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COVID-19: A Life Threatening Disease of Global Importance

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Abstract

Coronavirus 2019 disease is a globally declared pandemic viral disease affecting upper and lower respiratory tract, and it is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).The virus under the genus *Betacoronavirus* and it is enveloped and has single stranded positive sense RNA genomes with high mutation rate. Bats are suggested to be the natural reservoir of a wide range of coronaviruses. It can be transmitted through airborne droplets to the nasal mucosa in closed environments and direct/indirect contact. Clinical symptoms of the disease include high fever, chills, cough, and difficulty in breathing, diarrhea, myalgia, fatigue, expectoration, and hemoptysis. In addition, acute respiratory distress syndrome, heart failure, respiratory failure, and liver failure are most likely to occur. The general diagnosis of the disease includes consideration of clinical history/signs, travel history, and contact history of the suspected patient. Laboratory tests used to confirm the diagnosis include molecular tests, virus isolation, serological tests, and electron microscopy techniques. It has major public health and economic impact globally. Although viral diseases have no specific treatment, the treatment of the disease is almost supportive. Prevention and control measures of the disease include provision of protective equipment, disinfection, hygiene regulations, isolation and designing isolation rooms.

Keywords: COVID-19, Emerging, Pandemic, Public Health Importance, SARS-CoV-2

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1. INTRODUCTION

Coronavirus 2019 (COVID-19) is a globally declared pandemic viral disease affecting upper and lower respiratory tract, caused by a novel Coronavirus, a new strain of the virus that has not been previously identified in humans, and later designated SARS-CoV-2. It was observed in December 2019 causing a cluster of respiratory infections was first isolated from three patients with pneumonia, connected to the cluster of acute respiratory illness cases from Wuhan, China. Chinese authorities announced on January 7, 2020 that a new type of Coronavirus (novel Coronavirus, nCoV) has been isolated [1, 2].On January 9, 2020, China CDC reported a novel Coronavirus as the causative agent of this outbreak, which is phylogenetically in the SARS-CoV clade. The novel Coronavirus has thus been named 'severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), while Coronavirus disease associated with it is now referred to as COVID-19. This is a unique strain of RNA viruses that have not been previously observed in humans [3].

After the outbreak in Wuhan, Hubei province, China, the disease has spread globally, affecting most countries of the world, and was declared by the World Health Organization (WHO) as pandemic disease on January 11, 2020 [4]. This acute respiratory disease has spread throughout China and received worldwide attention. The emergence of SARS-CoV-2, since the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, marked the third introduction of a highly pathogenic and large-scale epidemic Coronavirus into the human population in the twenty-first century [5, 6].

The Chinese scientists rapidly isolated a SARS-CoV-2 from a patient within a short time on 7 January 2020 and came out to genome sequencing of the SARS-CoV-2. Moreover, this virus was named as 2019-nCoV by WHO on 12 January and COVID-19 on 11 February 2020 [7, 8]. WHO officially named the disease as coronavirus disease 2019 (COVID-19) and Coronavirus Study Group (CSG) of the International Committee proposed to name the new Coronavirus as SARS-CoV-2, both issued on 11 February 2020[5, 9]. This outbreak is associated with a large seafood and animal market [10].When given where the first case originated, the infection were transmitted probably as zoonotic agent (from animal to human) [11]. This disease has caused serious public health problems in humans more than its predecessors (SARS-CoV), and Middle East Respiratory Syndrome CoV (MERS-CoV), because, it has caused severe illness and death in China and has spread to several most other countries of the world [12].

Most people infected with SARS-CoV-2 developed severe acute respiratory illness (pneumonia) with symptoms of fever, cough, and shortness of breath, related to the disease called COVID-19. There have been several reported deaths. Investigators have tried to determine the source of SARS-CoV-2, and there is a link to a large wholesale fish and live animal market in Wuhan City. The virus has moved to other countries via travelers.

There have been several reported cases around the world. Prior to this, Coronaviruses have been linked to two major outbreaks, namely severe acute respiratory syndrome (SARS) and Middle Eastern respiratory syndrome Coronavirus (MERS-CoV). COVID-19 may result in mild, asymptomatic to life-threatening infections, equally affecting people living in both developing and developed countries [13, 14]. The aim of this chapter book was to overview Coronavirus 19 as a life threatening disease of global importance.

2. SARS-CoV-2 CHARACTERISTICS – ENVIRONMENTAL PUBLIC HEALTH IMPACTS

Coronaviruses are members of the sub-family Coronavirinae from the family Coronaviridae and the order Nidovirales. Based on phylogenetic relationships and genomic structures, the sub-family Coronavirinae is divided into four genera namely, *Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus, Alphacoronaviruses and Betacoronairuses* infect only mammals.

Gammacoronaviruses and Deltacoronaviruses infect birds and sometimes even infect mammals including rodents and bats. They are known to cause respiratory diseases in humans and gastroenteritis in animals [3, 15].

All Coronaviruses are pleomorphic RNA viruses characteristically containing crown-shape peplomers with 80-160 nm in size and are enveloped and have single stranded positive sense RNA genomes that range in size from 26 to 32 kilobases, have high mutation rate [3, 10]. This can lead to a greater possibility of errors, which can result in very rapid mutations. Some of these mutations can give the virus new properties, such as the ability to infect new cell types or even new species that can generate serious lung disease [16].

On electron microscopy, Coronaviruses show a characteristic appearance that resembles a crown (corona in Latin means crown) due to the presence of club-shaped surface protein projections, from which the name derived. The CoVs are pleomorphic virus with a unique replication strategy [17, 18]. Coronaviruses viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms [6, 19].

Genetic analysis revealed that SARS-CoV-2 is closely related to SARS-CoV and genetically clusters within the genus *Betacoronavirus*, forming a distinct clade in lineage B of the subgenus *Sarbecovirus* together with two bat-derived SARS-CoV-like strains [7]. Two-thirds of viral RNA, mainly located in the first open reading frame (ORF 1a/b), encodes 16 non-structure proteins (NSPs). The rest part of the virus genome encodes four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and also several accessory proteins. S glycoprotein of SARS-CoV-2 binds to host cell receptors, angiotensin-converting enzyme 2 (ACE2), which is a critical step for virus entry. The possible molecules facilitated membrane invagination for SARS-CoV-2 endocytosis is still unclear. Other virus proteins may contribute to pathogenesis. Host factors can also influence susceptibility to infection and disease progression. The elderly and people with underlying disease are susceptible to SARS-CoV-2 and tend to develop into critical conditions [5, 16]. The spike protein forms club-shaped protrusions that stick out all over the virion, resembling a crown or the sun's corona. These protrusions bind to receptors on host cells thus determine the cell types and the range of species that the virus can infect [15].

2.1. Epidemiological Characteristics

In December 2019, many pneumonia cases that were clustered in Wuhan city were reported and searches for the source have shown Huanan Seafood Market as the origin. The first case of the COVID-19 epidemic was discovered with unexplained pneumonia on December 12, 2019 [10]. Within a short time, this virus spread quickly throughout China during the Chinese New Year – a period when there is a high level of human movement among Chinese people. Although it is still too early to predict susceptible populations, early patterns have shown a trend similar to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) coronaviruses. Susceptibility seems to be associated with age, biological sex, and other health conditions [19].The increase in the number of cases in its origin and internationally after closing the market and evacuation of the cases in China has indicated a second transmission from human-to-human. New cases are identified and distributed all over the world [10].

Four human CoVs (HCoVs) (HCoV 229E, NL63, OC43, and HKU1) are endemic globally and account for 10% to 30% of upper respiratory tract infections in adults. Ecologically, there are several types of CoVs, and the greatest variety was noted in bats, suggesting that bats may be natural reservoirs for a lot of these viruses. Peri-domestic mammals can also serve as intermediate hosts, facilitating recombination, mutation, and genetic variations [3]. SARS-CoV-2 belongs to β-coronavirus, with highly identical genome to bat coronavirus, pointing to bat as the

natural host. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract [5].

COVID-19 has caused high morbidity as well as mortality in susceptible populations throughout the world. The disease has been spreading to most countries of the world including European, American, Asian, and African countries. In these countries, the death rates of the disease have been different. Even though deadly cases have been occurring throughout the world, the medical severity of COVID-19 is exactly not known, especially in terms of the recurrence of the infection, and the effects of infection in pregnant women, children, and other vulnerable populations SARS-CoV-2 has wide host adaptability that includes humans, birds, livestock, masked palm civets, mice, dogs, cats, camels, pigs, chickens, and bats, wherein they typically cause respiratory illness [11, 20].

Globally, the mortality rate of SARS-CoV-2 infection stands at 7.05%. Varied mortality rates have been noted in the WHO European Region (9.47%), American Region (5.23%), Eastern Mediterranean Region (4.08%), Western Pacific Region (4.12%), South-East Asia Region (3.86%), and African Region (3.79%), as determined from the numbers reported by the WHO. The WHO has categorized the SARS-CoV-2 transmission in the respective countries as a cluster of cases, sporadic cases, and community spread. The sporadic spread is when one or more cases are reported and most of them imported, and a few found locally. When cases are reported in a particular geographical region, in a cluster, and with common exposure history, it is considered as a cluster transmission. Community transmission is established when there are a greater number of cases reported with un-linkable transmission chains from various regions of a country [5, 21].

2.2. Reservoirs – Public Health Characteristics

Bats are the natural reservoir of a wide variety of CoVs, including SARS-CoV-like and MERSCoV- like viruses. Protein sequences alignment and phylogenetic analysis showed that turtles, pangolin, and snakes have been identified as alternative intermediate hosts for SARS-CoV-2 Upon virus genome sequencing, the COVID-19 was analyzed throughout the genome to Bat CoV RaTG13 and showed 96.2% overall genome sequence identity, suggesting that bat CoV and human SARS-CoV-2 might share the same ancestor, although bats are not available for sale in this seafood market.

Besides, protein sequences alignment and phylogenetic analysis showed that similar residues of receptor were observed in many species, which provided more possibility of alternative intermediate hosts, such as turtles, pangolin and snacks infections [5]. SARS-CoV-2 has wide host adaptability and is capable of causing severe diseases in humans, masked palm civets, mice, dogs, cats, camels, pigs, chickens, and bats [11].

2.3. Transmission – Environmental Health Impact Characteristics

The SARS-CoV-2 typically causes respiratory and gastrointestinal sickness in both humans and animals. It can be transmitted through airborne droplets to the nasal mucosa in closed environments and direct contact, touching contaminated and then touching your mouth, nose, or eyes, as well as during medical cases and laboratory sample handling[15,17].Human-to-human transmission of SARS-CoV-2 occurs mainly between family members, including relatives and friends who intimately contacted with patients or incubation carriers. There has been also transmission of the virus between healthcare workers. By contrast, the transmission of SARS-CoV and MERS-CoV is reported to occur mainly through nosocomial transmission. Infections caused by transmission of the virus in healthcare workers in 33-42% of SARS cases and transmission between patients is the most common route of infection in MERS-CoV cases. Direct contact with intermediate host animals or consumption of wild

animals was suspected to be the main route of SARS-CoV-2 transmission. However, the sources and transmission routines of SARS-CoV-2 remain elusive [4, 5].

The SARS-CoV-2 appears to be less lethal and highly transmissible than its predecessor SARS-CoV, which was more lethal but had low transmissibility rates. It is important to understand the host adaptability, interspecies interactions, and the mechanisms underlying the ability of the virus to undergo genetic variations to predict and prevent the potential future emergence and re-emergence of the existing and novel viral infectious agents [11].

2.4. Pathogenesis and Clinical Signs

Coronaviruses are divided into four genera, including α−/β−/γ−/δ-CoV. α- and β-CoV are able to infect mammals, while γ- and δ-CoV tend to infect birds. Previously, six CoVs have been identified as human-susceptible virus, among which α-CoVs HCoV-229E and HCoV-NL63, and β-CoVs HCoV-HKU1 and HCoV-OC43 with low pathogenicity, cause mild respiratory symptoms similar to a common cold, respectively. The other two known β-CoVs, SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infections [5].

Infection begins when the virus enters the host cell, the virus particle is uncoated and the spike protein attaches to its complementary host cell receptor. After attachment, a proteolytic enzyme of the host cell cleaves and activates the receptor-attached spike macromolecule. Depending on the host cell proteolytic enzyme available, cleavage and activation enable cell entry through endocytosis or direct fusion of the viral envelope with the host membrane. The chemical structure of Coronavirus RNA consists of 5' methylated head and a 3' polyadenylated tail, through which the RNA attaches to the free ribosomes of the host cell. This leads to the process of translation and formation of a long polypeptide chain. This protein has its enzyme (proteases) which break the polyprotein into multiple nonstructure proteins [21, 22].

Specific structural proteins, which might be found on the surface of the virus, play an important role in the pathogenesis and development of the complications[3].Additionally, it has been confirmed that angiotensin-converting enzyme 2 (ACE-2), a membrane exopeptidase, is the receptor used by SARS-CoV-2 for entry into the human cells, similar to SARS-CoV [7].

As an emerging acute respiratory infectious disease, COVID-19 primarily spreads through the respiratory tract, by droplets, respiratory secretions, and direct contact for a low infective dose. Based on epidemiological investigations, the incubation period is 1-14 days, mostly 3-7 days. And the COVID-19 is contagious during the latency period. It is highly transmissible in humans, especially in the elderly and people with underlying diseases. The median age of patients is 47-59 years, and 41.9-45.7% of patients were females. As it is designated SARS-CoV-2, COVID-19 patients presented certainly similar symptoms, such as high fever, chills, cough, and shortness of breath or difficulty in breathing [3, 5].

The infected people may also present with other symptoms, such as diarrhea, myalgia, fatigue, expectoration, and hemoptysis. Most adults or children with SARS-CoV-2 infection presented with mild flu-like symptoms and a few patients are in critical condition and rapidly develop serious complications, such as acute respiratory distress syndrome, heart failure, respiratory failure, and liver failure, and the infection may be severe in elderly and immunocompromised patients, even deaths can occur [11,23].

2.5. Diagnosis

The general diagnosis of COVID-19 includes consideration of clinical history, travel history, contact history, and clinical signs observed in the suspected patient. Other laboratory tests to confirm the diagnosis include molecular tests, such as the real-time polymerase chain reaction (rt-PCR), reverse transcription-polymerase chain reaction (RT-PCR) to detect the viral nucleic acid in the throat swab, and sputum specimens. Laboratories undertaking testing for COVID-19 virus should adhere strictly to appropriate biosafety practices [23]. Virus isolation, serological tests, electron microscopy techniques are

used to confirm the disease [24].

The viral research institution in China has conducted preliminary identification of the SARS-CoV-2 through the classical Koch's postulates, and by observing its morphology through electron microscopy. However, the golden clinical diagnostic method of COVID-19 is nucleic acid detection in the nasal and throat swab or other respiratory tract samplings by real-time PCR and further confirmed by next-generation sequencing [5]. Moreover, radiological imaging features that include the chest computed tomography scanning may be crucial in the management of infected patients [11,23].

2.6. Public Health and Economic Impact

The spread of the COVID-19 disease has strongly influenced the psychological and physical health of the general population, including the health care professionals [25]. The emergence of a novel coronavirus (2019-nCoV), which has caused an outbreak of unusual viral pneumonia in patients in Wuhan, a central city in China, is another warning of the risk of CoVs posed to public health [4].

It resulted in health, social, economic, and political problems across the globe. With wide host adaptability, and the ability to undergo mutations and genetic recombination, CoVs may continue to pose a potential threat to public health. It is important from the public health and economic point of view as it affects the growth of the country, which is majorly attributed to the restriction in the movement of the people and the cost associated with the control and prevention of the disease [11]. Several treatment, prevention, control measures are necessary that are presented below for public health protection.

3. Treatment – Prevention and Control Measures

There is the lack of effective antiviral therapy against COVID-19, thus, treatments mainly focused on symptomatic and respiratory support according to the diagnosis and treatment of pneumonia caused by COVID-19 issued by National Health Commission of the People's Republic of China[1,5].

Because of the unavailability of specific antiviral drugs, the therapeutic interventions in COVID-19 patients are almost always considered as supportive and most are repurposed drugs [4]. Antiviral treatment with interferon-alpha inhalation and Arbidol has been used [23]. Additionally, a protease inhibitor (Lopinavir/ritonavir) in combination with ribavirin may play a role as antiviral therapy in the early phase whereas nelfinavir is a promising alternative.

Other anti-viral treatments such as RNA interference, monoclonal antibody, synthetic peptides, and corticosteroids including dexamethasone are used to suppress excessive lung damage due to an inflammatory response [26]. The high flow oxygen supplementation and mechanical ventilation can be used for respiratory failure, and tracheotomy is required in patients requiring prolonged mechanical ventilation and intensive care [3, 5, 27].

Other therapeutic options include antiviral agents like remdesivir, fevipiravir, and EIDD-2801, rhACE2 (ACE-2 inhibitor), antimalarials (chloroquine, hydroxychloroquine), and vitamin supplementation (vitamin C, D, Zinc, and others). Convalescent plasma transfusion was found effective in the treatment and management of COVID-19 patients, although there is not much concrete evidence to establish its efficacy. It has been observed that the SARS-CoV-2 infection may affect various body systems that include the gastrointestinal system, the cardiovascular system, central nervous system, the kidneys, and liver apart from affecting the lungs to produce acute respiratory distress syndrome (ARDS).

Also, it was noted that the infection with SARS-CoV-2 may result in immune dysfunction (spleen and lymph node atrophy, myelocytopenia) [11, 28]. Oxygen therapy is nearly accepted by all patients, and WHO recommended extracorporeal membrane oxygenation to patients with refractory hypoxemia. Rescue treatment with convalescent plasma and

immunoglobulin G are delivered to some critical cases according to their conditions [1, 22]. In figure 1 are presented necessary measures that should be taken for the prevention and control of covid-19 in relation to proper application of sustainable designs to mitigate properly associated risks. Disease surveillance is necessary for qualitattive environmental health conditions at indoor, oudoor environments promoting proper use of sustainable designs within renewable resources so as to avoid air pollution emissions, water pollution, soil pollution so as to protect public health and to mitigate associated public health risks at post pandmic covid-19 era [31,32].

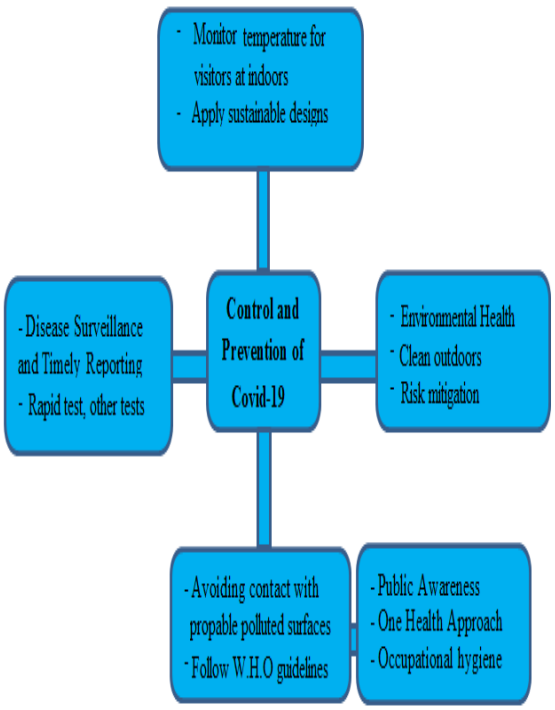

Figure 1. Measures to be taken for the prevention and control of COVID-19.

Various options are outlined to prevent COVID-19 caused by novel Coronavirus in order to protect the elderly who receive institutional care. These include the provision of protective equipment, disinfection, general hygiene regulations, isolation tests and designing isolation rooms. Special attention must be paid to preventive measures in nutrition and fluid intake. Having mental health can also help in maintaining normal balance [17].

To prevent the transmission of infectious agents in healthcare settings prevention measures of COVID-19 includes providing masks and hand hygiene products at all ports of entry to health systems (hospitals, physician offices, clinics), placing surgical masks on symptomatic patients immediately (clinically tolerable), rapid triage symptomatic patients in designated areas (negative pressure if available), immediate placement in isolation precautions (standard, contact, airborne) and use eye protection, and strict adherence to hand hygiene guidelines by healthcare workers [29, 30].

Proper control and preventive measures that include physical/social distancing, washing hands frequently with soap and water, disinfecting hands and objects with sanitizers and alcohol, avoiding contact of contaminated objects, using proper personal protective equipment, and public education could minimize the transmission [11, 22].

4. CONCLUSIONS

Coronavirus disease 2019 is an emerging zoonotic viral disease affecting respiratory systems of affected patients. Coronaviruses viruses cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms. COVID-19 has caused high morbidity as well as mortality in susceptible populations throughout the world.

It has wide host adaptability and capable of causing severe diseases in humans, masked palm civets, mice, dogs, cats, camels, pigs, chickens, and bats. As an emerging acute respiratory infectious disease, COVID-19 primarily spreads through the respiratory tract, by droplets, respiratory secretions, and direct contact for a low infective dose. The disease showed many clinical signs including fever, chills, difficulty in breathing, diarrhea, myalgia and other respiratory system signs.

It can be diagnosed using clinical signs and history, and different laboratory tests. The associated public health risks could be mitigated applying efficient monitoring schemes, taking right measures in time and

realise sustainable designs that improve a qualitative environmental health at indoor and outdoor. The treatment used against the disease is supportive, thus proper preventive measures should be taken to prevent the occurrence and spread of the disease.

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CONFLICT OF INTEREST

The authors declare that they do not have conflict of interest.

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