

Novel Coronavirus Disease 2019 (COVID-19): Emerging Public health Challenge

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ABSTRACT

COVID-19 Coronavirus (CoV) has been emerged as one of the serious pathogens that mainly target the respiratory system of human beings. COVID-19 disease is mainly caused by SARS-COV2 virus and presents the primary causative agent of this fatal disease which is of great human health issue. This has prompted us to summarize a review on COVID-19 (Corona virus Disease 2019) which would cover all essential details about the COVID-19 virus including its origin, symptoms and the possible treatments that have been discovered so far. Therefore this review would be very insightful for studies focusing towards identifying a better therapeutic approach against corona virus disease.

Keyword: COVID-19, SARS, Coronavirus, Phylogenetic Analysis, Disease

1. INTRODUCTION

COVID-19 was first identified in Wuhan city of China in December 2019 [1]. Earlier outbreaks of these corona viruses were SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome) which had emerged as a major threat to public health. [2]. Corona virus belongs to the Coronaviridae family of viruses and is a single stranded, positive sense RNA genome (size ranging from 26 to 32 kilobases in length) [1]. Coronaviruses have been elucidated in numerous hosts including several mammals such as bats, camels, dogs, mice, masked palm civets and cats. [p2]In 2018 a HKU2-related coronavirus (bat origin) was found to be responsible for a lethal syndrome in pigs (acute diarrhea) in 2018. Then in late December 2019, numerous patients with symptoms of viral associated pneumonia were reported to be epidemiologically linked with seafood market of Huanan in the city of Wuhan (in Hubei province of China). Next generation sequencing technology has made it possible to identify a novel human-infecting coronavirus (2019-nCoV). However, currently this 2019-nCoV has now been reported in several countries including Thailand, India, Japan, Indonesia, South Korea, USA, Malaysia, Italy, USA, UK, Singapore, and several other European and Asian countries. Numerous infected patients had exhibited high fever whereas some had reported dyspnoea with invasive lesions characterized in both infected lungs in their chest radiographs [1].

Wu et al. studied and reported a hospitalized patient (worker at a seafood market) as a potential source of the Corona outbreak. The diseased patient was reported with

severe respiratory syndrome along with abnormal chest radiographs. Author executed meta-transcriptomic sequencing of BALF (bronchoalveolar lavage fluid) to identify this aetiological agent and the analyses of the sequencing reads led to the identification of a novel coronavirus (2019-nCoV).

The authors compared the receptor binding domain of coronavirus COVID-19 with SARS-CoV to investigate the infecting potential of virus to humans. Experimental findings suggested that COVID-19 uses the similar entry receptor (the ACE2 protein) as SARS-CoV. Another study reported by Zhou et al. also confirmed the sequence similarity between COVID-19 and SARS-CoV. They collected oral swabs and BALF samples of seven patients who were admitted during the outbreak having severe pneumonia (out of which six were workers at a seafood market in Wuhan). The metagenomics analysis of a BALF sample identified a COVID-19 genome (~29.9 kb) which shares 79.5% sequence similarity with SARS-CoV. Further, the authors characterized the COVID-19 genome and studied the phylogenetic relationships between SARS-CoV, COVID-19, bat SARS-related CoVs. Their experimental analysis established a close phylogenetic relationship between COVID-19 and a bat CoV which was 96% identical at whole genomic level and suggested the bat origin of COVID-19. The authors created serological assays and qPCR, which helped in the diagnosis of COVID-19. Finally, they successfully cultured the virus and named it as 2019-nCoV. They further performed infectivity assays by using HeLa cells (either ACE2 proteins expressing or not expressing) and confirmed that ACE2 protein is responsible receptor for virus entry. In total, these reports

provided the details about the origin of 2019-nCoV, which could be significant in preventing its spread, and highlighted bats as viral carriers [3].

2. SYMPTOMS OF COVID-19 DISEASE

The symptoms of COVID-19 disease remarkably appear after an incubation period of approximately 5 days and the duration from the onset of COVID-19 disease symptoms to death ranges approximately from 6 to 42 days (with a median of 14 days). This duration depends on the age and immune system of COVID-19 patient. Several studies reported its large number of infected cases in patients with age more than 70 in comparison to patients with the age less than 70-years old [4]. A common symptom of COVID-19 disease includes fever, fatigue, respiratory issues, cough, sputum production, haemoptysis, headache, diarrhoea, lymphopenia and dyspnoea. Clinical features depicted by chest CT scan showed pneumonia whereas there were few abnormal features including acute respiratory distress syndrome, RNAemia, acute cardiac injury and ground-glass opacities that ultimately led to patient's death [5]. Some cases reported multiple peripheral ground glass opacities in sub pleural areas of lungs that resulted in both localized and systemic immune response leading to increased inflammation. Unfortunately, treatment with interferon inhalation in some cases showed no clinical efficacy and instead they worsened the condition by enhancing pulmonary opacities. Although there were similarities between the symptoms COVID-19 and previous reported betacoronavirus including dyspnea, dry cough, fever and bilateral ground glass opacities in chest CT scan. However, COVID-19 diseased patient showed few unique clinical features such as sore throat, rhinorrhoea, and sneezing. Patients infected with COVID-19 also showed gastrointestinal symptoms such as diarrhea in comparison to low percentage of SARS-CoV or MERS-CoV patients [7]. Thus, it is crucial to test urine and faecal samples to eliminate a potent alternative transmission route, specifically via health care workers and patients. Thus there is a crucial demand to develop methods to investigate several modes of transmission including urine and faecal samples in order to elucidate strategies for the inhibition of transmission in order to control the disease. The laboratory analysis also showed leucopenia with leukocyte counts of about 2.91×10^9 cells/L, out of which 70% were neutrophils. In addition, approximately 16.16 mg/L of blood C-reactive protein was also reported that was above the normal range i.e., 0–10 mg/L. D-dimer and high erythrocyte sedimentation rate were also found in

the analysis. Additionally high levels of cytokines and chemokines were noted in blood sample of COVID-19 patients such as included IL1RA, IL1- β , IL7, IL9, IL8, IL10, FGF2, IFN γ , TNF α , IP10, and VEGFA [2].

3. TRANSMISSION OF COVID-19 DISEASE OR INFECTION

Initial findings identified two snake species that could have been a probable reservoir of COVID-19. However, till date, no potential and reliable evidence of COVID-19 reservoir other than birds and mammals [5]. Numerous reports have indicated that person to person transmission is a possible route for spreading of COVID-19 infection. This report is further supported by cases which occurred within the families and among those people who had not visited the animal market of Wuhan [6]. Transmission occurs primarily through direct contact or via droplets spread during sneezing or coughing from an infected person. However a small study also confirmed that there was no transmission of corona virus from mother to her child [6].

Receptor binding expressed by the host cell is considered as the initial step of COVID-19 viral infection which is then followed by fusion with host cell membrane. Studies reported that lung epithelial cells are one of the main target of the corona virus. Therefore, it can be concluded that person to person transmission of SARS-CoV could occur via binding of the receptor binding domain of Corona virus spikes to cellular receptor ACE 2 (angiotensin-converting enzyme 2) [8]. Interestingly, the sequence of receptor binding domain of coronavirus COVID-19 virus spikes is found to be same as that of SARS-Coronavirus. This study strongly suggested that virus enters into host cells most likely via ACE2 receptor [4]. The genetic sequence of COVID-19 virus was found to be more than 50% to the MERSCoV and 80% identical to SARS-CoV [9], and these both MERS-CoV and SARS-CoV originated in bats. Thus, the phylogenetic analysis clearly indicated that COVID-19 virus belongs to the betacoronavirus genus that includes SARSCoV that infects bats, humans, and wild animal.

COVID-19 virus belongs to the 17th member of coronavirus family which infects human and was classified under the subfamily of ortho coronavirinae subfamily. Genomic sequence identity and phylogenetic analysis also revealed that COVID-19 can be considered as new betacoronavirus which infects humans.

4. AVAILABLE THERAPEUTICS OR TREATMENT POSSIBILITIES

The human to human transmission of COVID-19 disease leads to the isolation of patients who were administered with a variety of treatment. Currently, there are no corona specific vaccines or antiviral drugs against COVID-19 infection. Few drugs available against COVID-19 disease are antiviral drugs (Nucleoside analogues) and HIV protease inhibitors which could attenuate COVID-19 virus infection [7]. Another in vitro study reported that the broad spectrum antiviral drugs including chloroquine and remdesivir are highly effective in controlling the infection of COVID-19 disease [8]. These antiviral drugs have also proven safety records in human patients. Therefore, these therapeutic agents could be considered as significant therapeutic candidate for the treatment of COVID-19 infection [9]. Furthermore, numerous compounds which are in development include clinical candidate (EIDD-2801 compound) which has depicted high therapeutic potential against pandemic and seasonal influenza viral infections and represents another potential candidate drug for the treatment of COVID-19 disease [10]. It is further reasonable to consider other broad spectrum antiviral agent that could provide better drug treatment options for COVID-19 disease including Ritonavir or Lopinavir [11], RNA synthesis inhibitors and Neuraminidase inhibitors. However there is urgent need to identify potent chemotherapeutic drug candidate for the treatment of COVID-19 infections. Further there is a strong need to create an animal model to replicate the brutal disease currently reported in humans. Numerous researchers are currently trying hard to establish a non-human primate model for the study of COVID-19 infection in order to establish faster way of novel therapeutics and also for the testing of novel and potential vaccines for providing a better mechanism of virus-host interactions.

5. ACKNOWLEDGMENTS

We are highly thankful to Noida Institute of Engineering and Technology for providing the support and guidance for writing this review.

6. CONCLUSION

Numerous viruses would continue to grow via naturally induced mutations and thereby posing a threat to human health globally. This would not only affect health but greatly hampers the economy thus more studies should be focused towards identifying the inhibitory components which could inhibit the ability of virus to modify the immune response of host cell against it. Additionally there

is a need to explore the biological structural details of Coronavirus which could further provide us numerous ways to develop vaccines or drug against this lethal disease.

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