

UNDERSTANDING THE 2019 NOVEL CORONAVIRUS OUTBREAK***Dr. Mohamed Ashraf PT. and Dr. Nehal ElKilany**

Pharmacist-Seha-Ahs- Abu Dhabi- UAE.

***Corresponding Author: Dr. Mohamed Ashraf PT**

Pharmacist-Seha-Ahs- Abu Dhabi- UAE.

Article Received on 10/02/2020

Article Revised on 01/03/2020

Article Accepted on 22/03/2020

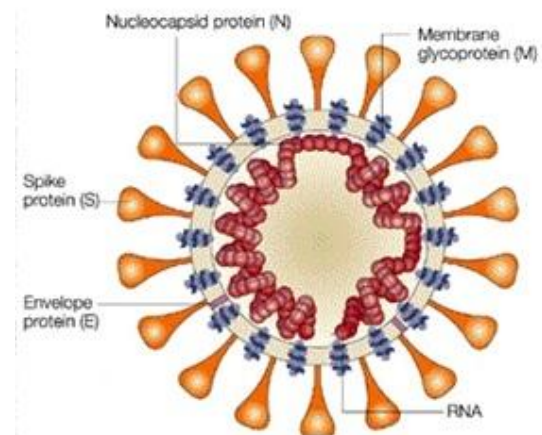
ABSTRACT

Coronaviruses are medium-sized enveloped positive-stranded RNA viruses, that belong to the beta coronavirus cluster, whose name is derived from the Latin “corona” meaning crown or halo, referring to their image under electron microscopy with crown like spikes on their surface similar to the solar corona. Covid-19 is the third known zoonotic corona virus disease after SARS and the Middle East respiratory syndrome (MERS). Coronaviruses cause acute and chronic respiratory, enteric and central nervous system (CNS) disease in many species of animals, including humans.

KEYWORDS: Beta coronaviruses, SARS, MERS, COVID19, zoonotic.**INTRODUCTION**

After the World Health Organization designated in February 2020 the disease COVID-19 (standing for coronavirus disease 2019), the organization announced COVID-19 outbreak a pandemic as of 13th of March 2020. The virus that causes COVID-19 is also known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); previously, it was referred to as 2019-nCoV.

In December 2019, China reported cases of a viral pneumonia caused by a previously unknown pathogen that emerged in Wuhan, a city of 11 million people in central China. The initial cases were linked to exposures in a seafood market in Wuhan where a large range of live animal and animal products were sold. The pathogen was identified as a novel (new) coronavirus (recently named Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is closely related genetically to the virus that caused the 2003 outbreak of Severe Acute Respiratory Syndrome (SARS). SARS-CoV-2 causes the illness now known as Coronavirus disease 2019 (COVID-19). Currently, there is no specific treatment (no vaccine and no antiviral) against the new virus.

**Figure 1: Schematic representation of the virus.**

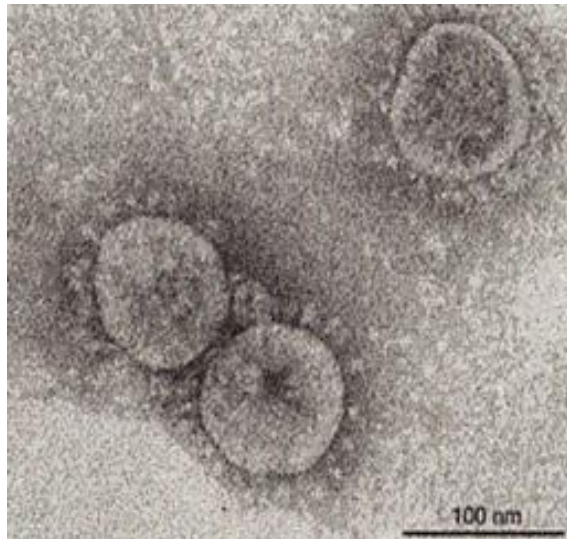


Figure 2: Electron micrograph of the Virus.

Cellular Receptor

Host receptor recognition is a determinant for virus infection. SARS coronaviruses (SARS-CoV) uses angiotensin-converting enzyme 2 (ACE2) as a receptor and primarily infect ciliated bronchial epithelial cells and type II pneumocytes, whereas MERS-CoV uses dipeptidyl peptidase 4 (DPP4) as receptor and infects unciliated bronchial epithelial cells and type II pneumocytes.^[1,2]

In 2013 Ge and colleague reported the whole genome sequence of SARS-like coronavirus in bats with ability to use human ACE2 as a receptor, thus having replication potentials in human cells.^[3]

According to early study it is suggested that 2019-nCov share the same receptor, (ACE2) with SARS-CoV. Based on the public database and the state-of-the-art single-cell RNA-seq technique that analyzed the ACE2 RNA expression profile in the normal human lungs. The results indicate that the ACE2 virus receptor expression is concentrated in a small population of type II alveolar cells.^[4] The study provides a biological background for the epidemic investigation of the 2019-nCov infection disease and could be informative for future anti-ACE2 therapeutic strategy development. Yet there is lack of analysis on receptor usage of 2019-nCov from the receptor perspective.

Mode of Transmission

There is limited knowledge regarding transmission of COVID-19, but the primary cases have been traced back to Huanan sea food market, with secondary cases occurring at hospitals among nurses and physicians who had extensive contact with COVID-19 patients. Also, several individuals who did not have direct contact with the Huanan seafood market were diagnosed with the disease. Transmission has been confirmed during close person-to-person contact, via respiratory droplets from coughs or sneezes.^[5,6]

Early on, many of the patients at the epicenter of the outbreak in Wuhan, Hubei province, China had some link to a large seafood and live animal market suggesting animal to human spread, and a growing number of patients reported did not have exposure to animal market, indicating human to human spread.

The three viruses (SARS, MERS, and COVID-19) are similar in zoonotic transmission from infected animals to humans. The MERS virus reservoir host is the dromedary camel, the SARS reservoir hosts are likely bats. It is still unclear whether COVID-19 was zoonotically transmitted from an infected civet cat, snake or other animal at the Huanan seafood market.

The common signs of COVID-19 infection include respiratory symptoms, fever, and cough, shortness of breath and breathing difficulties. Serious cases can lead to severe acute respiratory syndrome, kidney failure and death.^[7] Pneumonia appears to be the most frequent serious manifestation of infection and bilateral infiltrates on chest imaging. There are no specific clinical features that can yet reliably distinguish COVID-19 from other viral respiratory infections.^[7,8]

Leukopenia, leukocytosis and lymphopenia have been reported, although lymphopenia appears most common, elevated aminotransferase levels have also been described. On admission, many patients with pneumonia have normal serum procalcitonin levels; however, in those requiring intensive care unit (ICU) care, they are more likely to be elevated.^[9]

Clinical Management and Treatment

At present, there is no specific antiviral agent approved for treatment of this infection. Several existing antiviral agents are being used under clinical trial and compassionate use protocols based on in vitro activity (against this or related viruses) and on limited clinical experience.

Favipiravir, an antiviral drug that relies on RNA chain termination and possibly error catastrophe, was previously used against Ebola virus.^[20] The antiviral drug is currently approved as an investigational therapy to treat the COVID-19. Lopinavir-ritonavir is FDA-approved for treatment of HIV infection. As it targets protease, it has been used for other coronavirus infections; (used empirically for SARS) and is being studied in the treatment of MERS.^[10,11] In China, this combination in conjunction with Interferon alpha (IFN- α , an immunomodulatory drug used for hepatitis B & C) is used for treatment of some patients with COVID-19.^[12,13]

Remdesivir, an Ebola drug that targets polymerase, is an experimental antiviral agent with significant in vitro activity against coronaviruses^[14] with some evidence of efficacy in an animal model of MERS. Oseltamivir (Flu Drug that targets neuraminidase enzymes) used in Thailand in combination with Lopinavir and Ritonavir.

corticosteroids were used frequently to reduce inflammatory induced lung injury with high amount of cytokines induced by SARS-COV, MERS-COV, and 2019-nCoV infection. However the current evidence in patient with SARS and MERS suggest that receiving corticosteroid did not have an effect on mortality, but rather delayed viral clearance. Further evidence is urgently needed to know the beneficial or harmful effect for patient infected with 2019-nCoV.^[15, 16, 17, 18]

Supportive treatment includes oxygen supplementation and conservative fluid support. Management of septic shock includes cautious fluid resuscitation and use of vasopressors if fluid administration does not restore adequate perfusion. WHO provides guidance specific to the treatment of shock in patients with COVID-19.

In the absence of an approved vaccine, community mitigation measures are the primary way to reduce SARS-CoV-2 transmission among persons in the community, and adherence to recommended infection prevention and control measures can reduce the risk of SARS-CoV-2 spread in healthcare facilities. In the absence of an approved therapeutic with demonstrated safety and efficacy in patients with COVID-19, clinical management of COVID-19 patients includes supportive care of complications, including advanced organ support.^[19]

Preventive Measure for COVID-19 disease

Performing hand hygiene frequently with an alcohol based hand rub if your hands are not visibly dirty or with soap and water if hand are dirty is the most effective way to reduce the spread of the infection. Additional preventive measure include avoiding touching eyes, nose and mouth, practicing respiratory hygiene by coughing or sneezing into a bent elbow or tissue and then immediately disposing of the tissue, wearing medical

mask if respiratory symptoms appear and performing hands hygiene after disposing the mask. Moreover, it is essential to maintain social distance (minimum of 1 m) from individual with respiratory symptoms.^[20]

Risk of COVID-19 infection in Pregnant Woman

As intrauterine or perinatal transmission has not been identified yet, minimal information is available regarding Covid-19 during pregnancy. The approach to prevention, evaluation, diagnosis and treatment of pregnant women with suspected COVID-19 should be similar to that in non-pregnant individuals. The American College of Obstetricians and Gynecologists (ACOG) specifies that infants born to mothers with confirmed COVID-19 should be considered as patients under investigation, hence must be appropriately isolated and evaluated.

It is unknown whether the virus can be transmitted through breast milk; however, droplet transmission could occur through close contact during breastfeeding. ACOG recommends that mothers with confirmed COVID-19 or symptomatic mothers with suspected COVID-19 take precautions to prevent transmission to the infant during breastfeeding.^[21]

DISCUSSION

The new outbreak of respiratory illness caused by a novel coronavirus termed 'COVID-19' has emerged as a serious global public health concern. The illness was first announced on 31 December 2019, and the rapid spread of the virus is fueling fears as the global pandemic rises. During the initial period of the outbreak, from 8 December to 21 January 425 cases were identified and the number of cases reported and documented from the declaration of the initial outbreak, to date, has grown exponentially. At the time of writing, there are currently 153,527 cases of COVID-19, with 5735 deaths, and the virus has spread to 144 countries.

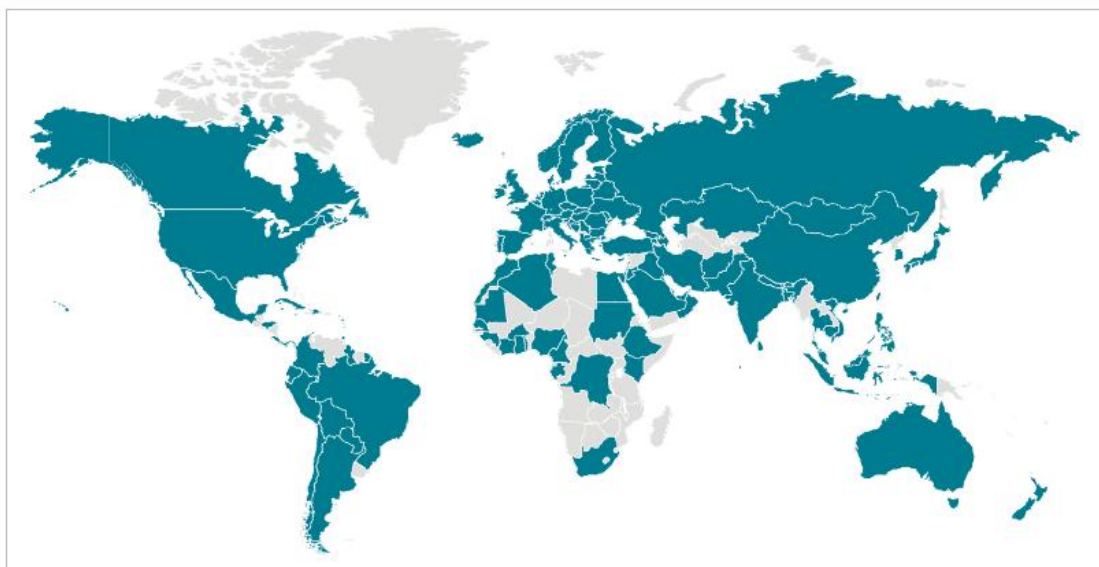


Figure 1: Global case numbers reported by the World Health Organization (WHO).

As now, countries are facing the hazard of community transmission and cluster horizontal spread of the disease across societies, quarantine & self-isolation measures are the most effective methods possible to reduce spread of the pandemic. Due to the ease of transmission of the virus, global rapid spread is affecting the global economy, hence emphasis must be put to develop measures to ease the economic pressures that societies will be facing after the economic fallout that will affect all the sectors of the community.

CONCLUSION

Presently COVID-19 spread from person to person, by the same mechanism as other common cold or influenza viruses, face-to-face contact with sneeze or cough or from contact with secretion of people who are infected. The three major patterns of the clinical infection is mild illness with upper respiratory tract presenting symptoms, non-life-threatening pneumonia, and severe pneumonia with acute respiratory distress syndrome that begin with mild symptoms for 7 to 8 days, and progresses to rapid deterioration, which is more likely among the elderly or those with comorbidities, such as diabetes, pulmonary disease, and other chronic conditions.

Non-pharmaceutical interventions remain central for management of COVID-19 because there are no licensed vaccines or coronavirus antivirals, continued research is important to understand the source of the outbreak by study of animals and animal handlers in markets to provide evidence necessary for prevention of future coronavirus outbreaks.

REFERENCES

- Li, W. H. et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*, 2003; 426: 450–454.
- Raj, V. S. et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature*, 2013; 495: 251–254.
- Ge X-Y, Li J-L, Yang X-L, et al. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature*, 2013; 503: 535–38.
- Zhou, P. et al. Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin. *bioRxiv*, 2020.2001.2022.914952, doi:10.1101/2020.01.22.914952 (2020).
- Huang C, Wang Y, Li X et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, 2020; 395: 497–506.
- Chan-Yeung M, Xu RH. SARS: epidemiology. *Respirology*, 2003; 8(Suppl 1): S9–14.
- Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA*, 2020.
- Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*, 2020.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*, 2020; 395: 507.
- Lopinavir-ritonavir is FDA-approved for treatment of HIV infection. It has been used for other coronavirus infections; it was used empirically for SARS 28 and is being studied in the treatment of MERS.
- Chu CM et al: Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*, 2004; 59(3): 252-6.
- Harrison C: Coronavirus puts drug repurposing on the fast track [news article]. *Nat Biotechnol.* ePub, 2020.
- Jin YH et al: A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*, 2020; 7(1): 4.
- Sheahan TP et al: Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun*, 2020; 11(1): 222.
- WHO: Clinical Management of Severe Acute Respiratory Infection When Novel Coronavirus (nCoV) Infection Is Suspected: Interim Guidance. WHO website. Updated January 28, 2020. Accessed March 2, 2020.
- Corticosteroid therapy for critically ill patients with Middle East respiratory syndrome. *Am J Respir Crit Care Med*, 2018; 197: 757-767.
- Corticosteroids as adjunctive therapy in the treatment of influenza. *Cochrane Database Syst Rev*, 2019; 2: CD010406.
- CDC: Coronavirus Disease 2019 (COVID-19): Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease 2019 (COVID-19). CDC website. Updated February 12, 2020. Reviewed February 25, 2020. Accessed March 2, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>
- CDC: Coronavirus Disease 2019 (COVID-19): How COVID-19 Spreads. CDC website. Updated March 4, 2020. Reviewed March 4, 2020. Accessed March 12, 2020. <https://www.cdc.gov/coronavirus/2019-ncov/about/transmission.html>.
- Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*, 2020; 395: 809.
- Guedj, Jérémie et al. “Antiviral efficacy of favipiravir against Ebola virus: A translational study in cynomolgus macaques.” *PLoS medicine* vol. 15, 3 e1002535. 27 Mar. 2018, doi:10.1371/journal.pmed.1002535.