

2019 Novel Coronavirus (COVID-19): A Review.

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ABSTRACT

2019 novel coronavirus (COVID-19) emerged in Wuhan in December 2019. (COVID-19) presents clinical symptoms which largely mimic the symptoms of viral pneumonia. Initially the virus showed association with other health conditions and age. These were similar trend with Middle East respiratory syndrome (MERS) coronavirus and Severe Acute Respiratory Syndrome (SARS) coronavirus such as fever, dry cough and dyspnea. However, COVID-19 shows some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat. Currently, there is no vaccine preventing 2019-nCoV therefore avoiding exposure to 2019-nCoV remains the best method to prevent the spread of the virus. Regular washing of hands with soap or disinfection with hand sanitizer containing at least 60% alcohol, covering sneezes and coughs with elbow or tissue papers which are then safely disposed off, use of face masks, avoiding contact with infected people and keeping as much distance as possible; at least 1 meter, refraining from touching the mouth, eyes and nose with unwashed hands are numerous preventive measures that may reduce the risk of exposure to the virus. This review aims to analyze the works on COVID-19 and suggest ways of staying safe at this time on global pandemic emergency.

Keywords: COVID-19, Fever, Dyspnea, SARS, MERS.

INTRODUCTION

Human coronaviruses (HCoVs) have been a major cause of "common cold" in healthy people for long although it has been considered negligible pathogens [1]. Nonetheless, in the 21st century, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), two highly pathogenic HCoVs and betacoronaviruses from animal reservoirs caused global epidemics which resulted in alarming morbidity and mortality [2]; [3]; [4]. However, most human coronavirus infections are mild [5]; [6]; [7].

Coronaviruses are positive stranded RNA viruses which are large and enveloped [8]. They belong to the order Nidovirales and family Coronaviridae and are distributed widely in mammals including humans and birds [9]; [10]. They cause enteric, respiratory, hepatic and neurologic diseases [11].

Coronaviruses are divided into 4 genera: alpha, beta, delta, and gamma. Of the 4 genera, alpha and beta CoVs are known to infect humans [12]. HCoV 229E, NL63, OC43, and HKU1 are four HCoVs which account for about 10 - 30% of upper respiratory tract infections in adults and are as well globally endemic [13].

Coronaviruses show great ecological diversity. Bats are seen to possess the greatest variety of coronaviruses. This suggests that the bats are reservoirs for many coronaviruses [14]. Peridomestic mammals may serve as intermediate hosts thereby enabling recombination and mutation processes which expand genetic diversity. There are possibilities of newer and more serious future outbreak as only few viruses have been identified [15].

In December 2019, 2019 novel coronavirus (2019-nCoV), another pathogenic HCoVs emerged in Wuhan,

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China. The 2019-nCoV presented clinical symptoms which largely mimic the symptoms of viral pneumonia (WHO, 2020a). This HCoV's emergence has resulted in serious illness and death across the globe. This outbreak is evolving quickly and this makes the effect of the outbreak unclear [16]. At the moment, there are thousands of confirmed cases across the globe with several confirmation of exported cases in other provinces in China, and in Thailand, Japan, South Korea, the USA and worldwide [17] [18]; [19].

In a space of one month, the virus rapidly spread throughout China and across the globe during the Chinese New Year when the Chinese travel in large number for the New Year celebration. In early trend, the virus has shown association with other health conditions and age. These were similar trend with Middle East respiratory syndrome (MERS) coronavirus and Severe Acute Respiratory Syndrome (SARS) coronavirus [20].

Epidemiology of Coronavirus

Cases of acute respiratory syndrome of unknown etiology were reported among people in the city of Wuhan, Hubei province of China in late December 2019 [21]. The infected people had link to seafood market in Wuhan [22]. It was found afterwards that secondary infection occurred by human-to-human transmission among close contacts. The infection grew in people who had no history of exposure to wildlife and people who had never visited Wuhan. Several cases of infection were also detected among medical personnel [23]; [24]; [25]. 2019-nCoV infection occurs as a result of exposure to the virus and studies have shown that both the immunocompromised and healthy individual appear to be susceptible to the virus. Identified cases among children and infants have been very few [26]; [27]. It has been suggested that people with lower immunity such as older people and people with health disorders such as renal and hepatic disorders [28].

2019-nCoV has higher transmissibility levels and pandemic risk than SARS-CoV

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[29]. As a result several public health measures such as environmental disinfection, case isolation and identification and follow-up of contacts have been laid down to reduce the transmission of the virus [30]. The incubation period of 2019-nCoV are believed to range from 2-11 days [31], with the Chinese health authorities reporting an average incubation period of 7 days, ranging from 2-14 days [32].

Pathogenesis

Coronaviruses are enveloped single strand positive RNA (+ssRNA) virus that are zoonotic in nature. It belongs to the order Nidovirales, family Coronaviridae, and subfamily Orthocoronavirinae [33]. They cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic and neurological symptoms [34]; [35]. The severe symptoms of COVID-19 are associated with an increasing numbers and rate of fatalities especially in the epidemic region of China [38].

Patients infected with COVID-19 showed higher leukocyte numbers, abnormal respiratory findings, and increased levels of plasma pro-inflammatory cytokines. One of the COVID-19 case reports showed a patient at 5 days of fever presented with a cough, coarse breathing sounds of both lungs, and a body temperature of 39.0 °C. The patient's sputum showed positive real-time polymerase chain reaction results that confirmed COVID-19 infection [32].

Other than 2019-nCoV, there are six known coronaviruses in human: HCoV-229E, HCoV-OC43, SARS-CoV, HCoV-NL63, HCoV-HKU and MERS-CoV. Coronavirus has caused two large scale pandemics in the last two decades: SARS and MERS [9]; [10]. The coronavirus isolated from the lower respiratory tract of patients with unidentified pneumonia in Wuhan is a new type of coronavirus (SARS-CoV-2) belonging to subgenus sarbe [5].

SARS-CoV-2 is different from the zoonotic MERSr-CoV and SARSr-CoV and becomes the seventh coronavirus to infect humans [34]. The phylogenetic analysis of the coronaviruses based on full-length

genome sequences shows that SARS-CoV-2 has the smallest genetic distance from bat coronavirus, but only about 45%-90% similarity with SARSr-CoV, and a lower similarity of 20%-60% with MERSr-CoV [2]. Therefore, a bat is probably the original host of SARS-CoV-2, although the intermediate host may still exist in the process of transmission from bats to human beings. Coronavirus has an envelope with particles that are round or oval, often pleomorphic, with a diameter of 50-200 nm [6]. S protein is located on the surface of the virus and forms a rod-shaped structure.

As one of the main antigenic proteins of the virus, the S protein gene is the main target used for typing [8]. Xu *et al.*, also reported that SARS-CoV-2 S-protein supports a strong interaction with human angiotensin-converting enzyme 2 (ACE2) molecules, which means that the virus poses a significant public health risk for human transmission by the S-protein-ACE2 binding pathway [11].

Clinical Presentation

Coronaviruses are distributed among humans, other mammals and birds and have been implicated to cause respiratory, hepatic, gastrointestinal and neurological infections [23]. Six coronavirus species are known to cause human infection, four of which typically cause cold symptoms in immunocompetent individuals, while the other two namely SARS-CoV (severe acute respiratory syndrome coronavirus and MERS-CoV (Middle East respiratory syndrome coronavirus) which are both zoonotic in origin were implicated in 2002 and 2003 outbreaks in Guangdong, China and 2012 outbreaks in the Middle East and can cause severe respiratory illness and fatalities [30].

Patients with confirmed 2019-nCoV infection have reported respiratory illness with fever, cough, and shortness of breath. Incubation period appears to range between two days to up to two weeks following exposure. To date the severity of illness has tended to be mild, however deaths have been reported. There is concern that patients with mild

symptoms may more easily spread the virus due to not seeking medical attention [16].

No vaccine exists to prevent infection; therefore, early identification and prevention of transmission is of paramount importance. Healthcare professionals' education is imperative as a majority of SARS-CoV and MERS-CoV cases were associated with healthcare-associated transmission. Based on experience with previous such outbreaks, those with advancing age and comorbidities such as diabetes and heart disease can be at high risk for adverse outcomes [9].

Symptoms

The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days [35]. The period from the onset of COVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days [1]. This period is dependent on the age of the patient and status of the patient's immune system. The most common symptoms at onset of COVID-19 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia [7]; [8]; [9]; [10].

Clinical features revealed by a chest CT scan presented as pneumonia, however, there were abnormal features such as RNAemia, acute respiratory distress syndrome, acute cardiac injury, and incidence of grand-glass opacities that led to death [25]. In some cases, the multiple peripheral ground-glass opacities were observed in subpleural regions of both lungs [35] that likely induced both systemic and localized immune response that led to increased inflammation. Regrettably, treatment of some cases with interferon inhalation showed no clinical effect and instead appeared to worsen the condition by progressing pulmonary opacities [27].

It is important to note that there are similarities in the symptoms between COVID-19 and earlier betacoronavirus such as fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest

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CT scans [4]. However, COVID-19 showed some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat [12]; [13]. In addition, based on results from chest radiographs upon admission, some of the cases show an infiltrate in the upper lobe of the lung that is associated with increasing dyspnea with hypoxemia [7].

Importantly, whereas patients infected with COVID-19 developed gastrointestinal symptoms like diarrhoea, a low percentage of MERS-CoV or SARS-CoV patients experienced similar GI distress. Therefore, it is important to test faecal and urine samples to exclude a potential alternative route of transmission, specifically through health care workers, patients etc [3]; [4]. Therefore, development of methods to identify the various modes of transmission such as faecal and urine samples are urgently warranted in order to develop strategies to inhibit and/or minimize transmission and to develop therapeutics to control the disease.

Transmission

Mammals including peridomestic animals such cattle, camels, cats, and wild animals such as bats serve as hosts for coronaviruses [6]. Generally, animal coronaviruses do not spread among human beings [8]. In the case of 2019-nCoV, early patients reportedly had link to the Huanan Seafood Market in Wuhan. This shows that the infections recorded in early patients were due to animal-to-person transmission. More cases were reported after the early cases among medical staff and people with no history of exposure to the Huanan Seafood Market or visited Wuhan. These later cases show that transmission mode was human-to-human transmission [11]; [12]; [13]; [14]. According to the Chinese health authorities, there are three main transmission routes for the 2019-nCoV. They include aerosol transmission, direct transmission and contact transmission [6]; [7]. Aerosol transmission might result when respiratory droplets mix into the air

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forming aerosols. The formed aerosols cause infection when inhaled into the lungs [34]; [35].

In direct transmission routes, transmission occurs when respiratory droplets from an infected person are ingested or inhaled by close by individuals. When humans touch a surface or object contaminated with the virus, the resulting transmission is referred to as contact transmission. Subsequently, individuals can be infected when they touch their eyes, mouth or nose [5]; [6].

Prevention and Control

Currently, there is no vaccine preventing 2019-nCoV therefore avoiding exposure to 2019-nCoV remains the best method to prevent the spread of the virus [23]. Regular washing of hands with soap or disinfection with hand sanitizer containing at least 60% alcohol, covering sneezes and coughs with elbow or tissue papers which are then safely disposed off, use of face masks, avoiding contact with infected people and keeping as much distance as possible; at least 1 meter, refraining from touching the mouth, eyes and nose with unwashed hands are numerous preventive measures that may reduce the risk of exposure to the virus [17].

It's recommended that medical personnel use the particulate respirator such as certified N95 or FFP2 when performing aerosols generating procedures. It's also recommended that medical professionals use medical masks in discharging their duties especially while providing any care to suspected or confirmed coronavirus patients. Individuals with respiratory symptoms are strongly advised to make use of medical masks both at the health care settings and home in line with the infection prevention guidelines.

Individuals without respiratory symptoms may not necessarily make use of medical masks but must cover their nose and mouth when coughing and sneezing with tissues papers or elbow. It is crucial to properly use and dispose the masks to avoid any increase in risk of transmission [8]. Different agencies across the globe such as the China CDC (Chinese Center

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for Disease Control and Prevention) have published guidelines aimed to raise awareness of the prevention and control of 2019-nCoV among the people.

This guideline contains numerous information such as the causes of 2019-nCoV, proper hand washing habits, disinfection methods, how to choose and wear face masks, preventive measures at different places such as homes, on public transport and in public space, and medical observation at home [2]. Other important guideline apart from preventive and control measures are aimed at eliminating panic among the people [29].

Vaccines and Treatments

Several efforts to develop vaccines are underway, but WHO estimates it will take about 18 months for the COVID-19 vaccines to be available [9]. At present, most treatment is symptomatic and supportive, though anti-inflammatory and antiviral treatments have been employed [5]. No effective antiviral treatment or vaccine is available for COVID-19.

However, a randomized multicentre controlled clinical trial is currently underway to assess the efficacy and safety of abidole in patients with COVID-19 (ChiCTR2000029573) [11]. First-line treatment for fevers includes antipyretic therapy such as paracetamol, whilst expectorants such as guaifenesin may be used for a non-productive cough [2]. Patients with severe acute respiratory infection, respiratory distress,

CONCLUSION

COVID-19 is a pandemic of global proportion. Since its emergence in Wuhan, it has thrown the world into a great challenge and panic. So many deaths have been recorded and although some drugs have been promising in handling the virus, no drug has shown to completely

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hypoxaemia or shock require the administration of immediate oxygen therapy [34].

Suspected and confirmed cases should be treated in isolation in hospitals with effective isolation and protective conditions. The suspected cases should be isolated in a single room, and the confirmed cases can be accepted in the same room. Critical cases should be treated in ICU as soon as possible [11].

Supportive treatment for complicated patients has included continuous renal replacement therapy (CRRT), invasive mechanical ventilation, and even extracorporeal membrane oxygenation (ECMO) [5]. Treatments include Bed rest, strengthen supportive treatment, ensure sufficient energy; pay attention to water-electrolytes balance and maintain the stability of the internal environment; closely monitor vital signs and finger oxygen saturation, and so on [17].

No specific antiviral drugs have been confirmed effective [5]. Since there is no effective therapy or vaccine, the best measures now are to control the source of infection, early diagnosis, reporting, isolation, supportive treatments, and timely publishing epidemic information to avoid unnecessary panic. For individuals, good personal hygiene, fitted mask, ventilation, and avoiding crowded places will help to prevent CoVs infection [8]

cure the disease. So far vaccines have not also been produced but researches are underway and the results encourage optimism. It is therefore advised that people follow the protective guidelines from WHO and relevant agencies.

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