

## A Novel Coronavirus (COVID-19) Pandemic: Origin, Clinical Picture, Transmission, Preventive Measures and Present Treatment

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### ABSTRACT

Viral diseases continue to emerge throughout the world and pose severe threats to health. Among the viruses, coronavirus is the leading pathogen of emergent respiratory disease epidemics. SARS-CoV2 is an etiological agent of COVID-19 that gains the attention of the world. This virus reported first in China and then became an epidemic. This new coronavirus originated in bats and transmitted to humans by the still unidentified intermediate source in Wuhan, China in December 2019. This disease transmits by respiratory aspirates, aerosols and air droplets. Recent researches reported that individuals without symptoms or convalescents can transmit the disease. Nosocomial transmission is also responsible for increasing the morbidity rate. The symptoms observed for this disease include mild to high fever, coughing, shortness of breath, myalgia, exhaustion, sputum production and sometimes diarrhea. Considering the severity, COVID-19 is categorized into four levels: mild, moderate, severe and critical. The incubation period reported is 3-7 days to up to 15 days. Currently, only supportive therapies are given to deal with the disease as no treatment is approved yet, however, oxygen therapy is used to deal with severe cases. Preventive measures are considered as the best weapon to contain the disease and isolation is the best option yet. Till date, there is no approved antiviral treatment and no vaccine.

This article review purposes to briefly summarize the recently published researches and progress on origin, clinical picture, transmissions, preventive measures and reported recent treatments of COVID-19 that will help frontline health workers in combating the coronavirus outbreak. This review will also improve the understanding of this pandemic to develop control measures.

**Keywords:** COVID-19, SARS-CoV2, Outbreak, Pandemic, Coronavirus

### INTRODUCTION

The novel coronavirus outbreak is posing threat to the population and healthcare workers all over the world. This respiratory viral infection spread very rapidly as in just few weeks, this virus spread from China to more than 80 countries and became pandemic [1,2]. According to the situation report-130 by WHO, from December 2019 to 29<sup>th</sup> May 2020, about 5,701,337 cases have been reported worldwide and the highest cases are reported in the USA followed by Brazil, Russia, Spain and in the UK. In addition to this, a total of 357,688 patients lost their lives. Furthermore, the new cases are reporting every day [3].

This coronavirus also caused destruction in the past and became the reason for two pandemics in the last two decades that are SARS “Severe Acute Respiratory Syndrome” and MERS “Middle East Respiratory Syndrome” [4]. The morbidity and mortality rate were higher as well as these two outbreaks emerged from animal reservoirs [5].

COVID-19 was first identified by the Chinese CDC after the throat swabbing of a coronavirus positive individual. WHO on 7<sup>th</sup> Jan named this virus as 2019-nCoV [6]. The etiological agent of this disease is SARS-CoV2. It is enveloped single-stranded RNA virus having 80 to 120 nm in diameter [7]. Interestingly, just like two other deadly SARS-CoV and MERS-CoV, SARS-CoV-2 is also  $\beta$ -coronavirus. Upon further analyses, it is found that SARS-CoV and SARS-CoV-2 use ACE2 or ‘Angiotensin-Converting Enzyme-2’ as its receptor [8]. Conversely,

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SARS-CoV-2 has greater transmission and infectivity rate than SARS-CoV and MERS-CoV and has a lesser mortality rate [9].

Novel coronaviruses pose a major threat to the health of people globally. This review purposes to briefly summarize the recently published researches and progress on origin, clinical picture, transmissions, preventive measures and reported recent treatments of COVID-19 that will help frontline health workers in combating the coronavirus outbreak. This review will also improve the understanding of this pandemic virus to develop control measures and to help in follow-up researches.

## ORIGIN

Since 8<sup>th</sup> December 2019, a bunch of pneumonia cases of anonymous etiology started to occur in Wuhan, China around Huanan seafood wholesale market, a place in which live animals are being sold [10]. These cases were similar to viral pneumonia. Later examining the respiratory samples, the researchers at CDC confirmed that the etiological agent of these pneumonia cases is new coronavirus [11]. Afterward, WHO entitled this disease as COVID-19 and Taxonomy Committee termed this etiological agent as "Severe Acute Respiratory Syndrome Coronavirus 2" or "SARS-CoV-2" [12,13].

As stated by Fan [1], the results of genome analysis of SARS-CoV-2 sequence showed similarity at recognition rate of bat SARS coronavirus (SARSr-CoV-RaTG13) and SARS-CoV and as 96% and 79.5% respectively that indicates that this virus may be originated from the bat. In addition to this, similar to SARS and MERS, this virus has several potential and intermediate hosts that are posing a great challenge in the containment of this pandemic.

## CLINICAL PICTURE

The symptoms of coronavirus start appearing soon after the incubation period that is reported as 5 days by Li [11] is somewhat alike to SARS-CoV specifically 2 to 10 days [14]. As stated by Wang, Tang and Wei [15], the phase ranging from the beginning of symptoms to the loss of life is 6-41 days and an average of 2 weeks. On the other hand, Hui [10] informed the average incubation period is 3 days, while the average time between starting symptoms to death as again 2 weeks. They further added that this period depends upon the age and immune system of the patient. It is mainly short in patients older than 70 years as the immune system becomes weak.

The symptoms reported by most researchers include fever, cough and difficulty in breathing while some researchers also reported lymphopenia, diarrhea and vomiting [13,16,17]. Huang [12] found that many patients have complained of dyspnoea and the median from starting symptom to the progression of Acute Respiratory Distress Syndrome (ARDS) is just nine days. In addition to this,

other complications like ARDS, arrhythmia, heart injury, secondary infections, compromised kidney function and irregular liver functions are also reported in severe cases [6]. It is also reported that besides lungs, this viral infection can damage different tissues and organs of the body. Xu [18] in their case report presented moderate micro vesicular steatosis in liver tissue.

It can be noted that some of the symptoms of COVID-19 and earlier coronavirus pandemics are similar. But on the other hand, COVID-19 presented a few unique clinical pictures including targeting the lower airways that are evident by symptoms like rhinorrhea, sneezing and sore throat [19]. Chest CT scans of pandemic cases present pneumonia. However, some abnormal features like RNAemia and incidence of grand-glass opacities are also seen [20].

## DIAGNOSIS

CT scan is the diagnostic technique, mainly used to analyze this viral infection. In the study of Guan [9], more than 96% COVID-19 patients that were positive by RT-PCR presented same results on chest CT scans. Similarly, another researcher proved that various examinations of CT scans can be implied to determine the treatment effect [21]. Conversely, by overlapping of novel coronavirus and other viral pneumonia on CT scan can present false-positive results of COVID-19. However, numerous imaging features are also seen in these patients, which includes ground-glass opacity, consolidation, even or abnormal interlobular septal widening, air bronchogram and widening of the nearby pleura [22]. Another investigation by Ai [23] reported that around 90% patients of COVID-19 showed bilateral chest CT results, while the sensitivity of CT scan was found to be 97%. Moreover, chest CT scan results along with symptoms and laboratory tests can help in early diagnosis of COVID-19.

Laboratory analysis presented that more than half of the patients had lymphopenia while some of the patients had thrombocytopenia [9]. Some patients showed higher level of C-reactive proteins and different enzymes like lactate dehydrogenase and creatinine kinase, however, some individuals had raised transaminase, abnormal myocardial enzyme spectrum or higher serum creatinine [12]. Novel coronavirus patients also showed lower CD4+T, CD8+T and oxygenation index whereas raised levels of IL-6 and IL-10 [24].

## TRANSMISSION

Liu [25] define reproduction number ( $R_0$ ) as "the number of secondary infections that patients may have in a susceptible population with no interventions." A researcher presented the reproduction number of SARS-CoV-2 between 2.47 to 2.86 [26]. Whereas Majumder [27] described reproduction number as 2.0 to 3.3 in their research. The assessed reproduction number of SARS-CoV and MERS-CoV was

2.2 to 3.6 and 2.0 to 6.7 respectively [28]. This indicates that COVID-19 has higher transmissibility.

The SARS-CoV-2 viral infection had spread from Wuhan to several countries in just a few months. At present, pathophysiological characteristics of COVID-19 is somehow known, however, the mechanism of spread is still unknown [7]. The present knowledge is obtained from the SARS and MERS that it is transmitted among humans through respiratory droplets [19,28].

### SOURCE OF TRANSMISSION

Based on the reporting of initial cases from Wuhan's live animal market as well as increased cases of novel coronavirus in the city, it is proposed that this viral infection is from the zoonotic origin. Banerjee [29] found that bats are the reservoir of several coronaviruses like SARS-CoV and MERS-CoV-like viruses. For that reason, bats are believed to be the host of SARS-CoV-2, whereas pangolins and snakes are supposed as the intermediate hosts. Zhou [30] sequenced the genome of bat and COVID-19 and presented that 96.2% of the overall genome sequences were identical and hence share the same ancestors. Therefore, bats are considered as the source of SARS-CoV-2. In addition to this, Xu [31] isolated SARS-CoV-2 from pangolins and from infecting humans and used several molecular techniques and electron microscopy and showed 99% similarity between them revealing that pangolins are the intermediate host of COVID-19 virus. Another research by Ji [32] suggested that COVID-19 is possibly caused by snakes, but Zhang [33] proved that snakes are not the host of SARS-CoV-2.

### ROUTE OF TRANSMISSION

Interpersonal transmission merely occurs by direct contact or via respiratory droplets that are spread by the cough or sneeze of SARS-CoV-2 infected individual. These two routes are the most common modes for transmission of the virus while aerosols can be another important route. Besides this, SARS-CoV-2 is also found in saliva, stool, and urine samples [26]. Furthermore, a report reported that the digestive tract might be a route of SARS-CoV-2 infection [34]. Xiao [35] also detected RNA of SARS-CoV-2 in gastrointestinal tissue in COVID-19 patients. SARS-CoV-2 is also found in fecal swabs and blood [6]. Another researcher found this virus in tears and eye secretion of COVID-19 cases showing the probability of several routes of transmission [36]. However, the transmission of the virus from mother to baby through the placenta is still under investigation.

### SUSCEPTIBLE POPULATION

An investigation reported that people between 30 to 79 years are infected most with novel coronavirus with the average age of 47 years. While the ratio of people with 80 years or more for this disease is very less [4]. In addition to this, females had relatively less ratio. Another researcher noted

that the ratio of male patients is higher than the females among 99 COVID-19 positive patients [6]. Interestingly, it is found that MERS-CoV and SARS-CoV infected males most while the ratio of infected females was less [33]. The reason behind this could be the X chromosome and sex hormones as they play a crucial role in providing resistance to infections [34]. Wang, Tang and Wei [15] reported that people with older age are more susceptible to COVID-19 and the infected individuals who died most had the pre-existing respiratory disease or a history of surgery. The finding of this research supports the research of Channappanavar [37] and Jaillon, Berthenet and Garlanda [38] that stated that coronavirus infects older males most having comorbidities. Therefore, this indicates that males are who are elder and also to those who have underlying chronic health conditions like diabetes, hypertension, and cardiac diseases are at great risk. Furthermore, cancer patients are also reported to be more susceptible to COVID-19 [39].

### TREATMENT

As a result of the rapid interpersonal transmission of this viral infection, the patients are kept in isolation for the treatment. Till date, there is no specific treatment option is approved by the FDA against this viral infection. The only option to treat COVID-19 patients is to use broad-spectrum antiviral drugs and to provide supportive therapy. Present therapies primarily focus on symptomatic and respiratory sustenance [2,10].

### ANTIVIRAL MEDICINES

Currently, the treatment option for COVID-19 patients is based upon relieving symptoms. Antipyretic therapy is given for fever and for that paracetamol is given to patients. For producing expectorants in non-productive cough, guaifenesin is being suggested by doctors [15]. Patients with severe cases may face respiratory distress or hypoxemia. These patients are immediately administered supportive oxygen therapy.

Remdesivir is reported by several researchers as a favorable antiviral drug against different RNA viruses [35]. Moreover, chloroquine poses immunomodulatory activity and has activity against SARS-CoV-2 in vitro as stated by Chen [6]. Gao, Tian and Yang [40] also supported chloroquine as it showed positive results in the COVID-19 patients. Numerous experimental trials to determine the effectivity of Remdesivir is still going on whereas the efficacy of Remdesivir is unclear currently. However, a combination of remdesivir and chloroquine is proved effective to prevent the growth of virus *in vitro* [34].

Arbidol is too under investigation. It showed positive effects on SARS-CoV; therefore, it is suggested that it can be a possible drug to treat COVID-19 patients [41]. Another study reported that as compared to Kaletra, Arbidol showed better therapeutic effects and can be used against SARS-CoV-2. Furthermore, remdesivir, lopinavir/ritonavir,

nucleoside analogs and neuraminidase inhibitors gain major importance in the investigation. As reported by Jin [42], the antineoplastic drug, carmofur, is under investigation too as it inhibited SARS-CoV-2 protease ( $M^{pro}$ ). This drug inhibits the replication of the virus and could be an effective compound for treating COVID-19 cases.

### CHINESE MEDICINES

Chinese medicines are also important to treat COVID-19 cases. Several traditional Chinese medicines like ShuFeng JieDu or Lianhua Qingwen are developed by the researchers to test for COVID-19. The research reported that Shuanghuanglian oral liquid can inhibit this viral infection [43]. Another study reported that baicalin, chlorogenic acid and forsythine when added to Shuanghuanglian oral liquid, showed effectivity on certain viruses as well as bacteria [44].

### IMMUNOENHANCEMENT THERAPIES

Immunity plays a very important role in combating COVID-19. Boosting the immune system can protect from the SARS-CoV-2 pandemic. Interferons are responsible for inducing an immune response and by inhibiting viral infections. Previously, synthetic interferon-alpha showed effectivity against the SARS-CoV pandemic. According to Mustafa, Balkhy and Gabere [45], interferon showed activity against MERS-CoV by inhibiting the replication of the virus.

Administration of intravenous (IV) immunoglobulin can be the safest immunomodulator for providing lasting effects that can also restrict pro-inflammatory cytokines production and can enhance the anti-inflammatory mediator production [46]. Thymosin alpha-1 (Ta1) also acted as an immunity enhancer in SARS cases that help to efficiently control the disease. However, due to the effectivity of these two immune enhancers, they can be administered for treating COVID-19 cases [45].

### CONVALESCENT PLASMA THERAPIES

Convalescent plasma therapy can be an efficient treatment to ease disease when no vaccine or drug is available. In one study, this therapy is proved efficient more as compared to high dose of hormonal shocks in SARS cases that reduce death rate and shortened hospital stay [47]. Another study reported that when patients with the H1N1 influenza pandemic were given convalescent plasma therapy, they pose a significantly lower morbidity rate [48].

Conversely, most recovered individuals from COVID-19 can produce antibodies against the COVID-19 that can prevent from reinfection [49]. The plasma of these recovered patients can be used as convalescent plasma therapy by collecting plasma globulins. During the viral infection, the viral load peaks in the initial week so in this period, convalescent plasma therapy can effectively clear out the viral load. Therefore, this therapy can be used as a therapeutic option [50,51].

### BLOOD PURIFICATION

Currently, blood purification is adopted for treating severe COVID-19 cases. As ACE2 express more in the kidney than lungs, therefore, the kidney can become the target of COVID-19. Frequent blood purification can ease the kidney load as well as can stimulate the recovery of kidney function [52]. Moreover, the imbalance of pro-inflammatory and anti-inflammatory factors leads to the destruction of the immune system. Thus, this technology can eliminate inflammatory factors and cytokine storms, as well as by correcting imbalances of electrolytes and can retain acid-base balance. As a result, the symptoms can be eased and blood oxygen saturation can be improved. [53].

### PREVENTIVE MEASURES

As the transmission rate of this viral infection is very high, therefore, it is needed to adopt effective preventive measures to control the spread of this disease. As till date, no effective treatment and vaccine are available, therefore, it is needed to diagnose the disease at the early stage and separate the patient so the transmission is reduced. Individuals following protective measures can efficiently prevent COVID-19. These preventive measures as indicated by CDC and WHO include self-hygiene, wearing medical masks, avoiding contact with infected individuals. Basic hand hygiene measures are proved effective in combating COVID-19 [26]. Additional measures are taken by the countries including countrywide lockdowns, avoiding social gatherings and restriction in traveling [4].

### VACCINES

Currently, there is no approved vaccine that is effective in preventing COVID-19. Several researches are being undertaken to test vaccines. Few vaccines are made by researchers that are under trial.

Bacillus Calmette-Guerin or BCG vaccine is reported by Miller [54] to provide protection from numerous respiratory infections. These researchers indicated that countries with BCG vaccination policy are affected less than the countries without the BCG policies. Countries without BCG policy (USA and Italy) is severely affected [55]. Moreover, it is also found that countries like Iran who started the BCG policy in the late 90s showed a high mortality rate. Therefore, the link between the BCG vaccine and novel coronavirus needs to be investigated and the BCG vaccine can be effective for vaccination against COVID-19 [56].

An mRNA based recombinant protein from SARS-CoV strain Urbani (AY278741) was inoculated to animal models that produced antibodies and immunity against SARS-CoV. This vaccine was developed for COVID-19 and is under trial and thought to provide immunity against SARS-CoV-2 [57]. Another vaccine, INO-4800 DNA-based will also start human testing [19].

## SUPPLEMENTS

Vitamin C has the ability to prevent the proneness to lower respiratory tract infections (LRTIs). Similarly, COVID-19 can cause LRTIs. For that reason, an adequate dose of vitamin C supplementations can help in preventing SARS-CoV-2 [58]. Likewise, the decreased level of vitamin D and E can lead to bovine coronavirus infections. Therefore, it is suggested that vitamin D and E supplementations can boost immunity against COVID-19 [59,60].

## CONCLUSION

The SARS-CoV-2 outbreak is posing a severe threat to the health worldwide. The new cases continued to rise worldwide as the transmission rate of this disease is very high. This disease is very similar to two other pandemics SARS-CoV and MERS. It is reported by several researchers that this virus is originated in bats. To date, there is no approved treatment and vaccine while researches are undertaken to develop vaccine and treatment. Effective preventive measures can be taken to prevent this disease.

Currently, it is necessary to control the transmission of COVID-19 for the containment of disease-19. Researchers are working exclusively on treatment and vaccine development.

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