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The Outbreak, Epidemic and Pandemic of Coronavirus Disease (COVID-19)

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Abstract

SARS-COV2 causes the most lethal Coronavirus disease COVID-19 and constitutes the emissary of conclusively contagious disease that turned out to be a universal public apprehension. Incident that is based on the people who got infected by the subjection to the Wuhan City animal market of People's Republic of China. This has substantially advocated the zoonotic genesis of COVID-19. The transmission of contagious infection spread by the contact which leads to the quarantine of suspected patients; hence they were then subjected to a variety of treatments. Considerable amount precautionary measures were adopted to reduce the subsequent amount of the disease transmission to get the epidemic under control. Specific efforts had been laid for the cautionary protection of individuals with susceptible conations for catching the infection including elderly people, children, and health care professionals. Focusing on this review the main highlight is on the large array of symptoms, epidemiology along with modes of transmission and pathogenesis combined with phylogenetic analysis that will shape the future of this lethal disease.

Keywords: Coronavirus, COVID-19, Wuhan city, Pneumonia and Pathogenesis

1. Introduction

The human respiratory system is the prime target of pathogen known as Coronavirus. Earlier outbreaks caused by viruses of corona family include the well-known Middle East respiratory syndrome (MERS)-CoV and severe acute respiratory syndrome (SARS)-CoV, they both have been most significantly identified and characterized as a threat towards public health. During the period of late December in the year 2019, a group of convalescent patients were hospitalized followed by the initial diagnosis of pneumonia like symptoms of unknown causes. Such individuals were closely linked with the areas of wholesale markets of wet animals and seafood market of Wuhan, Hubei Province of China (Bogoch et al., 2020; H. Lu et al., 2020). Many reports foretold the potentially lethal outbreak by the Coronavirus turning into large number victims it produced in the year 2019 Novel (New) Coronavirus (COVID-19, denominated by WHO, on 11th Feb 2020) which was adjudged to be remarkably larger to 1 (diversification from 2.24 to 3.58) (Zhao et al., 2020). The summary and sequence of COVID-19 infections are as follows. The very first cases came under consideration were sequentially reported during the period of 18th December 2019 (Du Toit, 2020). Further during the period of 18th to 29th December 2019, five patients were admitted to the hospital with

symptoms like acute respiratory distress syndrome and among them one patient succumbs to death (Ren et al., 2020). Moreover, since 2nd January 2020, 41 individuals were hospitalized and their cases had been confirmed by the pathology laboratories of COVID-19 infection, inculcating more severity to the medical conditions less than half of the diseased individuals had underlying complications of cardiovascular diseases, diabetes mellitus and hypertension (Huang et al., 2020).

Researchers evaluated data from more than 5,000 U.S. patients, involving those at Michigan Medicine, who were hospitalized in the intensive care unit for COVID-19. 14% of them underwent Cardiac Arrest (CA) within two weeks of being admitted to the ICU. "Cardiac arrest is mutual in older patients with COVID-19, and survival rates after an arrest are deprived," Although one of three COVID-19 patients undergoing in hospital cardiac arrest (IHCA) may achieve Return of spontaneous circulation (ROSC), almost 90% may not survive at 30 days or to hospital discharge (Ippolito et al., 2021). CA causes global ischemia and multiple pathways are affected (Choudhary et al., 2021; Shoaib et al., 2020). Several studies have supported the use of Near-infrared Spectroscopy (Takegawa et al., 2021), electrophysiological technique like electroencephalogram and somatosensory evoked potential (Leanne Moon et al., 2016) as a predictor of brain recovery after cardiac arrest. CA is also a complex disease and till date not an approved drug which shows beneficial effect in survival and neuroprotection have been developed, although few therapies like lipids (Nishikimi et al., 2021), gases (Hayashida et al., 2020), and metformin (Rishabh Choudhary, 2021) and probably mitochondrial transplantation (Hayashida et al., 2021) has been predicted with some benefits.

COVID-19 patients were the ones who caught infection from the hospital visits, most of them known as a condition of nosocomial infection. But earlier it was concluded by the analysis that COVID-19 was not found to be a highly contagious virus that spreading from individual to an individual, but it is more likely to spread because of many patients catching infections at various locations all over the hospital via an unknown mechanism. Adding more to the severity to the situation, only the individually who were found to be sick were tested, hence there were many more who got clinically sick. When cases proceeded further on 22nd Jan 2020, there were a total of 571 new cases of COVID-19 that were substantially reported in other 25 provinces of China (Lu, 2020). The National Health Commission of China has reported the information of the very first deaths until the 22nd Jan 2020 that comprised of a total 1975 individual cases that were reported to be confirmed by contagious infection by COVID-19 in the Chinese mainland with overall 56 deaths (W. Wang et al., 2020). On the other hand, a report on 24th Jan 2020 that summarized the rapidly increasing number of cases that reached up to 5502 in number (Nishiura et al., 2020). When the situation turned critical new 7734 cases were confirmed in China by 30th Jan 2020 and 90 cases were also have been reported by that time form countries like Germany, Taiwan, France, Thailand, Sri Lanka, Japan United Arab Emirates, and India. Overall, fatality of COVID-19 was about 2.2% (Bassetti et al., 2020).

The very first case related to COVID-19 contagious infection were also confirmed in the United States that lead to the further progress in the identification, diagnosis of symptoms, clinical courses and including the disease management of every case. When development pattern of disease was studied carefully, it came out to be the infected individual's initial mild symptoms that steadily progressed into pneumonia after the 9 days of severe illness (Holshue et al., 2020). The CDC emphasizing on a great effort has successfully screened >30,000 passengers arriving at US airports for the symptoms of novel Coronavirus. In the series of initial screening of 443 individuals that have been reported to be tested for Coronavirus in the 41 states of United States of America. A critical research report was published in Nature that unleashed the fact that Chinese health authorities concluded on 7th Feb 2019, that there were 31,161 individuals who caught this infection in China, so far more than 630 people were reported to be dead because of infection. While preparing this research papers, WHO reported 51,174 confirmed cases on the other hand 15,384 critical cases and 166 deaths in China. In New York, a case series for Pneumatosis intestinalis in the setting of COVID-19 for four critically ill patients experiencing from pneumatosis intestinalis (PI) during their hospital admittance has been reviewed. All patients got the biological agent tocilizumab (TCZ), an interleukin (IL)-6 antagonist, as an experimental medication for COVID-19 before emerging PI. COVID-19 and TCZ have been individually associated to PI risk, yet the source of this relationship is unspecified and under assumption. PI is an unusual situation, identified as the existence of gas in the intestinal wall, and although its pathogenesis is

inadequately recognized, intestinal ischemia is one of its connective agents. Based on COVID-19's involvement with vasculopathy and ischemic insults, and IL-6's protective role in intestinal epithelial ischemia–reperfusion injury, an adverse synergistic association of COVID-19 and TCZ can be recommended in the setting of PI (Miyara et al., 2021)

2. Symptoms

The signs and indications of contagious COVID-19 infection are exhibited after the incubation period that is around estimate period of 5.2 days (Li et al., 2020). The time span that is required by COVID-19 symptoms towards death ranged up to from 6-41 days following a median time of 14 days. Further, this period is totally based on factors like age of an individual combined with status of the immune system that how strong it is. Eventually, it was observed that it was way shorter in the patients those were of >70-years old in substantial comparison with those who are under the age of 70 years old. When facts are studied regarding the onset of the commonly observed onset symptoms of COVID-19 the illness was combined with cough, fever and combined with sputum production, followed by hemoptysis, lymphoenia, dyspnonea and lymphopenia (Carlos et al., 2020; Huang et al., 2020; Ren et al., 2020; W. Wang et al., 2020). Analysis of CT scan reports revealed the presence of pneumonia, but also many other abnormal features such as RNAaemia, acute cardiac injury, incidence of grand glass opacities combine with respiratory stress syndrome that will finally lead to the death of the patient (Huang et al., 2020). In the minority of the cases multiple peripherical ground glass opacities were clearly observed in the correct location that was sub pleural areas of both lungs (Lei et al., 2020) that further develops into both localized and systematic response of the immune system that transforms into the inflammation. But it was a pity that treatment of some cases that was subjected to interferon inhalation showed no clinical affects and transformed into a worsen situation that was followed by the progressing pulmonary opacities (Lei et al., 2020).

Most crucial and different thing that researchers noticed is that the corresponding signs and symptoms in between beta coronavirus and COVID-19 such as dry cough, fever, bilateral ground glass opacities and dyspnea were found particularly on chest CT scans (Huang et al., 2020). But COVID-19 demonstrated exceptional features that especially included the injury to the lower airway as readily apparent due to the upper respiratory tract symptoms those include sore throat, rhinorrhea, and sneezing (Assiri et al., 2013; Lee et al., 2003). Moreover, such results established that results that were obtained from chest radiographs upon admission of an individual and some cases also show the peculiar cases of infiltration in the upper lobe of the lung that has been always associated with hypoxemia and dyspnea (Phan et al., 2020). It is eminent that many patients infected with COVID-19 also tuned on the gastrointestinal signs and symptoms including diarrhoes, a minority in patient numbers developed gastrointestinal distress those were very similar to the SARS-CoV and MERS-CoV patients. Hence, it is essential to pay pathological attention to the fecal and urine samples preclude a high possibility in the development of new transmission mode for COVID-19, very particularly via health care workers and patients (Assiri et al., 2013; Lee et al., 2003). Accordingly, proper development of protocols that are particularly meant for the identification of various transmission modes including urine and fecal samples are urgently required for the development of strong methodologies to stop and inhibit and reduce the disease transmission.

3. Pathogenesis

One of the grave symptoms of COVID-19 are linked with an ascending number of mortality most specifically from the widespread epidemic Chinese regions. Dealing with the serious conditions of health emergency from the period in between 22nd to 25th of Jan 2020 the Chinese National Health Commission announced the information about initial 17 deaths that further enhance the numbers up to 56 deaths (W. Wang et al., 2020). Data proclaimed the number of individual demised were 2684 cases reported because of COVID-19 which turn out to be 2.84% in comparison with the prior information of 25th Jan 2020 and the death ranges in median of 75 covering the age of 48 to 89 years (W. Wang et al., 2020). The long-suffering individuals because of the contagious infection of COVID-19 displayed a much higher leukocyte numbers, associated with the abnormal respiration, also an increment in the levels of plasma pro-inflammatory cytokines. When taking a case of COVID-19 into consideration reports and analysis showed a patient suffering with fever for 5 days, presented with a cough and coarse breathing sounds from both the lungs, most importantly the body temperature of 39°C. The collected samples of sputum gave positive real time PCR results that also

confirmed COVID-19 contagious infection (Lei et al., 2020).

The intense laboratory studies gave the results showing the condition of leucopenia with the leukocyte counts of 2.91 × 10^9 cells/L of which 70.0% were identified as neutrophils. Adding more to the fact of studies a value of 16.16 mg/L of blood C-reactive protein was reported above the normal range (0–10 mg/L). Increase rate of erythrocyte sedimentation rate and D-dimer was also closely studied (Lei et al., 2020). Later on, the main symptoms of contagious nature of COVID-19 infection were intense pneumonia that subsequently targeted the respiratory system, but it also observed that RNAaemia, in combination with the incidence of ground-glass opacities, and acute cardiac injury also occurred after a while in a patient (Huang et al., 2020). Most remarkable fact were the high levels of cytokines in the blood along with chemokines were precisely notable in COVID-19 infections that also included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. Most of the serious cases that were subject to ICU displayed very high levels of pro-inflammatory cytokines also including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα that are main factors in promoting the disease lethality (Huang et al., 2020).

4. Transmission

Establishing the fact that majority of the infected individuals acquired their disease from their exposure particularly to the wet animal market of Wuhan City, as it was a place where live animals sold on daily basis, hence, this fact concluded the zoonotic genesis of COVID-19 particularly. Large endeavor focused for the exploration for a possible source or some intermediate vector from which infection that has spread among humans. Earlier reports and analysis most importantly identified two species of snakes expected to be a possible source COVID-19. Nonetheless in later studies it was concluded that there is not a single solid evidence to conclude that Coronavirus has a mammalian or avian reservoirs (Bassetti et al., 2020; Ji et al., 2020). When studies concentrated on molecular level, the thorough analysis of COVID-19 genome exhibited 88% similarity with two bat-driven severe acute respiratory syndrome (SARS)-like Coronaviruses that are proving to be highly dangerous (R. Lu et al., 2020; Wan et al., 2020). When the focus of research diagonally shirted on a molecular level the analysis of genome of COVID-19 exhibited 88% similarity with two bat-derived severe acute respiratory syndrome (SARS)-like Coronaviruses at genetic level (R. Lu et al., 2020; Wan et al., 2020), such facts opened the gate way to the conclusion that mammals are more likely to the connecting link in between humans and COVID-19. Many other reports also figured out the factor of human-to-human transmission that is the most expected and reasonable passage for COVID-19 contagious infection spread out. Such cases also promoted the solid facts related to the occurrence of contagious COVID-19 infection among relatives and family members, who never visited the wet animal market at Wuhan (Carlos et al., 2020; Wu et al., 2020). Hence, one on one transmission occurred most importantly at primary level via personal contact or droplets spread because of coughing and sneezing by an infected person. In a miniature investigation conducted on pregnant females in their third trimester who were tested positive of COVID-19 infection, there was no proof of its transmission from mother to child. Despite of this all-pregnant females underwent cesarean sections. Hence, it remained a mystery that Coronavirus can be contracted via vaginal birth directly. This is essentially important because pregnant females are more liable to the catch severe pneumonia as contagious infection (H. Chen et al., 2020). When it comes the host cell invasion by COVID-19, it binds to the receptors expressed by host cell that is later followed by the fusion with the cell membrane. Earlier, it was questioned that why Coronavirus always targets the lung's epithelial cells as its primary target. Although, it has been particularly reported that man-to-man spread of SARS-CoV takes place by the binding between the receptor-binding ability of virus spikes combine with the cellular receptor which has been subjected as angiotensin-that is converting enzyme 2 (ACE2) receptor (Jaimes et al., 2020; Wan et al., 2020). It is very eminent that the genomic sequence of the receptor-binding domain of COVID-19 spikes has been found to be corresponding to of SARS-CoV. Data obtained by analysis and examination revealed and suggests that entry inside the host cells is most likely via the ACE2 receptor (Wan et al., 2020).

5. Phylogenetic analysis

After several studies and research COVID-19 has been categorized specially as a β CoV of group 2B by the World Health Organization (WHO) (Hui et al., 2020).

Overall, ten different genomic sequences the COVID-19 were obtained from 9 different patients showcased 99.98% identity of the sequence (R. Lu et al., 2020). Dealing with same issue at molecular level another research study concluded that 99.8-99.9% nucleotide identity that has been isolated from five different patients and finally the sequence result revealed the confirmation of new beta-CoV strain (Ren et al., 2020). The result of the genomic sequence obtained from experimentation of COVID-19 displayed correspondence in its specific identity particularly 50% with MERSCoV (R. Lu et al., 2020; Ren et al., 2020), and about 80% with SARS-CoV that originated among bats (Cui et al., 2019). Such strong evidence that was obtained from the molecular phylogenetic analysis determined that COVID-19 is from the genus beta-coronavirus that also includes SARSCoV that infects wild animals, bats, and humans alike (Zhu et al., 2020). When classified under the sub family of Orthocoronavirinae, COVID-19 exemplify as the seventh member of Coronavirus family tree. The Coronavirus has also been adorned within the subgenus Sarbecovirus (Zhu et al., 2020). COVID-19 has obtained a special status as a new Betacoronavirus that infects humans, this fact is based on reports on phylogenetics, and genome sequence studies concluded that, Coronavirus is particularly peculiar from SARS-CoV. As, it has been always said that COVID-19 has originate from bat, hence, another piece of proof suggesting the same factors that supports the COVID-19 has a bat origin because it consists of the existence of a high degree of homology of the ACE2 receptor from a large diversity of animal species, hence, suspecting these animal species as possible intermediate hosts or animal models for COVID-19 contagious and infectious in nature (Wan et al., 2020). Most particularly such viruses hone a single intact open reading frame on gene 8, eventually that indicates its bat origins clearly. But when it comes to the sequences of amio acids the domain of tentative receptor-binding is very similar to SARS-CoV, pointing that such kind of viruses also uses the same receptor (Ren et al., 2020).

6. Antidotes/ remedy alternatives

The widespread transmission of COVID-19 contagious infection among the individuals made the way to the patients quarantine that were practiced via composition of variety of treatments. Although, currently there is no effective antiviral vaccines for COVID-19 viral infection that can act as a possible therapeutic solution for humans globally. The method in practice is the last resort of using the combination of antiviral drugs of broad spectrum like HIV-protease inhibitor and analogues of Nucleosides that can reduce and diminish the viral infection until unless any solution rises for the treatment of such contagious infection (Lu, 2020). After the critical observation the treatment protocol designed for the effected individual reached only the 75percent patients because of the lack of antiviral drugs. The treatment procedure that involved the oral drug administration twice a day for the time duration of 14 days included the drugs like intravenous administration of 0·25 g ganciclovir, 500 mg ritonavir and 75 mg oseltamivir (N. Chen et al., 2020). On the other hand, additional report stated that drugs belonging to the broad spectrum like chloroquine and remdesivir administered twice a day were found to be highly fruitful in the management of 2019-nCoV infection under the in vitro conditions because such strong antiviral agents have a safe record for human usage. Hence, such a cocktail of these antiviral drugs is being considered a highly effective treatment for COVID-19 infection so far (M. Wang et al., 2020). Moreover, there are several other compounds that are under the development procedure, many of the can be named as the clinical candidate EIDD-2801, this compound has exhibited an effective therapeutic potential against the pandemic and seasonal viral diseases and this whole scenario indicates and predicts the promising potential drug against the contagious infection of COVID-19 (Toots et al., 2019). Medical professionals and scientists are working hard and expecting the development of antiviral drug for the COVID-19 infection and until then their only source of support comes from the reasonable treatment from the broad spectrum of antiviral drugs that includes RNA synthesis inhibitors, Neuraminidase inhibitors, peptide (EK1) and Lopinavir/Ritonavir. But this viral agent has exposed our weakness and need for the development and identification of antiviral and chemotherapeutic drug agents for the effective treatment.

There is a great requirement for the proper development of prevention and protection against the COVID-19 with pre and post exposure scenarios, but there is also a great need to establish itself in animal models to duplicate the severity of infections in humans. Therefore, many different groups of scientists are working hard under current situation to develop a primary model to study COVID-19 that model is nonhuman and primate model of study for the establishment of rapid track of novel therapeutics combined with the testing of such antiviral agents that

be providing a better understanding of host virus interaction in case of COVID-19.

7. Subsequent administrative measures for the outbreak management

Considerable amount of safety measures has been taken in consideration to reduce the individual-to-individual COVI-19 transmission that is essential in breaking the chain of current viral outbreak. Exceptional awareness and attentiveness have been paid for the reduction and protection against the transmission is required against the highly susceptible population that particularly includes elderly people, researchers, and health individuals.

Special recommendations were instructed for healthcare professionals and individuals working in the research laboratories (Jin et al., 2020). Prior death cases of were profound among the senior citizens, because of their weak immune system that provides enough opportunities for a fast progression of COVID-19 viral infection (Li et al., 2020; W. Wang et al., 2020). The public facilities and services were instructed for the sanitization on routine basis. Moreover, contact with contaminated and wet objects were to be considered as dealing with virus, especially in the case of urine and fecal samples that were expected to be potentially serving an alternative route of person-to-person transmission (Assiri et al., 2013; Lee et al., 2003). Major control and prevention measures were adopted by countries like US and China. Travel restriction and screening were implemented to stop the further spread of virus (Carlos et al., 2020). Protocols were designed for the hygiene and sanitation changes for dealing with COVID-19 infections, such actions are meant to be monitored restricting the possibilities of nosocomial infections in combination with other transmission routes. Further, inculcating a lot more information evolution, adaptation and virus spread predicted to have transmitted from possible intermediate animal reservoirs to the humans. There are a considerable number of quarries that should be addressed to create more and more public awareness.

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