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COVID-19 outbreak, prevention and treatment: A Review

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Abstract

In December, 2019 a cluster of pneumonia cases of unknown etiology occurred in Wuhan, Hubei Province, China, and was confirmed to be caused by a new coronavirus. This was named as coronavirus disease 2019 (COVID-19) and the World Health Organization declared it an emerging pandemic in March 2020. The virus responsible for the disease was named as SARS-CoV-2. The disease is diagnosed by fever, sore throat, body ache, shortness of breath, cough and further complicated by pneumonia and in some cases leading to sever acute respiratory distress with potential damage to vital organs such as lung, heart, liver, and kidney. It is found to be spread by human-to-human transmission through droplets or direct contact, and the incubation period of the disease has been estimated from 5 to14 days. By August 07, 2020, SARS-CoV-2 had led to 19111123 confirmed cases, and 715163 dead of COVID-19 in more than 200 countries. To combat COVID-19, a number of repurposed antiviral drugs such as chloroquine, hydroxychloroquine, remdesivir,ravipiravir and some anti-inflammatory corticosteroid likedexamethasone, etc. have been applied. It is claimed that some of these drugs are able to restrict further spread of the virus, whereas some can only provide relief from severe inflammation, and thereby lead to better recovery from the disease. Based on the current published evidence, we systematically summarize the origin, symptoms, transmission, treatment and prevention of knowledge associated to COVID-19 in the hope of helping the public better understand and combat the disease and also to provide reference for future studies.

Keywords: COVID-19; Transmission; Symptoms; Prevention; Treatment; Vaccines

1 Introduction

A novel single strand RNA coronavirus strain disease, COVID-19 or severe acute respiratory syndrome coronavirus 2 (SARSCoV-2), emerged in Wuhan, China (Huang et al., 2020; Li et al., 2020a). It has rapidly spread globally (Holshue et al., 2020; Lupia et al., 2020; Wang et al., 2020a). WHO has declared it as a pandemic in March 2020 (Liu et al., 2020a). On January 31, WHO declared the pandemic as a global health emergency (Chang, Yan, & Wang, 2020; WHO, 2020a). COVID-19 is a highly infectious disease, and it has been found to be transmitted through person-to-person (Fuk-Woo et al., 2020; Nishiura et al., 2020). It is well established that fever along with respiratory symptoms such as cough and dyspnoea are the common symptoms of COVID-19 that are very much similar to the diseases caused by the other two highly pathogenic coronaviruses: Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in 2003 and Middle East Respiratory Syndrome Coronavirus (MERS-Cov) in 2012 (Chan et al., 2020a; Hamming et al., 2004; Memish et al., 2014a; Su et al., 2016). In 2002-2003, more than 8000 people were affected and 774 out of them had died from SARS coronavirus, whereas in 2012, there were 2494 confirmed cases and 858 deaths from MERS coronavirus according to the WHO (WHO, 2004a; WHO, 2013). The present corona virus is expected to infect a large proportion of the world's population. The epidemic has been spreading to more than 200 countries, with 19111123 confirmed cases and 715163 deaths, as reported by the World Health Organization (WHO) on 07 August (WHO, 2020b). All of these emerging infectious diseases leading to a global spread were caused by β-corona viruses. The emer-

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gency faced by the scientific community in addressing the pandemic provides the justification for the use of drugs that have not yet been approved and with still preliminary scientific evidence. So far, the treatment of this disease have been a combination of certain repurposed antiviral drugs and supportive care, and to some extent some anti-inflammatory steroids. The mushroom, plant and other polysaccharides draw a lot of attention due to their several difficult biological properties, such as, anticancer, antiviral, immunomodulating, antimicrobial, anticoagulant, antidiabetic, antioxidant, and antitumor activities (Maity et al., 2015; Wasser, & Weis, 1999; Wasser, 2002; Zou et al., 2014). This report reviews the genetic structure, infection source, symptoms, transmission, treatment and ongoing research for the quicker detection and prevention of COVID-19, so that it can provide references for follow-up research, prevention and treatment, and may help readers to have the latest understanding of this new infectious disease.

2 Origin of SARS-CoV-2

The source of SARS-CoV-2 is quite complex. COVID-19 is the third known zoonotic coronavirus disease after SARS and MERS (Chan et al., 2020b; Ithete et al., 2013; Li et al., 2005; Paden et al., 2018; Shi, & Hu, 2008). Emerging novel coronavirus shows 88% identity to the sequence of two bat-derived SARS-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, and about 50% identity to the sequence of MERS coronavirus (Lu et al., 2020). The novel coronavirus was then named "SARS-CoV-2" by the International Virus Classification Commission. The origin of the virus is not clearly known, but initially diagnosed patients were associated to the Huanan Seafood Wholesale Market, Hubei Province, China where wild animals are sold (Guo et al., 2020a; Li et al., 2020a; Wang et al., 2020b). Thereafter, it continued to emerge all over the world through human to human viral droplet transmission. The probability of a mammal and bird intermediate host for SARS-CoV-2 has been suggested by Bassetti et al (2020) and Zhang et al (2020a). A study by Ji et al (2020a) showed that snakes are the most likely wildlife repository for the SARS-CoV-2. Snakes often hunt bats in the wild. As per a recent study pangolinhave been suspected to be an intermediate host of the virus (C, 2020; Han, 2020; Lam, et al. 2020; WHO, 2020c; Wong, et al. 2020; Xiao, et al. 2020a; Zhang, Wu, & Zhang, 2020). Benvenuto et al (2020), Chan et al (2020b), Hui et al (2020), Perlman (2020), and Yang et al (2020a) confirmed that SARS-CoV-2 has very intimate relationship with bat. Recently, Zhou et al (2020a) and Wu et al (2020) found that the sequence homology between SARS-CoV-2 and SARS-CoV was 79.5% and also found that the SARS-CoV-2 had a bat coronaviruses. So, bats have been considered as the most likely natural reservoir of SARS-CoV-2 as suggested by WHO, although the intermediate hosts remain to be determined (WHO, 2020d).

3 Structure of SARS-CoV-2

The name Corona originated from Latin word corona, meaning "crown" or "wreath", and since in the outer surface around the viruses there are crown-like spikes these are named as coronaviruses (Figure 1; Prasad et al., 2020; Sohrabi et al., 2020; Shereen et al., 2020). Coronaviruses belong to the family Coronaviridae (order Nidovirales) and include viruses with a single-strand, positive-sense RNA genome approximately 26–32 kilobases in size (Chen, 2020a; Chen et al., 2020a; Paraskevis et al., 2020; Woo et al., 2010). Its RNA genome consists of 29891 nucleotides, encoding for 9860 amino acids and shares 99.9% sequence identity, suggesting a very recent host shift into humans (Lu et al., 2019; Zhou et al., 2020). The disease arising out of it is known as COVID-19 where 'CO' stands for corona, 'VI' for virus, and 'D' for disease, and 19 indicates the year of its initiation. Formerly, the virus was referred to as '2019

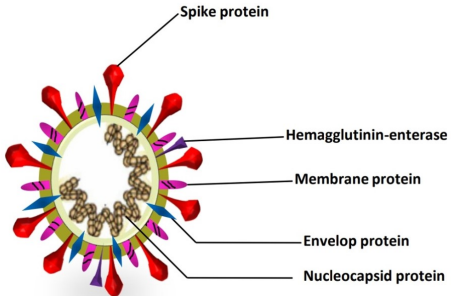

Figure 1: Schematic representation of the structure of SARS-CoV-2.

novel coronavirus' or '2019-nCoV'(Gorbalenya et al., 2020). International Committee on Taxonomy of Viruses (ICTV) named the virus as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The Coronaviridae family contains four genusesnamely α, β, γ and δ (Saminathan et al., 2014; Yin, &Wunderink, 2018). The novel virus is classified as a β-CoV and bears considerable similarity to SARS-

CoV (Chen, Liu, & Guo, 2020; Xu et al., 2020a; Zhu et al., 2020a). Six coronaviruses (HCoV-229E, NL63, MERS-CoV, SARS-CoV, HCoV-OC43 and HCoV-HKU1)) were previously known to cause disease in humans. SARS-CoV-2 therefore is the seventh member of the coronavirus family that infects human beings after SARS-CoV and MERS-CoV (Perlman &Netland 2007; Zhu et al., 2020). The four important structural proteins essential for regulating the function and structure of the virus are envelope protein (E), membrane protein (M), spike protein (S) and the nucleocapsid protein (N)(Schoeman and Fielding, 2019; Walls et al., 2020). The arrangement of nucleocapsid protein (N), envelope protein (E), and membrane protein (M) among betacoronaviruses are different (Lu et al., 2019; Mousavizadeh, &Ghasemi, 2020).The genomes of SARS-CoV-2 and SARS-CoV share more than 79% sequence similarity on average, and their S proteins share 76.47% identity (Xu et al., 2020a; Zhou et al., 2020).

4 Transmission

4.1 Transmission from animal to human

Coronaviruses are zoonotic in nature. They first develop in animals before developing in humans. For passage of the virus from animal to humans, a person has to come into very close contact with an infected animal. Various studies reported that the animal to humantransmission of MERS-Co-V and SARS-C0-Voccurred via direct contact of humans with intermediary host animals like camels,bats, or uncooked meat (Annan et al., 2013; Cui, Li, & Shi, 2019; Huynh et al., 2012; Paden et al., 2018; Woo et al., 2016; Yin and Wunderink, 2018). The intermediate hosts of SARS-CoV-2 are predicted to be the unknown but different reports showed that the source of the virus is Huanan seafood wholesale market in Wuhan city, where live animals are sold, that include frogs, camels, wild rabbits, reptiles, snakes, deer, crocodiles, marmots, Peacocks, swans, pangolins, bats, birds, kangaroos, snails, civet cats, goats, centipedes,cicadesand hedgehogs (Chen et al., 2020b; Ji et al., 2020a; Ji et al., 2020b; Hui et al., 2020; Lu et al., 2020a; Wan et al., 2020; Wu et al., 2020; Zhou et al., 2020).

4.2 Transmission from human to human

Coronaviruses (MERS and SARS) can be spread from person to person through respiratory droplets of infected people (Fuk-Woo et al., 2020; Jennifer et al., 2016; Kang et al., 2017; May et al., 2004). The COVID-19 pandemic has also been driven due to human-to-human transmission, especially during close contact of people (within 1-2m) as well as via respiratory droplets produced when infected persons cough or sneeze (Chan et al., 2020c; Guo et al., 2020b; Ghinai et al., 2020; Huang et al., 2020; Li et al., 2020a; Rothe et al., 2020; WHO, 2020e; Yu et al., 2020; Zhu et al., 2020a). SARS-CoV-2 uses the angiotensin converting enzyme II (ACE2) receptors like

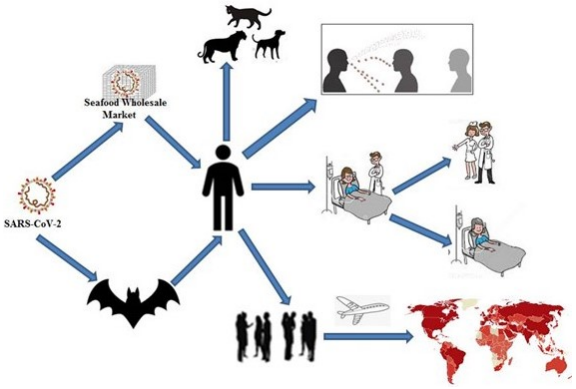

Figure 2: The key reservoirs and mode of transmission of coronaviruses.

its very close analogueSARSCoV (Zhou et al., 2020b). It has been reported that a newborn baby of a COVID-19 infected mother was also found to be COVID positive after 30 hours of birth (CCTV.COM, 2020). This indicate that COVID-19 may transmitfrom mother to child but there is currently no special evidence (Chen, 2020b; Chen et al., 2020c; Schwartz and Graham, 2020; Zhu et al., 2020b). Figure 2 presents the possibility of COVID-19 transmission from respiratory droplets.

4.3 Asymptomatic transmission

Whether or not the asymptomatic carriers transmit the disease is quite controversial (Zange et al., 2020). Different recent studies showed that there is a rapidly increasing incidence of infections by asymptomatic carriers (Bai et al., 2020; Chang et al., 2020; Carlos et al., 2020; Kupferschmidt, 2020). However, we also should attach importance to asymptomatic cases, which may play a critical role in the transmission process (Chan et al., 2020a; Shen et al., 2020a).

4.4 Transmission via infected surfaces and aerosols

It has been reported that COVID-19 might be indirectly transmitted from one susceptible person to an-

other during touching the surface, followed by eyes, nose, or mouth (Figure 2; Lu et al., 2020; Ong et al., 2020; Phan et al., 2020; Riou& Althaus, 2020). Recent studies have shown that SARS-CoV-2 can be transmitted via saliva of infected people (Hoffmann et al., 2020; Peng et al., 2020; Sabino-Silva et al., 2020; To et al., 2020). Experimental results showed that the viability of the coronavirus in aerosol is for about 3 h, on copper surface for about 4 h, on cardboard about 24 h, but up to 72 h on the surfaces of plastic and stainless steel (Van Doremalen et al., 2020a; Van Doremalen et al., 2020b). Fomites may also be a large source of transmission, as SARS-CoV has been found to persist on surfaces up to 96 h and other coronaviruses for up to 9 days (Kramer et al., 2006; Kampf et al., 2020). Moreover, studies indicate that SARS-CoV-2 is transmitted mainly through respiratory droplets rather than through the air (Jin et al., 2020a).

4.5 Transmission through feces

Previous learning on SARS-CoV and MERS-CoV identified their viral RNA in feces (Corman et al., 2016; Leung et al., 2003). A number of recent studies showed that SARS-CoV-2 can spread among people through feces transmission, although this route of transmission is very limited (Gu et al., 2020; Guan et al., 2020a; Holshue et al., 2020; Xiao et al., 2020b; Zhang, Wang, &Xue, 2020).SARS-CoV-2 has been detected in excreta specimens, such as feces and anal/rectal swabs (Bowser, 2020; Gao et al., 2020; Tang et al., 2020a; Wolfel et al., 2020; J. Pan et al., 2020a).That's why maintaining good hygiene and cleanliness after using the toilet and before eating definitely lowers the risk of getting infected from the disease.

4.6 Transmission from human to animal

Recently, there is a patient dog infected from its nasal and oral cavity with a low level of COVID-19 virus (COVID, 2020). This is the first case of human-to-animal transmission that has been confirmed by the World Organization for Animal Health (WOAH). On April 6, 2020, the tiger in New York City's Bronx Zoo of USA was infected by coronavirus, which might be due to transmission of virus from an asymptomatic zookeeper (BBC, 2020; USDA 2020). This topic is still an ongoing study by WOAH. The transmission of SARS-CoV-2 from humans to domestic cats is also reported (AP News, 2020; Halfmann et al., 2020a; Shi et al., 2020).

4.7 Transmission due to environmental factors

Previous reports showed that the combination effects of low humidity, low temperature, surface and ground-waters, lack of sunlight, deficiency of vitamin D are responsible for various diseases (Auffret et al., 2019; Eng et al., 2015; Givens et al., 2016; Gardner et al., 2019; Kuiken et al., 2003; Kokolus et al., 2013; Lin et al., 2006; Leigh et al., 2015; Sims and Kasprzyk-Hordern, 2020). Different studies have shown that temperature is a vital factor in the transmission and survival of coronaviruses (Altamimi, & Ahmed, 2019; Bi et al., 2007; Cai et al., 2007; Casanova et al., 2010; Chan et al., 2011; Guionie et al., 2013; Tan et al., 2005; Van Doremalen et al., 2013). During the early days of its outbreak, it was concluded that the transmission rate and stability of SARS-CoV-2 can be varied with different environmental parameters, i.e., temperature, humidity, sunlight etc. (Huang et al., 2020; Luo et al., 2020a; Moriyama et al., 2020; Ma et al., 2020a; Ong et al., 2020; Tosepu et al., 2020; Wang et al., 2020c; Xie, & Zhu, 2020). It was also oversimplified by the thought that the spread would decrease during summer. However, there is no concrete evidence to say that the virus would die off in summers (Martinez-Alvarez et al., 2020).Also the outbreak of COVID-19 in tropical countries do not even support this concept.

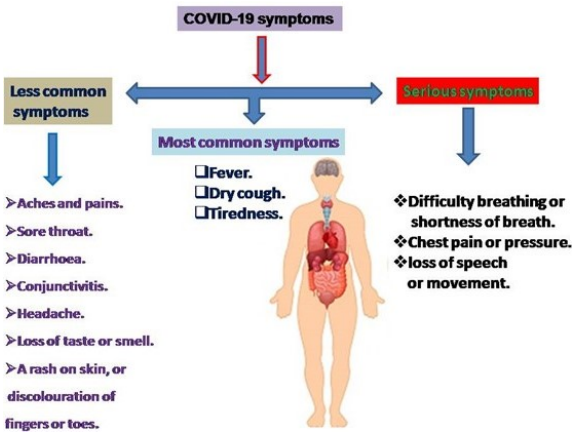

Figure 3: The most common symptoms of COVID-19 according to the WHO.

5 Symptoms

The first symptoms of COVID-19 disease appear after an incubation time of around 5 to 6 days according to the WHO reports (Li et al., 2020b). The episode from the start of COVID-19 symptoms to

death ranged from 6 to 41 days with a median of 14 days (Wang, Tang, & Wei, 2020). COVID-19 affects different people in different ways. Doctors and scientists are still learning new things about the virus every day. The most common symptoms of COVID-19 disease are fever, cough, and fatigue, while other symptoms include pains, nasal congestion, dyspnoea, runny nose, headache, sore throat or diarrhea (Assiri et al., 2013; Carlos et al., 2020; Hopkins, 2020; Iacobucci, 2020; Lee et al., 2003; Lai et al., 2020a; Pan et al., 2020b;Palus, 2020; Ping et al., 2020; Figure 3). In some people, COVID-19 causes more severe symptoms like high fever, severe cough, and shortness of breath, which often indicate pneumonia (Huang et al., 2020). Less common symptoms are gastrointestinal disorder, anosmia, dysgeusia etc. (Cheung et al., 2020; Zhang, & Xu, 2020; Zhou et al., 2020b). The severe symptoms include sepsis and septic shock, multi organ failure, including acute kidney injury and acute cardiac injury (Chen et al., 2020b; WHO, 2020f). Many a people infected with the virus showed no symptoms (Kupferschmidt, 2020). Hu et al (2020a) reported that, the occurrence of symptoms like fever, cough, fatigue, and dyspnea occurred roughly 85.6 %, 65.7 %, 42.4 % and 21.4 % respectively in COVID-19 patients. Children show similar symptoms to adults but generally suffer from mild illness (WHO, 2020; Xia et al., 2020a; Zhou et al., 2020c). Lu et al (2020b) reported that, 41.5% of the children develop illness due to fever whereas other common signs and symptoms are cough and pharyngeal erythema. Common symptoms reported in adults with COVID-19 are fever, dry cough, and fatigue; severe cases have been associated with dyspnoea and bilateral ground-glass opacities on chest CT (Rothan, &Byrareddy, 2020). A study by Zhan, Qin, Xue, and Zhu (2020) showed that the health care workers in China effected by COVID-19 disease suffer from acute respiratory distress syndrome (ARDS) including cardiac injury, septic shock, multiple organ dysfunction syndrome, hypercoagulability, intracardiac thrombus, and bacteremia. Goyal et al (2020) reported that the most common symptoms in New York City, USA were cough (79.4%), fever (77.1%), dyspnea (56.5%), myalgias (23.8%), diarrhea (23.7%), and nausea and vomiting (19.1%). SARS-CoV-2 may also infect the central nervous system (CNS), which might lead to a high incidence of neurological symptoms (Baig et al., 2020; Filatov et al., 2020; Li et al., 2016; Li, Bai, &Hashikawa, 2020; Lau et al., 2004; Mao et al., 2020). In addition to clinical symptoms, SARS-CoV-2 was identifying in the endoscopic specimens of the esophagus, stomach, duodenum and rectum from various patients (Jin et al., 2020b; Lin et al., 2020a). According to WHO, COVID-19 symptoms for pregnant and non pregnant women are almost equal (WHO, 2020). Fan et al (2020) reported that SARS-CoV-2 may directly bind to such ACE2 bearing cells and damage the kidney and testicular tissue of patients.

6 Effect of COVID-19

6.1 COVID-19 and Society

Unlike in the past year history of the century, the entire human civilization has been facing an international public health crisis(Sohrabi et al., 2020). People are being killed, human sufferings are increased, and public lives have been in distresses. But this is not merely a health calamity but is largely associated with economic and socio-political crisisas well(Nicola et al., 2020). COVID-19 has been characterized as a pandemic by the WHO, is attaching societies at their core. Although the outbreak affects all sectors at the people, the effect has been much more damaging to those residing in the most exposed conditions, including economically week section of people, older persons with disabilities and others (Ferneini, 2020). Since the virus is a new one and nobody has any kind of immunity against it, theoretically the entire human population is susceptible to be infected. But as per the reports of transmission and death toll is concerned, aged persons with pre-existing health complications are at a high risk of infection (Ali et al., 2020). Refugees, migrants, or displaced persons are also expected to suffer extremely both from the pandemic and its aftershock (Chakraborty, & Maity, 2020). They might suffer from restricted movement, crunching of employment opportunities, increased xenophobia etc. COVID-19 pandemic is most likely to increase inequity, marginalization, discrimination and worldwide joblessness in the medium and long-term (Kabir, Afzal, Khan, Ahmed, 2020; OECD Interim Economic Assessment, 2 March 2020). Widespread worldwide societal protection system might play a resilient role in defending workers and in reducing the predominance of poverty.

6.2 COVID-19 and Pregnancy

Alfarajet al (2019) and Wong et al (2004) reported that around onethirdof infected pregnant women have diedfrom illness due to SARS-CoV and MERS-CoVepidemics. Pregnant women and their fetuses are exposed to a high risk during contagious COVID-19 outbreaks (Qiao, 2020; Wanget al., 2020f; Zhang et

al., 2020d).Till date, COVID-19 effected cases data in pregnancy are limited(Lei et al., 2020; Liu, Chen, Tang, Guo, 2020;Liuet al., 2020b,c; Wong et al 2020; Zhuet al., 2020b). Chen et al (2020f) reported that good maternal and fetal outcomes of nine pregnant women in a hospital. Yan et al (2020) reported that the general symptoms of 116 pregnant women were fever (59 out of 116) and cough (33 out of 116), and 27out of 116 patients presented without symptoms.Most of the newbornswere not infected with COVID-19. Yang et al (2020d) reported that among 55 pregnant women cases, 13 patients were found COVID-19 positive and also 20 new born babies (from confirmed mother and from normal mother) were tested SARS-CoV-2 negative.

6.3 COVID-19 and Risk Factors

The correct reasons for COVID-19 risk are yet to be recognized.But different studies showed that a maximum percentage of COVID-19 patients are suffering from comorbidities (Guan et al., 2020; Huang et al., 2020; Tang et al., 2020b). Guan et al (2020b) reported that hypertension (14.9%) and diabetes mellitus (7.4%) are the most frequent illness due to COVID-19 outbreak.Chen et al (2020b) reported that COVID-19 infected people with chronic comorbidities such as cardiovascular and cerebrovascular diseases and diabetes.It was reported that after liver transplantation of patients, COVID-19 infection arose (Massoumi et al., 2020; Saigal et al., 2020; Zhang, Shi, & Wang, 2020). COVID-19 patients are suffering with cardiovascular disease (10.5%), diabetes (7.3%), hypertension (6.0%) and respiratory disorders (6.3%) as high (Xie, & Chen, 2020; Yang et al., 2020e). Xie, and Chen (2020) reported that 73.3% COVID-19 patients are suffering comorbidities in Wuhan, China. The highest percentage of COVID-19 cases occurs in patients with the medium age was between 34 and 59 years and less number of cases shows in children, whose age less than 15 years (Bai et al., 2020; Cai et al., 2020; Huang et al., 2020; Wang et al., 2020b Wang et al., 2020g).

7 Prevention and control of COVID-19

To prevent the spread of COVID-19, the relative measures have been initiated throughout the world.

7.1 Primary prevention tips

People can help protect themselves from respiratory illness including COVID-19 with everyday preventive actions (Cheng, Lam, &Leung, 2020; Feng, et al., 2020; Leung et al., 2020; Leung, Lam, & Cheng, 2020; WHO, 2020g), such as

- Frequently washing hands with soap and water or with sanitizer.
- Maintaining physical distance.
- Avoiding close contact with infected people.
- Not touching mouse, nose or eyes without properly washing hands.
- Maintaining cough etiquettes.
- Eating well cooked foods.
- Keeping an infected or suspected person isolated.
- Use of masks when going outside.

7.2 Fast confirmed cases detection

The different methods of testing COVID-19 are RT-PCR, Isothermal Amplification Assays, Antigen, Serology, Medical Imagine, and Pulse Oximeter. Transmission of SARS-CoV-2mainly occurs by direct contact with infected people and in many cases through indirect contact with surfaces (known as fomite) in the immediate environment or with objects used by the infected person. It is therefore very much essential to identify the infected people, including those who are either asymptomatic or with minor symptoms (HKSAR, 2020a, b). All confirmed cases should stay in the hospital for isolation and treatment until fully recovered (Temporary test, 2020). Suspected cases are also required to isolate in the hospital until a negative result of SARS-CoV-2 is observed. So it is necessary to rapidly identify the COVID-19 confirmed cases so as to minimize the spread of the disease (Lauer, et al., et al., 2020).

7.3 Restriction on community or mass gathering

The World Health Organization defines mass gatherings (MGs) as “events attended by a sufficient number of people to strain the planning and response resources of a community, state or nation” (WHO, 2015). Every year, various religious, cultural, social, scientific, sport, and political mass gathering festivals take place in different parts of the world (Abubakar et al., 2012; Memish et al., 2012; Memish et al., 2014b; Rashid et al., 2008). Any such mass gatherings exaggerate many of the risk factors for transmission of infectious diseases like COVID-19, and have historically been associated with outbreaks of the disease both in local and international levels (WHO, 2020h). As per the data available so far, COVID-19 is mainly transmitted from person to person through direct contact

(Riou, & Althaus, 2020; Figure 4). Thus, the spread of respiratory illnesses during the mass gathering is a major public health concern with the potential of dissemination of diseases.

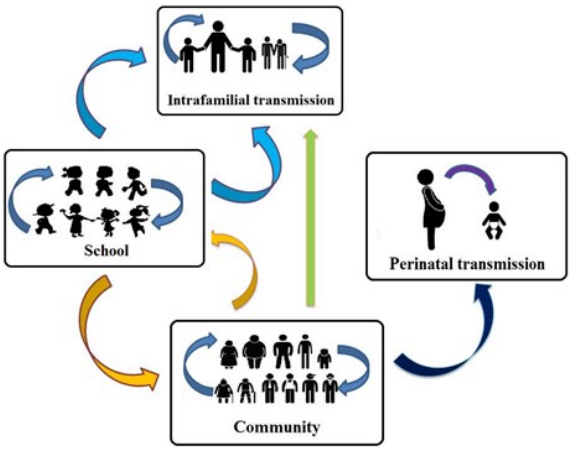

Figure 4: Transmission dynamics of COVID-19 disease in People

The outbreak did not slowdown in many of the affected countries, moreover it has been found that the disease is being transmitted to the other countries through the pilgrims and other fellow travelers (Wu, Leung, &Leung, 2020). It has been observed that it generally takes 5 to 14 days (counting from the date of infection), known as incubation period (approximate time required to develop symptoms in the infected individual) and before that period the personremains asymptomatic but might be capable to infect people in close contact.These asymptomatic SARS-CoV-2 carriers might play a vital role in the transmission and thus pose a significant challenge to infection control in context of mass gathering. Governments of different countries have decided to close schools, colleges, universities and academic institutions at different time durations, mostly with effect from first week of February, 2020. Central and local administrations have restricted any sorts of religious, cultural, social, sports or commercial mass gathering events throughout the country for the time being. Many countries have suspended travel to and from other countries by adjourning international flights (Bogoch et al., 2020; Mahase, 2020; New York Times, 2020; Touitre News, 2020). Some international events such as Umrah, Hajj and the Olympic games etc. have officially been postponed as these are some of the largest and most geographically and ethnically diverse mass gatherings throughout the world (Ebrahim, &Memish, 2020a,b; Gallego et al., 2020; Gautret, Al-Tawfiq, & Hoang, 2020). So all the people are avoiding community and mass gathering event to control the rapid spread of COVID-19 (Ebrahim, &Memish, 2020c).

7.4 Avoiding close contact

People are high risk of contracting SARS-CoV-2 if they come into contact with someone who's carrying it, especially if exposed to their sputum or come near them when they cough, sneezeor even speak loudly throwing droplets from their mouth (Hellewell et al., 2020). In several places throughout the world home or institutional quarantine for 14 dayshas been made compulsory for people who arrived from COVID stricken places or countries (Guidelines on Prevention, 2019). In this quarantine period daily body temperature, and symptoms monitoring are required. The best way to prevent the spread of infection is to avoid or limit contact with people who are showing symptoms of COVID-19 or any respiratory infection. That's why avoiding close contact with suspected and confirmed COVID-19 persons and even with unsuspected people might be a very important step towards preventing the disease from further spread to a large extent (Feng, Damon-Feng, & Zhao, 2020).In this regard it has been suggested to maintain a distance of 1 meter (better 2 meter) from one another.

7.5 Protection of healthcare workers

Due to the unprecedented lockdown, globally millions of people stay at home in order to contain the spread of the disease. Butfrontline COVID warriors including doctors, nurses, support staff, medical techniciansand other health care providers prepare to walk in exactly opposite way (Lai et al., 2020b). They go to the hospitals, clinics, laboratories, testing centres, quarantine centresand are compelled to expose themselves at high risk from COVID-19 (Lau et al., 2004; Zhan, Qin, Xue, and Zhu, 2020). If health-care workers are infected by COVID-19 the infection might pass to their families. Moreover, this will definitely hamper the healthcare sectors asa whole. Since health-care sectors are every country's most precious resource, their safety must be ensured in the following ways: All healthcare staff must be well acquainted with COVID-19. They must know clearly how it is transmitted and how they can defend themselves. So rigorous and hands on training must be provided to health workers.
Increased access of personal protective equipment (PPE)including N95 masks for an aerosol generated procedure, face shield or goggles, gloves and isolation gowns should be made to the healthcare providers.
Many healthcare staff have tocontinue long shifts

without break. So, family support and psychological support are necessary to health workers.
Many health workers have faced violent onslaughts from people in the society. So it is highly expected that govt. should make necessary steps to protect health workers under attack during covid-19 pandemic. Some countries including India have already implemented an act in this regard.

8 Treatment

The outbreak of COVID-19 has been designated as a global pandemic situation. Although a number of processes are available for identifying the diagnosis such as chest CT radiography or a number of laboratory testing, unfortunately in spite of rigorous research works there is no approved drugs/ vaccines available so far that can contain the spread of the disease or prevent mankind from the outbreak of COVID-19. Doctors, scientists, and researchers throughout the world are working whole heartedly beyond the clock for discovery of new drugs/vaccines for the treatment of COVID-19.

8.1 Commercially available drugs

Despite the worsening trends of COVID-19, no drugs are validated to have significant efficacy in clinical treatment of COVID-19 patients in large-scale studies. The treatment going on so far is mainly symptomatic. Patients are treated to relief them from their sufferings based on their local symptoms only. In search of medicines for combating COVID-19, a very effective strategy is the repurposing of some drugs that have previously been successfully used for treatment of other viral diseases without substantial adverse effect on humans. Therapeutic targets against SARS-Co-V-2 exist at various stages of infection such as (i) viral attachment, viral entry and viral fusion (ii) Viral proteolysis (iii) viral replication and (iv) host cytokine response. In different parts of the world a number of clinical trials are going on to evaluate the efficacy of these drugs alone or in combination with others as well as to test certain immunosuppressive drugs to improve critically ill patients. But a number of repurposed drugs have been used indifferent parts of the world. Remdesivir is an antiviral drug initially developed for Ebola treatment but it has shown positive result in COVID-19 disease (Cao, Deng, & Dai, 2020; Ko et al., 2020; Wang, 2020). Chloroquine and hydroxychloroquine have been used as an anti-viral drugs in COVID-19 infection (Rolain, Colson, &Raoult, 2020; WHO, 2020i). Kelleni (2020) says that Nitazoxanide/Azithromycin combination are used a drug for COVID-19 treatment. Cao et al (2020) reported that lopinavir-ritonavir is clinically used as a drug in COVID-19 treatment. Azithromycin has been shown to have a clinical efficacy against (Gautret et al., 2020). Dexamethasone shows good result in clinical trial (Foxnews, 2020). Dexamethasone showed decent result in clinical trial (Foxnews, 2020). Dexamethasone have been reported to cut down death rates significantly in critically ill COVID-19 patients and the British government authorized the use of dexamethasone for COVID-19 patients. The Indian health ministry approved the use of dexamethasone for COVID-19 patients showing certain specific signs of worsening status (MoHFW, 2020). Favipiravir is the first oral drug approved in India for restricted emergency use for the treatment of mild to moderate COVID-19 patients. Studies show that the drug offers a rapid reduction in viral load and also provides a faster symptomatic and radiological improvement. A list of probable drugs is provided in Table 1. But this is not the solution to prevent the disease. So exact drug discovery is important as early as possible to control the pandemic COVID-19.

Table 1: The detailed report of commercially available drugs for treatment of COVID–19

Sl. no.	Name of drug	Diseases treated	References
1	Remdesivir	Ebola, SARS, MERS, COVID-19	Agostini et al., 2018; Gordon et al., 2020; Grein et al., 2020; Ja, Ah, & Za, 2020; Tchesnokov et al., 2019; Wang et al., 2020d
2	Baricitinib	COVID-19	Richardson et al., 2020; Stebbing et al., 2020
3	Ivermectin	COVID-19	Caly et al., 2020
4	Favipiravir (Avigan)	Ebola, COVID-19, Influenza	Jin et al., 2014; Sissoko et al., 2016; Wang, 2020
5	Ritonavir	MERS, SARS, COVID-19	Chan et al., 2015; Chu et al., 2004; Lin et al., 2020b
6	Darunavir	COVID-19	Beck et al., 2020; Lin et al., 2020b

7	Lopinavir	COVID-19, SARS, MERS	Chu et al., 2004; Chan et al., 2015; Lin et al., 2020b; Yao et al., 2020a
8	Alcohol Vaporization or Nebulization Inhalation Therapy	COVID-19	Cao, 2020
9	Chloroquine	SARS, Human Coronavirus OC43, COVID-19	Colson et al., 2020; Devaux et al., 2020; Gao, Tian, & Yang, 2020; Keyaerts et al., 2009; Vincent et al., 2005; Wang et al., 2020d
10	Azvudine	COVID-19	Hu, Jiang, Yin, 2020
11	Ruxolitinib	COVID-19	Stebbing et al., 2020
12	Carfilzomib	COVID-19	Wang, 2020
13	Indinavir	SARS and COVID-19	Contini, 2020; Tan et al., 2004
14	TMPRSS2 inhibitor Camostat mesylate	MERS, Coronavirus 229E and COVID-19	Bertram et al., 2013; Hoffmann et al., 2020b; Shirato et al., 2014
15	Oseltamivir	COVID-19	Lu, 2020
16	Baloxavir marboxil	COVID-19	Li and Clercq, 2020
	Tocilizumab	COVID-19	Alattar et al., 2020; Diao et al., 2020; Luo et al., 2020b; Xu et al., 2020b
17	Hydroxychloroquine	COVID-19	Colson et al., 2020; Chen et al., 2020d; Gautret et al., 2020; Magagnoli et al., 2020; Yao et al., 2020b
18	Umifenovir (ArbidolTM)	COVID-19, Ebola	Deng et al., 2020; Dong, Hu & Gao, 2020; Hulseberg et al., 2019
19	Teicoplanin	COVID-19, Ebola	Baron et al., 2020; Wang et al., 2016
20	Azithromycin	COVID-19	Fantini et al., 2020; Gautret et al., 2020
21	Glycyrrhizin	COVID-19, Influenza	Luo, Liu, Li, 2020; Michaelis et al., 2011
22	Ribavirin	COVID-19	Hung et al., 2020
23	Galidesivir	COVID-19	Li & De Clercq, 2020

8.2 Traditional Chinese medicine

Traditional Chinese medicine (TCM) has plentiful experience in the treatment of infectious diseases for thousands of years and has been employed previously as effective treatments for SARS and MERS (WHO, 2004b; Su, & Liu, 2019).Now TCM, including herbal formulas has played an important role in the prevention and treatment of COVID-19 (Gao et al., 2020; Guo, & Li, 2020; Hu et al., 2020b; Lu et al., 2020c; Ling, 2020; Ma et al., 2020b; Niu et al., 2020; Ren, Zhang, & Wang, 2020; Wang et al., 2020e; Xia et al., 2020b; Yang et al., 2020b, Yong et al., 2020). In China, more than 90% of people use TCM for treatment (National Administration of Traditional Chinese Medicine, 2020). Chen et al (2020e) reported that Chinese patent medicines are used for treatment novel coronavirus. A list of probable TCM drugs is provided in Table 2.

Table 2: Traditional Chinese medicine commercially used in treatment of COVID–19

Sl. no.	Name of medicine	diseases treated	References
1	Jinhua Qinggan granule	H1N1 influenza, COVID-19	CIIC,2020; Yang et al., 2020b; Zhang et al., 2020b
2	Lianhua Qingwen capsule	COVID-19, SARS	CIIC,2020; Yang et al., 2020b; Zhang et al., 2020b
3	Xuebijing injection	COVID-19, SARS	CIIC,2020; Yang et al., 2020b; Zhang et al., 2020b
4	Qingfei Paidu decoction	COVID-19	Yizhy, Fang, & Xianglin, 2020; Zhang et al., 2020b
5	Huashi Baidu decoction	COVID-19	Zhang et al., 2020b
6	Xuanfei Baidu decoction	COVID-19	Zhang et al., 2020b
7	Astragalus membranaceus	COVID-19	Luo, et al., 2020c; Yang et al., 2020c
8	Glycyrrhizae uralensis	COVID-19	Luo, et al., 2020c
9	Saposhnikoviae divaricata	COVID-19	Luo, et al., 2020c; Yang et al., 2020c
10	Lonicerae Japonicae Flos	COVID-19	Yang et al., 2020c
11	Agastache rugosa	COVID-19	Xu, et al., 2020c; Yang et al., 2020c
12	Radix platycodonis	COVID-19	Yang et al., 2020c
13	Scrophularia ningpoensis	COVID-19	Xu, et al., 2020c; Yang et al., 2020b

14	Ophiopogon japonicas	COVID-19	Xu, et al., 2020c
15	Tan Re Qing Injection	COVID-19	Yang et al., 2020c
16	Lian Hua Qing Wen Capsule/Granule	COVID-19	Yang et al., 2020c
17	Shen Qi Fu Zheng Injection	COVID-19	Yang et al., 2020c

8.3 Indian medicine

Traditional Indian medicinal (TIM) schemes are considered as one of the oldest treatments in human various diseases (Ravishankar and Shukla, 2007). TIM has a rich history of its effectiveness. They are- Ayurveda, Siddha, Unani and Yoga, Naturopathy and Homoeopathy (Adhikari, & Paul, 2018).The TIM, particularly Ayurveda, Siddha, Unani and Homoeopathy medicines largely use plant based ancient texts had documented medicinal uses of large number of plants (Pundarikakshudu and Kanaki, 2019). As COVID-19 cases continue to rise across the world, the Ministry of AYUSH government of India, published an advisory suggesting that the use of alternative medicines might act as immunity booster against COVID-19 (AYUSH, 2020a). The ministry claimed that 'AYUSH KWATH' formulation can help boost the immune system, the body's first line of defense against bacteria and viruses. AYUSH KWATH is a combination of four medicinal herbs commonly used in every Indian kitchen - Tulsi (Ocimum sanctum), Dalchini (Cinnamomumzeylanicum), Sunthi (Zingiber officinale), and Krishna Marich (Piper nigrum) (AYUSH, 2020b). The Ministry of AYUSH recommended Indian preventive and immunity-enhancing medicinal plants for COVID-19 are shown in Table 3 (AYUSH, 2020 c,d).

Table 3: AYUSH recommended Indian medicinal plant for COVID-19 treatment

Indian medicinal plant	Trade name	TIM system	Recommended usage	Helpful against
Preventive and prophylactic				
Tinospora cordifolia	Samshamani Vati	Ayurveda	Twice a day with warm water for 15 days	Fever, Immuno-modulatory,
Andrograhis paniculata	Nilavembu Kudinee	Siddha	Decoction 60 ml. twice a day for 14 days	Viral Fevers Including Dengue
Cydonia oblonga Zizyphus Jujube Cordia myxa	Behidana Unnab Sapistan	Unani	Twice a day for 14 days	Antioxidant activity, Immuno-modulatory, antiallergic, smooth muscle relaxant activity and Anti-influenza activity
Arsenicum album 30	Arsenicum album 30	Homoeopathy	Daily once in empty stomach for three days. The dose should be repeated after one month by following the same schedule.	Effective against COVID-19; Macrophages activator.
Symptom management of COVID-19 like illnesses				
AYUSH-64		Ayurveda	02 tablets twice a day	Malaria
Agasthya Hareetaki		Ayurveda	05 gm twice a day with warm water	Immunomodulatory, and upper respiratory infections

Anuthaila	Sesame oil	Ayurveda	02 drops in each nostril daily in the morning	Respiratory infections
Nilavembu Kudineer	Kaba Sura Kudineer	Siddha	Decoction 60m1 twice a day	Pyretic and Anti bacterial effect
Adathodai Manapagu		Siddha	Syrup 10 ml twice a day	Fever and cold
Btyonia alba	Btyonia	Homoeopathy	Tablets as prescribed by physician	Reduce lung inflammation
Rhus toxico dendron	Rhus tox	Homoeopathy	Tablets as prescribed by physician	Viral infections
Atropa belladonna	Belladonna	Homoeopathy	Tablets as prescribed by physician	Asthma and chronic lung diseases
Bignonia sempervirens	Gelsemium	Homoeopathy	Tablets as prescribed by physician	Asthma
Eupatorium perfoliatum	Eupatorium perfoliatum	Homoeopathy	Tablets as prescribed by physician	Respiratory symptoms
Add on Interventions to the conventional care				
Vishasura kudineer		Siddha	Decoction 60 m1 twice a day	Fever
Kabasura kudineer		Siddha	Decoction 60 m1 twice a day	Fever, cough

8.4 Plasma therapy

Convalescent plasma (CP) therapy involves transfusion of the blood plasma of a recovered patient into another patient. Plasma of the recovered patients contains crucial components of immunity known as antibodies that have sufficient potential to fight an invading pathogen - an antigen, and to defeat it. After a successful infusion, some blood cells in the patient's body act as memory cells to identify and defeat the same antigen by quickly producing the same antibodies. Different countries including India have been using this on trial basis for treatment of COVID-19 infected patients. Convalescent plasma has also been previously used as an alternative to recover the survival rate of patients with different viral infections, such as SARS, MERS, influenza, and severe Ebola virus infection (Arabi et al., 2016; Cheng et al., 2005; Hung et a., 2009; Syal, 2020; WHO, 2014; Zhou, Zhong, &Guan, 2007). Duan et al (2020a) reported that CP treatment improved 10 patients, who are effected COVID-19 symptoms especially fever, cough, shortness of breath, and chest pain. Shen et al (2020b) concluded that CP treatments of 5 critically ill patients with COVID-19 are giving positive result. Ahn et al (2020) reported that two COVID-19 patients in Korea are recovered in CP therapy. Zhang et al (2020c) and Ye et al (2020) also reported the convalescent plasma therapy. So CP therapy used to improve the survival rate of patients, who are effected SARS-CoV-2 infection (Chen et al., 2020e; Duan et al., 2020b).

8.5 Vaccines

There is no specific vaccines available yet (Burton, and Walker, 2020). Currently, researchers are trying to develop more than 135 vaccines against the coronavirus around the world (WHO, 2020j). The first vaccine safety trials in humans started in March. Some trials will fail, but a little may succeed in stimulating the immune system to generate efficient antibodies against the virus. The British-Swedish company AstraZeneca and the University of Oxford is developed a SARS-CoV2 vaccine called ChAdOx1 (ChAdOx1, 2020), now which is beginning Phase II/III testing and may deliver by October. BioNTech, Fosun Pharma, and Pfizer collaboratelly develop 3 LNP-mRNAs vaccine and it was in human trials in the month of May 2020. (2020a). Moderna's LNP-encapsulated mRNA vaccine is eyeing Phase III trials in July and may be ready by early 2021 (mRNA, 2020b). A regularly updated landscape document has been prepared by the WHO for the status of vaccine development worldwide (Leet al., 2020; WHO, 2020j). In India a vaccine, namely Covaxin, a vaccine candidate for Covid-19 has been developed by Hyderabad-based Bharat Biotech, and is currently in the stage of human trial.

8.6 Nutrition supplement

Good nutrition is very important before during and after an infection. Apart from the constant untiring efforts of our scientists to develop effective antidote of the disease, emphasis have also been given on enhancing individual immunity levels through intake of healthy diets, fresh vegetables, natural antioxidants along with regular exercise and meditation. In this pandemic situation a healthy immune system is one of the most important weapons due to non-availability of efficient protective medicine (Koff, & Williams, 2020). There are many vitamins and trace elements which are important for the usual functioning of the immune system (Wintergerst, Maggini, Hornig, 2007). Recently the Ministry of AYUSH, Govt. of India, being driven by Ayurveda, the plant based science, has recommended regular intake immunity boosting material, such as warm water, Haldi, herbal tea, turmeric, cinnamon, coriander, cumin, black peeper, dry ginger, basil leaves etc, as a preventive health care measure for boosting immunity levels of individuals with special reference to respiratory systems (AYUSH, 2020e). Regular intake off foods containing vitamin C, zinc and antioxidants help fight COVID-19 by raising one's immunity level (Hemila, 2003, Roy et al., 2020). Polysaccharides isolated from edible mushrooms are natural immunomodulators, antioxidants and have been found to be effective for its fight against certain viral diseases (Maity et al., 2015; Wasser, & Weis, 1999; Wasser, 2002). There are some immunity enhancing vitamins and trace elements for COVID-19 are shown in Table 4.

Table 4: Nutrition supplement for COVID-19 treatment

Sl. no.	Name of nutrition supplement	Diseases treated	References
1	Vitamin A	Bovine coronavirus, HIV-1, malaria, and diarrheal	Jee et al., 2013; Villamor et al., 2002
2	Vitamin B	MERS-CoV	Keil, Bowen, Marschner, 2016
3	Vitamin C	Avian coronavirus, SARS	Atherton, Kratzing, Fisher, 1978; Hemila, 2003
4	Vitamin D	Bovine coronavirus, cancers, and cardiovascular disease	Holick, 2004; Nonnecke et al., 2014
5	Vitamin E	Bovine coronavirus	Nonnecke et al., 2014
6	Iron	Viral mutations	Wessling-Resnick
7	Selenium	Influenza virus, bronchitis virus	Beck et al., 2001; Ma et al., 2019
8	Zinc	SARS-CoV, COVID-19	Read et a., 2019; Roy et a., 2020; Velthuis et al., 2010
9	Copper	Influenza viruses	Rupp et al., 2017
10	Magnesium	EBV infection	Chaigne-Delalande et al., 2013

9 Conclusion

In this review, we summarize all the potential interventions for COVID-19 infection. SARS-CoV-2 emerged as a novel virus to which humans had no immunity, it spreads very fast, and carries a high mortality. To date, there is no specific antiviral drug/vaccine for COVID-19, and the case fatality rate is still high. Till the development and application of the vaccine to the entire population, the people in general have no other option than to survive with SARS-CoV-2. Our citizens need adopting the practice of wearing masks, washing hands, maintaining social distancing-cough etiquettes-personal hygiene Maintaining healthy lifestyle, regular exercise, and healthy diet might boost the immune systems as well. Intake of certain immune modulating plant derived materials may also effectively protect from the virus to a certain extent. Large scale studies are required to identify the clinical features of the disease. Researchers, scientists, and doctors are working to make out the correct source of disease, modes of transmission, virus structure, most efficient treatment policy, nutrition supplement, and drugs/vaccines development. Finally, vaccination is highly demand for future prevention of emerging corona virus related epidemics or pandemic.

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