



Bird's Eye View on the Diagnosis, Treatment, & Prevention of the COVID-19 Outbreak

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ABSTRACT

In December 2019, an outbreak of a new infectious disease occurred in Wuhan in the Hubei Province, China and spread across other Asian and non-Asian countries. The COVID-19 virus was known earlier as 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On February 12, 2020, the World Health Organization (WHO) officially named the disease caused by the novel coronavirus as Coronavirus Disease 2019 (COVID-19). Meanwhile, several independent research groups have identified that COVID-19 has a 79% genome sequence identity with SARS-CoV, the virus which caused a major outbreak in 2002–2003 when compared to MERS CoV. Even though some promising results have been achieved but Clinical studies of these candidate drugs need to be confirmed their safety and efficacy in the treatment of COVID-19. Till then the spread may be controlled only by following the strict quarantine protocols and preventive measures as there is no effective drug available for the treatment at this moment. This article gives a bird's eye view about the current knowledge on the diagnosis, treatment, & prevention of the COVID-19 outbreak. Readers should renovate themselves regularly as the information about the virus is developing gradually at a greater rate.

Keywords: COVID-19, Diagnosis, Treatment, Prevention

1 Introduction

The epidemic of unknown acute respiratory tract infection (COVID-19) broke out first in seafood market, Wuhan, China, since 12 December 2019 and received worldwide attention. On 11 March 2020, the World Health Organization (WHO) classified the outbreak as a pandemic. This new virus was unknown before the outbreak began in Wuhan, China [1]. Interestingly some confirmed COVID-19 positive patients did not visit the suspected market [2]. This indicates that human-to-human transmission was occurring. On 30 January 2020, World Health Organization (WHO) officially declared the outbreak as a public health emergency of international concern [3]. Based on phylogeny, taxonomy and established practice, the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses designated this virus as a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) finally on February 11, 2020 [4]. SARS-COV, MERS-COV were the first and second epidemic corona viruses which emerged in 2002 and 2012 respectively. Like SARS-COV, MERS-COV also started with a patient suffering from pneumonia. SARS-CoV and novel corona virus causes severe respiratory illness in humans and animals than MERS-CoV. SARS, MERS and Novel Corona virus are members of the family Coronaviridae, because all of these show influence on respiratory tract. SARS-COV spreads from a bat to civet cats and then to human. MERS-

CoV originated from a bat via camel to a human [5]. Several studies suggested that bat may be the potential reservoir of SARS-CoV-2.

Based on the WHO report, no specific association with an animal is confirmed yet for COVID-19. 229E, OC43, NL63, HKU1, SARS-CoV, MERS-CoV and SARS-CoV-2 are the seven coronavirus species that are known to cause diseases in humans currently. COVID-19 is the seventh corona virus [6]. Among them, 229E, OC43, NL63 and HKU1 only cause mild symptoms. Severe illness can be caused by the remaining three viruses, namely SARS-CoV, MERS-CoV and SARS-CoV-2 [7]. SARS-CoV, and COVID-19 uses the same receptor, angiotensin-converting enzyme 2 (ACE2) [8]. The nucleocapsid (N) protein of novel corona virus has nearly 90% amino acid sequence identity with SARS-CoV. Corona viruses are enclosed +ve sense RNA viruses ranging from 60 nm to 140 nm in diameter. The treatment which now providing are the medications that are used for normally treating the cold, cough, fever, body pains, throat pain. Several viruses will attack our body daily but we are defending them with our immunity, otherwise humans can't live and this leads to epidemic when the immunity level is low. It is clear now that SARS-CoV-2 can be transmitted by human-to-human through droplets [9], contact and fomites. However, compared to SARS-CoV, MERS-CoV has shown for more limited human-human transmission. As COVID-19 an emerging virus, control measurements and effective prevention should be needed as there is no effective drug or vaccine approved for the treatment of SARS-CoV-2 infection yet. So, early detection, diagnosis, treatment, and quarantine in order to block human-to-human transmission should be necessary.

2 Current knowledge on the diagnosis, treatment, & prevention of the COVID-19 outbreak

2.1 Diagnosis

Firstly, COVID-19 genome sequencing studied in china and that lead to the development of the diagnosis kits. It takes more time to prepare the drug even after analyzing the sequence. Virus is not visible with our naked eye. Generally, virus infect our upper nasal cavity. The virus has their own genetic material as every single living organism have. The genetic material of virus is positive single stranded RNA. Confirmed patients are classified into mild, moderate, severe, and critical types according to the clinical manifestations [10]. Nucleic acid detection in the nasal and throat swab sampling or other respiratory tract samplings by real-time PCR and the rapid blood test are the clinical diagnosis methods of COVID-19 so far.

Molecular approaches are based on Real Time-PCR (RT-PCR) or Northern blot hybridization targeting specific COVID-19 genes [11]. Nasal secretions, blood, sputum, and bronchoalveolar lavage (BAL) samples are subjected to specific serological and molecular tests for laboratory diagnosis to detects specific COVID-19 proteins. Samples are collected from suspected patient [12]. The sample which we used is nasopharyngeal or oropharyngeal (NP/OP) swab for RT PCR technique and blood sample by using needle prick for blood test kit. NP/OP is a medical term for nose swab. Neither of the test will give standalone result because RT PCR test is not a exactly diagnostic test. It is the kit for process of search purpose. We are using it as a diagnostic purpose because we don't have other option but both kits provide 98% almost accurate.

The blood test kit consists of five columns i.e., buffer solution, sample, IgM, IgG, and control. Buffer solution is a liquid solution which will take your blood in forward direction to reach the control column. Body can produce both types of antibody IgG and IgM. IgM is known as primary immune response antibody. This is the antibody that our body normally produces for the first time when we infected with bacteria or virus. IgG produces for the second time when we infected with same bacteria or virus. If the body have more IgG then it indicating that the body is infected with virus couple of times. If we have more IgM and no IgG then the body is infected with the virus for first time [13]. Remember, there must be a line in control section. It indicating that blood is reached till the end of the control column of the kit. If there

is no line in control column then it means that the kit is faulty or the buffer solution may be less. If there is a line in IgG, and IgM indicating that affected with virus couple of times and for the first time respectively. If there is no line in IgG and IgM then the person is not affected with the virus that is -ve result [14]. In laboratory examination results, the lymphocyte counts and interleukin-6, interleukin-10, tumor necrosis factor- α (TNF- α), the neutrophil count continued to decrease and increase respectively indicating the immune status in severe patients. The data showed that ICU patients had higher plasma levels of Interleukin (IL)-2, IL-7, IL-10, 10 kD interferon gamma-induced protein (IP-10), macrophage inflammatory protein 1- α (MIP-1 α), granulocyte colony-stimulating factor (GCSF), monocyte chemoattractant protein-1 (MCP-1), and TNF- α [15].

2.2 Treatment

To inhibit the recently emerged COVID-19, a combination of chloroquine which functions at both viral entry and post-entry stages and remdesivir which does only at post-entry stage were proven to effectively [16]. Remdesivir shows broad spectrum antiviral activity effectively against several RNA viruses including SARS-CoV and MERS-CoV. Remdesivir is another potential drug which is developed for Ebola previously has been now reported to treat the first US case of COVID-19 successfully as it was provided intravenously to the patient without any adverse events observed on the day 7 and is undoubtedly excellent news [7]. Chloroquine is a drug used for an autoimmune disease and malarial infection for many years and shows great potential to treat COVID-19. This drug is widely available and low cost. Chloroquine effective concentration was 0.77 μ M and remdesivir effective concentration was 1.13 μ M. Encouragingly, chloroquine and remdesivir are under phase 3 clinical trial currently [7]. Recent publications have brought attention that chloroquine phosphate is higher-ranking to the treatment in inhibiting the worse situation of pneumonia, promoting a virus negative conversion, improving lung imaging findings, and shortening the disease course [17, 18].

Recently, hydroxychloroquine is broadly used in autoimmune diseases such as rheumatoid arthritis and lupus. The side-effects are generally mild and transitory for chloroquine and hydroxychloroquine. So, they are considered to be safe but self-treatment is not recommended [19]. Favipiravir had significantly fewer adverse effects than the lopinavir/ritonavir group as it shows more potent antiviral action than those. Patients treated with the combination of ribavirin along with lopinavir-ritonavir had better outcome [20]. Ritonavir and lopinavir are the protease inhibitors which are used to treat infection with human immunodeficiency virus (HIV) showing the effective results of treating the outbreak COVID-19. Several drugs such as chloroquine, darunavir, remdesivir, hydroxychloroquine, and favipiravir are currently undergoing clinical studies for to treat the coronavirus disease 2019 (COVID-19) in China. Studies have also revealed that some other drugs may have potential efficacy in treating the outbreak COVID-19. One is darunavir and other is Favipiravir. The ribonucleic acid in corona is same as which is present in AIDS. Darunavir is a second-generation of HIV-1 protease inhibitor and Favipiravir is the Japanese anti-flu drug (brand name Avigan) is a RNA-dependent RNA polymerase (RdRp) inhibitor [20]. Both were approved for treatment of COVID-19 in China.

On February 14, a clinical trial on favipiravir for the treatment of this outbreak initiated by the National Clinical Research Center for Infectious Diseases at the Third People's Hospital of Shenzhen achieved promising results and on February 4, 2020, researchers in China announced that darunavir inhibited novel corona virus infection in china [21]. The commonly used systemic corticosteroid treatments and antiviral drugs including Peramivir, oseltamivir, zanamivir which are the neuraminidase inhibitors, acyclovir, ribavirin, ganciclovir for influenza virus, are not recommended for the treatment of COVID-19 [22]. Scientists are trying hard to find suitable drugs to treat this disease. Even though some promising results

have been achieved but Clinical studies of these candidate drugs need to be confirmed their safety and efficacy in the treatment of COVID-19 as there are no verified antivirals to this outbreak at present. However, more evidence is needed before drawing conclusions as no data has been provided yet officially. Fluids and oxygen ventilators are the supportive care for treatment. The antiviral plasma is the enemy for the novel coronavirus. When there is no vaccine and specific medicine, then antiviral plasma becomes the treatment called convalescent plasma. But the plasma treatment cannot be used as a mono-theory. It has to be combined with clinical manifestation while applying other antiviral and maintenance therapy at the same time. In late February, 91 among 197 patients who were treated with plasma and monitored for a 48-hour period showed significant improvement in their condition. So the patients who recovered from corona recently can donate to other patients to save [23]. Zhang Dingyu, the director of Wuhan Jinyintan Hospital has said that recovered patients have to be between 18-55 years old and have recovered for at least 14 days before can donate their blood. If the person is in good health, the age range could be extended to 60 years old. Before the donation, he or she has to undergo screening tests to make sure the blood is free from the novel coronavirus, HIV, syphilis, hepatitis B and C. Uncertain reactions and allergic reactions which can lead to acute respiratory disease syndrome and multiple organ failure are the plasma treatment side effects. This is the biggest risk with the treatment for severe ill patients. Plasma treatment has also been used in the fight against SARS, H1N1 (SWINE FLU) [24], H5N1 (BIRD FLU), Ebola. During SARS-CoV, patients who were treated with plasma had more favourable prognosis. And fewer side effects than those treated with antiviral drugs.

2.3 Prevention

WHO situation reports indicate that COVID-19 is spreading globally in a rapid manner as of 12 February 2020. Infection is acquired either by inhalation of these droplets or touching surfaces contaminated by them and then touching the nose, mouth and eyes [25]. The person with mild illness should ensure adequate isolation having ventilation at home with sunlight, wear surgical mask [26] and maintain hand hygiene for every 15-20 mins, hydration, nutrition and controlling fever and cough. Coughing in sleeve/tissue rather than hands should be practiced [9]. People with fever, cold, and difficulty in breathing should seek medical attention and who are tested positive should be isolated, monitored and followed up their contacts. Some of the people will be recovered from the disease without needing special treatment because of their immunity. Other non-specific symptoms include fever, cold, cough, myalgia, dyspnea with or without diarrhea and nausea a few days prior to fever [27]. Small number of patients can have headache or hemoptysis. Severe illness rapidly develops to pneumonia, acute respiratory distress syndrome (ARDS), multiple organ failure, arrhythmia, shock, and secondary infection, even deaths [28]. Mechanical ventilation or assisted ventilation in Intensive Care Unit (ICU) with quarantine facilities may be required at this stage. Those with underlying medical problems like high blood pressure, diabetes, heart problem and older people are more likely to develop severe illness.

More attention and care should be needed to a newborn child and the elderly due to their immature or weak immune system. COVID-19 in children show milder cases than adults [29]. The use of mask by healthy people is currently not recommended by WHO but wearing mask in crowded places and large gatherings is necessary. Transplacental transmission from pregnant women to their fetus has not been described as per current information. The 11 million population of Wuhan from 23rd January, was placed under lock down with restrictions of entry and exit from the region. This lock down was extended to other countries as the number of cases started increasing exponentially [12]. Big problem of novel corona is the virus will mature only after entering into human body then only the symptoms of the disease will get to know. There is also a scope of spreading to others during the incubation period. For COVID-19 testing,

different countries including India put in screening mechanisms in airport to detect the people who have symptoms returning from China and then placed them in isolation [30]. It is important to note that the number of cases has reduced in China lately and increased exponentially in other countries including USA, Germany, Italy and Iran. Vaccine is very necessary for this type of viruses because the doctors who are treating the diseased people will have the chance of getting. Minimum period for development of vaccine is 1 year. Scientists are trying to develop drugs for this outbreak by conducting drug trials on animals all over the world.

3 Current outbreak status

As of May 2, 2020, a total of 3267184 confirmed cases globally, with 229971 deaths (7.03%) had been reported by WHO (Fig. 1). Among those, USA is the first country which reported 1067127 total confirmed cases and 57406 total deaths till date. COVID-19 is moving like a wave which causing severe shock to social, economic and political aspects. Every day, a large number of people are losing their jobs and deduction in income parallelly shops, restaurants, theatres are closing world wide as dozens of the world's greatest cities are abandoned as people stay indoors by government order.

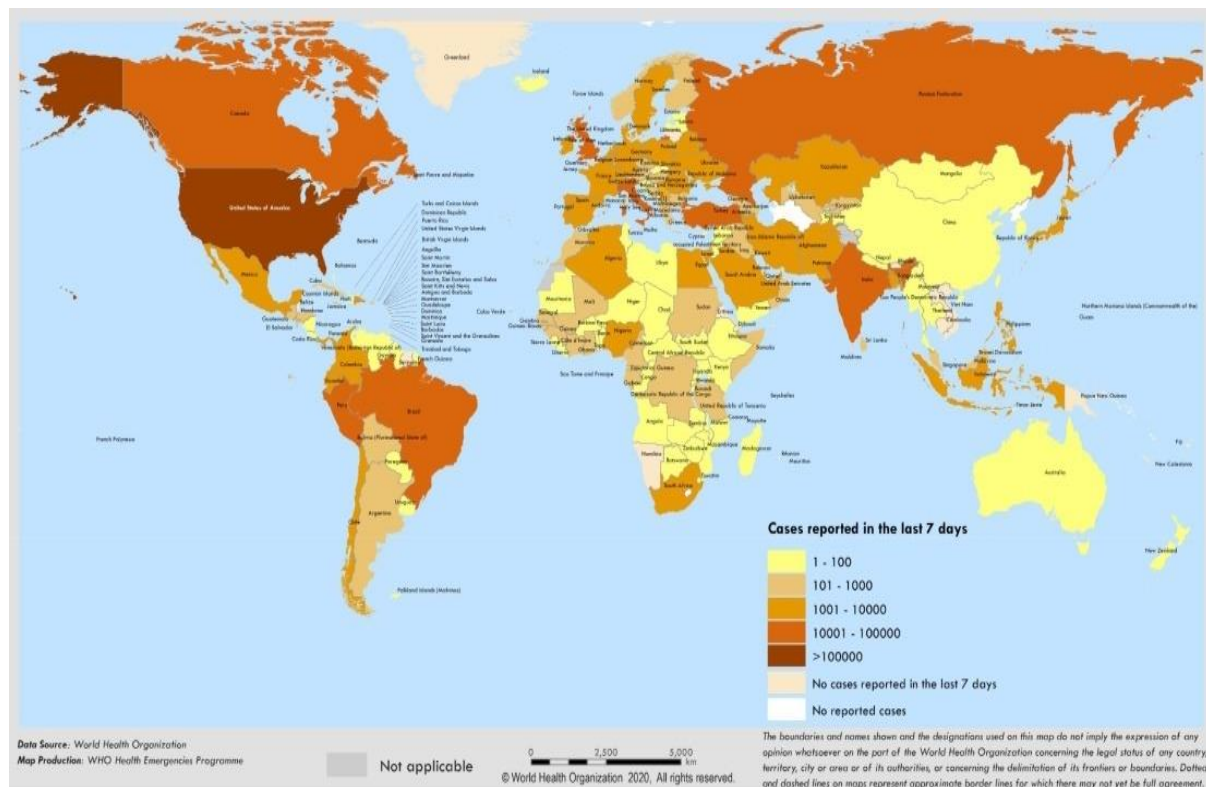


Figure 1: WHO Situation report dated 2 May 2020. (Adapted from WHO).

4 Conclusion

Pathogen identification, genome publication, diagnostics development within weeks of the initial case detection of COVID-19 were characterized by rapid and effective scientific response. COVID-19 is an emerging pathogen which spreads quickly and ranges from mild symptoms to severe pneumonia and even deaths. COVID-19 spread may be controlled only by following the strict quarantine protocols to maintain social distancing as there is no effective drug available for the treatment at this moment. In addition, effective preventive measures must be implemented to control it and on the development of vaccine and antiviral drugs. Meanwhile, great effort should be made to prevent the outbreak of COVID-19 and other novel viruses in future, legislation should take necessary steps in order to prohibit the trade of wild animals,

and the potential intermediate host(s) of various viruses. This novel virus is also becoming a wider threat to public health, global economics, and posing governance challenges. All global government authorities have launched psychological intervention, and I sincerely hope that people from the whole world should overcome the epidemic as fast as possible.

5 Conflict of Interests

The authors declared that no conflict of interest exist regarding this publication.

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