Evolving Through COVID- 19: Can it be any Better for us?

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Abstract

Human evolution has witnessed a various eras of pandemic outbreaks in past . Each time evolving through them has given mankind the opportunity to develop the skill of coping and developing a new scientific thinking process. COVID19 is the most challenging for the twenty first century, in terms of identifying, isolating and controlling the transmission of the pathogenic virus. The unidentified source of origin, its complicated transmission dynamics and exponential rate of disease progression makes it difficult for the health care professionals to contain the infection and its spread. The genomic clues obtained at the molecular level is employed both at diagnostic and therapeutic level is the only hope that helps us to survive this crisis. The determination to find a cure has struck all the fundamental researchers and the ultimate zest to conquer this pandemic is preset globally. This is evident through the escalated experimentation and clinical trials that wasn't witnessed anytime prior.

Keywords: COVID 19, Unidentified Source, Transmission Dynamics, Healthcare Professionals, Genomic Clues, Survive.

1. INTRODUCTION

Dawn of this decade came to a fast still when China reported its first confirmed case of SARS-CoV-2. In December, 2019, a local outbreak of pneumonia of initially unknown cause was detected in Wuhan (Hubei, China), and was quickly determined to be caused by a novel corona virus 1 namely severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). The outbreak has since spread to every province of mainland China as well as 27 other countries and regions, with more than 70 000 confirmed cases as of Feb 17, 2020 [1]. And it turned out to be the worst nightmare ever witnessed by this generation; it had its hardest stroke at the European and American population. It had birched down the normal lives of people all around the world and turned itself as global pandemic in just a matter of weeks. Looking forward to survive this viral tragedy it is utmost important for all of us to be stay aware of the virus; origin, mode of spread, primary symptoms, the pattern of viral shedding, precautionary measures to be taken.

Addressing a viral attack can be much challenging task for health care professionals. Being employed at the preliminary level in identifying the disease and treating the same, sadly we are included in the high-risk group criteria. Therefore, it's highly critical to make ourselves equipped with best precautionary measures currently available. Providing any medical or dental care at this stage is highly vulnerable by exposing ourselves to the disease directly or indirectly, and risking it for our personal healthcare workers and other patients who come in contact with us. Discussing the current available preventable objectives and precautionary measures both at professional and community level can be the very step towards it.

2. OUTBREAK HISTORY OF COVID 19

The history of the viral outbreak can be traced back to its origin and initial spread in China. Cracking the viral genome and its evolutionary evidence links it to a SARS-CoV-2-like CoV (named Pangolin-CoV) in dead Malayan

pangolins. Pangolins are part of the mammalian family and closely resembles as anteaters in Indian context. Pangolin-CoV is 91.02% and 90.55% identical to SARS-CoV-2 and Bat CoV RaTG13, respectively, at the whole-genome level. Aside from RaTG13, Pangolin-CoV isthe most closely related CoV to SARS-CoV-2. The S1protein of Pangolin-CoV is much more closely related to SARS-CoV-2 than to RaTG13. Five key amino acid residues involved in the interaction with human ACE2 are completely consistent between Pangolin-CoV and SARS-CoV-2, but four amino acid mutations are present in RaTG13. Both Pangolin-CoV and RaTG13 lost the putative furin recognition sequence motif at S1/S2 cleavage site that can be observed in the SARS-CoV-2. Conclusively, recent studies suggests that pangolin species are a natural reservoir of SARS-CoV-2-like CoVs [2].

Similar to the cases for SARS-CoV and MERS-CoV , the bats are considered as a probable species for the origin of SARS-CoV-2, as it shares 96% whole-genome identity with a bat CoV, Bat CoV RaTG13, from Rhinolo-phus affinis from Yunnan Province of china [3,4]. The concept of SARS-CoV and MERS-CoV usually tend to pass into different species of intermediate hosts, such as civetsor camels, before leaping to humans as been taken into account [4]. The fact indicates that SARS-CoV-2 was probably transmitted to humans by other animals. However, the earliest coronavirus disease 2019 (COVID-19) patient reported no direct exposure at the seafood market [5,6]. This definitely highlights the fact that mode of transmission or identifying the vector responsible for the disease is still not known. Strangely the mode of initial spread makes it difficult in fully understanding the viral transmission spread and its interspecies dispersion mechanism both in humans and other animals.

The only scientific clue was based on report of Liu and his colleagues (24 October, 2019), from the Guangdong Wildlife Rescue Center of China first detected the existence of a SARS-CoV-like CoV from lung samples of two dead Malayan pangolins with a frothy liquid in their lungs and pulmonary fibrosis [3], and this fact was discovered close to when the COVID-19 outbreak occurred. This however, leaves us to revolve around more pondering questions and answers that are obviously not known to us.

Coronaviruses are enveloped viruses with a positive sense single-stranded RNA genome (26–32 kb) and are categorised into corona virus genera α, β, γ, δ [7]. Human corona viruses (HCoVs) detected in the α corona virus (HCoV-229E and NL63) and β corona virus (MERS-CoV, SARS-CoV, HCoV-OC43 and HCoV-HKU1) genera [8,9]. The novel corona virus belongs to β genera and is identified β-CoV and named as "SARS-CoV-2" by the International Virus Classification Commission.

The genome of SARS-CoV-2 is similar to typical CoVs and contains at least ten open reading frames (ORFs). The first ORFs (ORF1a/b), about two-thirds of viral RNA, are translated into two large poly proteins. In SARS-CoV and MERS-CoV, two poly proteins, pp1a and pp1ab, are processed into 16 non-structural proteins (nsp1-nsp16), which form the viral replicase transcriptase complex[10]. Those nsps rearrange membranes originating from the rough endoplasmic reticulum (RER) into double-membrane vesicles where viral replication and transcription occur [11,12]. The other ORFs of SARS-CoV-2 on the one-third of the genome encode four main structural proteins: spike (S), envelope (E), nucleocapsid (N) and membrane (M) proteins, as well as several accessory proteins with unknown functions which do not participate in viral replication

3. THE VIRAL REPLICATION AND TRANSMISSION DYNAMICS IN HUMANS

Coronavirus S protein has been reported as a significant determinant of virus entry into host cells and it is found that a critical proteolytic cleavage event occurred at SARS-CoV S protein at position (S2') mediated the membrane fusion and viral infectivity [13]. The envelope spike glycoprotein binds to its cellular receptor. The entry of SARS-CoV into cells was initially identified to be accomplished by direct membrane fusion between the virus and plasma membrane [14]. After the virus enters the cells, the viral RNA genome is released into the cytoplasm and is translated into two polyproteins and structural proteins, after which the viral genome begins to

replicate [15]. The mechanism of all viral diseases are likely similar.

The entity that captures the immune attention is the most striking feature of this disease process that makes its ultimately fatal. As increased incidence of Acute Respiratory Distress Syndrome (ARDS) symptom clearly highlights the exaggerated of immunopathological response with the release of uncontrolled systemic inflammatory release of large amounts of pro-inflammatory cytokines (IFN-α, IFN-γ, IL-1β, IL-6, IL-12, IL-18, IL-33, TNF-α, TGF-β, etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10, etc.) by immune effector cells in SARS-CoV infection [16-19]. Similar to those with SARS-CoV and severly infected MERS-CoV. IL-6, IFN-α, and CCL5, CXCL8, CXCL-10 levels were also elevated in severely infected individuals when compared to those with the mild-moderate disease [20]. The cytokine storm will trigger a violent attack by the immune system to the body, cause ARDS and multiple organ failure, and finally lead to death in severe cases of SARS-CoV-2 infection, just like what occurs in SARS-CoV and MERS-CoV infection [21].

The most common symptom associated with this disease is its targeted approach on the upper respiratory tract and affecting lower lobes of the lung. As SARS-CoV-2 belongs to the SARS family it definitely shares the immune-physiological events. The SARS virus enters the body through the respiratory tract and first infects the epithelial cells of the trachea, bronchi, bronchioles, and lungs. The virus infects resident, infiltrating, and circulating immune cells. The circulating immune cells carry the virus to other organs. The virus infects and damages the immune cells of the spleen, peripheral and central lymph nodes, and other lymphoid tissues [22].

Apart from causing symptomatic acute upper respiratory tract diseases chances of it invading the CNS, inducing neurological diseases is also critical. The neuro-invasive propensity of CoVs has been documented almost for all the beta corona viruses, including SARS-CoV [23], MERS-CoV [24], HCoV-229E [25], HCoV-OC43 [26], mouse hepatitis virus (MHV) [27], and porcine hem-agglutinating encephalomyelitis corona virus (HEV) [28,29]. In light of the high similarity between SARS-CoV and SARS-CoV2, it is quite likely that the potential neuroinvason of SARS-CoV-2 plays an important role in the acute respiratory failure of COVID-19 patients [30]. The prognosis of the disease is highly linked to the extent of immune-mediated damages primarily affected the organ of lungs. Much of the emphasis of the disease progression has to be highly monitored with increasing count of immune cells especially of the T lymphocytes, monocytes and macrophages. The response of immune cells with reduction or exaggerated proliferation is always associated in predicting the immune mechanism of individuals[31-35]. However, focussing on stimulating the immune activity or suppressing them through the use of various steroidal therapies is still at debate [29].

4. WHAT'S NEXT IN LINE FOR TREATMENT CONSIDERATIONS???

Chloroquine, typically used in the context of malarial or autoimmune disease it acts through the affects glycosylation of the ACE-2 pulmonary cell receptors, impairing viral cell entry [36-39]. The alteration of pH alkalinising the cellular cytoplasm impairs the endosome function and is ideally considered to be less toxic and effective.

Camostat mesylate, a serine protease inhibitor, partially blocks SARS-CoV-2 entry into the pulmonary cells by inhibiting S protein priming and endocytosis [42]. However, the current studies on treatment with camostat mesylate are currently pending.

Tocilizumab is a humanized monoclonal antibody against interleukin-6 receptor (IL-6R Ab), is commonly used as an immunosuppressive in the treatment of rheumatoid arthritis and systemic juvenile idiopathic arthritis [38-41]. Small studies in China have found some success with the treatment of severe cases of COVID-19 with tocilizumab [43].

Identifying the pathogen and developing a vaccine against it, is considered as the most effective measure to contain the outbreak of an infectious disease. However, isolating the different viral strains (differs across different geographical locations) and identifying the antibodies against it, is highly challenging task [45]. The mutational changes are continuous and seeking approval from various regulatory bodies

are of time bound challenge for researchers worldwide [44]. Cancer immunotherapeutic agents are however considered at the moment [43].

Apart from developing a vaccine, a recent use injecting convalescent sera to high risk group of patients. Concept is based on 'Passive immunity', passive antibody therapy has a storied history going back to the 1890s and was the only means of treating certain infectious diseases prior to the development of antimicrobial therapy in the 1940s [46,47]. Experience from prior outbreaks with other corona viruses, such as SARS-CoV-1, shows that such convalescent sera contain neutralizing antibodies to the relevant virus can be used as an adjuvant therapeutic measure [48]. A group of U.S. researchers working to set up clinical trials for convalescent plasma, called the National COVID-19 Convalescent Plasma Project is currently refocusing on this [49,50].

5. CONCLUSION

To conclude the present situation is highly crucial for all of us. The individual preventive measures when taken personally can definitely make a mark in reshaping and redefining the spread of the infection. Considering our community health, each individual can play an important role in preventing the disease spread. In turn can cause a drastic reduction of disease associated mortality and morbidity rates. At times, simple acts of frequent hand washing, use of sanitizers, facemasks and gloves and most importantly self-governed quarantine are the most efficient way to save lives.

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