE-2 receptor on human lung cells. S-glycoprotein has 2 subunits, S1 having key function

domain (RBD) controls host-virus range and cellular tropism, and S2 having two tandem domains named as Heptad repeats 1(HR1) and (HR2) mediates viral cell membrane fusion to these two domains.[10,11] After viral cell membrane fusion, the viral RNA genome enters into the cytoplasm and translates into two polyproteins, pp1ab and ppa1. In the double-membrane vesicle of the host cell, these polyproteins encode into nonstructural proteins and form replication transcription complex (RTC), which replicates continuously and synthesize a large amount of sub-genomic RNAs translating into structural and accessory proteins.[12,13] Mediating endoplasmic reticulum, golgi apparatus, newly synthesized genomic RNA, envelope, and nucleocapsid proteins assemble to synthesize virion particle vesicles. In the end, these virions containing vesicles release virus fusing with the plasma membrane. The binding of s-glycoproteins of SARS-CoV-2 and ACE-2 receptors is under study by various advancement approaches. It seems through a systemic study of β -COV receptors, SARS-CoV-2 entry is increased in the patients expressing ACE2 receptor in human but not Dipeptidyl peptidase-4 (DPP4) or Aminopeptidase N (APN). Verified through Cryo-EM structure of SARS-Cov-2 S- glycoprotein in the perfusion conformation, it is seen that ACE2 receptor and S-glycoprotein binding is 10 to 20 folds higher than that of SARS-Cov-2.[14] Cell surface-associated Transmembrane protease serine 2 (TMPRSS2) and Cathepsin activates the cleavage of S-glycoprotein of SARS-CoV-19, while the likely molecules (enzymes) involved in SARS-Cov2 endocytosis are yet unclear. [15,16] Studies and researches have shown that SARS-CoV-2 although transmits readily to human beings but is less virulent than SARS-CoV-19.

This virus has a high infection and high mortality rate. The possible factors for this global outbreak were:

1. Unknown pneumonia out break at China Spring Festival.
2. Further studies are needed to understand the pathophysiology of virus
3. Available data sho

wed that the virulence of SARS-COV-2 is less than SARS-COV-19 and MERS, with the mortality rate of COVID-19 being 4%, which is lower than that of MERS being around 35% and SARS 9.6%, respectively.[17] With time, under advancement approaches, the pathophysiological mechanisms, virulence, pathogenicity, and human-to-human transmission of the SARS- CoV-2 mechanism are understudies.

INCUBATION PERIOD

The reported incubation period ranges from 1-14 days

but in a few patients' symptoms seen even after 21 days. The average incubation period is around 7-8 days. Due to antigenic mutations it is no immunity exists against it, and it has high infectivity and fatality (especially in immune-compromised individuals like the elderly, heart failure patients, chronic respiratory disease patients, chronic kidney disease and malnourished patients. It is more virulent in cold and humid conditions) as compared to other coronaviruses. The survival time of coronavirus at 20°C is 4 hours in the air, 8 hours on fabric, 24 hours on stainless steel, and 48 hours on wood. While sustained heat of more than 55°C, chlorine-containing disinfectant, chlorhexidine, lipid solvent, and 75% alcohol effectively inactivates the virus.[11,14,18]

TREATMENT AND PROMISING THERAPEUTICS

Recent studies have shown that drugs used for the human immunodeficiency virus can be used for the treatment of Coronavirus. Remdesivir results in the blockage of enzymes needed for replication of HIV. Chloroquine, an antimalarial drug is efficacious in declining inflammation among people suffering from severe COVID-19. In cell culture, this drug represses the replication of SARS.[19] The prodrug, Remdesivir, gets metabolized in the body to its potent form GS-441524. This potent metabolized form is an analog of adenosine nucleotide that gets inserted in the place of actual nucleotide but is null when viral exoribonuclease tries to read it, thus halting the viral RNA product.[20] This drug inhibits viral RNA production by diminishing the viral RNA polymerase activity thus shutting down translation and transcription. Remdesivir in an intravenous form (200 mg on day 1 and 100mg for nine days, one dose daily) in patients of COVID-19.[21] The main concept of present line treatment is to treat the patient symptomatically. Others include the multivitamins and supplements that boost up the immune system to be active against the invading viral organisms. The following drugs are being used in hospitals across Pakistan for the treatment of patients. Though there is no such guideline or recommended treatment by WHO and FDA.

DNA VACCINES AGAINST CORONAVIRUS

During the assessment of vaccines on animals, especially mice, the final results showed us that it leads to the induction of the immune system against the virus. Due to the limitation of data when it comes to humans there is no documentation of authentic response.[22] While experimenting with mice the

vaccines containing E, M, N, and SRS-COV proteins were injected and it resulted in combination vaccines as a result. Out of all the structure-forming proteins of the corona, the S protein is a major antigenic component. This component induces host response after neutralization of antibodies thus leading to protective immunity against the viral pathogen. Thus, the results revealed that combination vaccines are a major trigger in the induction of the host immune system. Combination vaccines were shown to be more effective in triggering immunity when used in 2 doses followed by immunization with an inactive form of the virus than either of the vaccines used alone.[22] This induction of the immune system resulted in both humoral and cell-mediated immunity. To increase the effectiveness of available vaccines for corona these combination vaccines are shown to be more effective. The lessons from these vaccinations can provide a strong basis to help us in organizing the development of effective vaccines against already established coronavirus.[23]

INACTIVATED CORONAVIRUS VACCINE

Some experimental studies in animals proved the immunogenicity and effectiveness of inactivated SARS-CoV-2 vaccines, and one of them is being assessed in clinical trials. Until now, there has been no practical applicability of live attenuated vaccines against SARS-CoV. However, some cDNAs have been approved that encode CoV genomes, counting coronavirus. Recombinant viruses can be saved from cDNAs that are obtained through in vitro ligation. Genetic analysis was used to evaluate the functioning of SARS-CoV-2 proteins and has led to the development of some researches that can produce some attenuated coronavirus vaccines by engineering specific attenuated mutations or modifications into the viral genome. Even if live attenuated vaccines against influenza and adenovirus are available for humans. The presence of an infectious virus in the feces of coronavirus patients increases the risk that a live attenuated SARS-CoV-2 vaccine stain may accumulate in the feces of infected people and can be a source of infection for unvaccinated people. Some other risks are ways of engineering the vaccines and combing it's with other types of wild CoV to reduce the threat of infection.[24]

CONTACT TRACING AND QUARANTINE

An additional method to control the spread of SARS-CoV-19 is tracing all the close contacts of those who

are symptomatic, separating them, and keeping in isolation those who are asymptomatic for the 10 days incubation period after their contact. Many countries applied such measures in the recent pandemics, including China, Taiwan, Hong Kong, Canada, and Singapore. In the start, as less was known about the transmission of the disease, direct and remote contacts of symptomatic and asymptomatic patients with COVID-19 were isolated in some countries. Opposite to this, quarantine is now limited to only close contacts of symptomatic patients with the disease, because these are now considered to be the only contacts who have a notable danger for developing the disease. The quarantine was limited in Beijing, so the number of patients was related to a specific infection, and it also made it easy to diagnose and deal with the cases by enforcing the reporting of current symptoms. So, quarantine in Beijing was successful because an infected but quarantined person could not transmit the disease to his close ones. A study has proved that quarantining only those who had close contact with the symptomatic patients would not have compromised its efficacy. Local public health authorities should also be taken into consideration while deciding to implement quarantine. Typically, quarantined persons were directed to stay isolated, use surgical masks when near others, check their temperature 2-3 times a day, seek medical attention immediately if they develop fever or other symptoms like dry cough, sore throat, flu, or muscle aches that are compatible with SARS. Regular visits and phone calls were made regularly to check the health of quarantined patients. There are some objections to the quarantining procedures because it might not be supported by the law or the morals of the society by restricting a patient's right to be free. Also, it's difficult to trace all the contacts who are at risk and ensuring that rules of quarantine have been observed in all quarantined individuals.

CONCLUSION

The review paper delivers information about COVID-19 transmission and its recent understandings and future possibilities which can be adopted to prevent this disease. It is a series of threats for the population of the world. Till now there is no proper cure and treatment of this virus. Researches are working on the making of the vaccine against this virus. To this date, we know how to prevent this disease as much as we can by taking some precautionary measures. Wearing a mask, hand washing, social distancing, and quarantine are some preventive measures. Remdesivir has a great beneficial effect on both animals and humans having SARS-CoV-2 infection. It is a novel nucleotide analog

and has shown beneficial effects on patients with fast recovery. We need to know that it is very likely that the coronavirus will continue to emerge and will cause many human and animal infections resulting in outbreaks. Policies and coping strategies for the developing world can be in many possible ways. As the pandemic's epicenter and likewise destruction moved from Asia to Europe, to America and then to the whole world brought about a great pandemic and while some countries have already opened their businesses, two big problems have attracted the attention of the whole world that how to formulate and implement recovery economic strategies to develop a more wide-ranging and maintainable post-crisis world on a whole. As well as how to lift international support for evolving countries to ensure their commercial survival and to support their breakable healthcare systems, while spreading the seeds for a better future on the prospect. Both of these issues have major consequences for industrial development opportunities and policies of third-world states. The pathogenesis and spread is the basic and primary cause of this virus, If we will get information about it then eventually we will find out many possible ways to treat coronavirus patients, making vaccination but up to now, we will have to adopt some initial practices to ensure everyone's and our safety which involves isolation methods currently called quarantine, adopting precautionary measures on different levels and supporting others.

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CONFLICT OF INTEREST

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