Epidemiology and Pathogenesis of COVID-19, a Pandemic Novel Coronavirus Disease; Review from Global Perspectives

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) is an emerging global public health issue that was declared as a pandemic by the World Health Organization (WHO) on March 11, 2020. The disease is causing substantial mortality and morbidity after the first case emerged in the Wuhan city of China from the Huanen Seafood Market in late December 2019. This mini-review summarizes the information regarding the virology of the etiological agent, epidemiology, pathogenesis, clinical manifestation, laboratory diagnosis, and prevention by reviewing published literature as well as situation reports of WHO and other international organizations. The chronological incidence of COVID-19 uncovered a significant increasing trend ($P<0.01$) of confirmed and death cases in all regions of WHO. As of November 22, 2020, total cases of 57,882,183 and 1,377,395 deaths have been reported globally. Among WHO regions, the regions of the Americas and West Pacific contributed to the highest and lowest confirmed cases and death cases, respectively. Minimizing person-to-person contact, travel, and gathering is an effective way to control the current pandemic situation together with increased coverage of vaccines developed as specific antiviral drugs are not available to date for treatment. To combat the underlying serious global health problem caused by COVID-19, a controlling framework in the joint effort from governments is essential following the WHO guidelines at the global and regional levels.

***Keywords**: COVID-19; Coronavirus; Epidemiology; Pandemic; Pathogenesis; WHO*

INTRODUCTION

Taxonomically, Coronaviruses belong to the genus *Coronavirus* within the family Coronaviridae, subfamily Coronavirinae, and order Nidovirales, which comprises single-strand, positive-sense RNA viruses (Sahin, 2020). Morphologically, they are enveloped with size 120-160 nm in diameter, containing crown-shaped peplomers, from which the name 'Corona' was derived (Woo, Huang, Lau, & Yuen, 2010). They are remarkable among all RNA viruses due to the largest genome size i.e., ranging from 26 to 32 kb in length. Coronaviruses can rapidly replicate in a wide range of hosts i.e., humans, pigs, turkey, guinea fowls, bats, cats, dogs, camels, whales, ducks, and

avian hosts (Lu et al., 2020; Miłek & Domańska, 2018). Till now, there are seven types of Coronaviruses reported to cause human diseases i.e., 229E, NL63, OC43, HKU1, MERS-CoV, SARS-CoV, and COVID-19. Former four human Coronaviruses are low pathogenic, confined to upper respiratory tract infections, and cause cold-like respiratory illness, meanwhile, the latter three are highly pathogenic human Coronaviruses that predominantly infect the lower respiratory tract and cause fatal pneumonia (Channappanavar & Perlman, 2017). As the antigenic structure of Coronaviruses infecting animals, avian species, and humans are similar; there is a possibility of a shift between the hosts (Sahin, 2020). Previous epidemiological incidences caused by Coronaviruses i.e. SARS (Severe Acute Respiratory Syndrome), and MERS (Middle East Respiratory Syndrome) uncovered that derived strains are more pathogenic and could cause severe infection in humans. Recently, a new strain of Coronavirus first isolated from Wuhan, China in late December 2019 is causing massive infections and millions of deaths worldwide. This new strain of Coronavirus is also believed to have originated in bats but the intermediary animal host form which it jumped into a human is yet to be determined.

EPIDEMIOLOGY OF COVID-19

Incidences of pneumonia cases of unknown etiology were officially reported in December 2019. Later, it was disclosed that the outbreak is associated with Huanan Seafood Wholesale Market, Wuhan, China. The etiological agent of the disease i.e., a new type of Coronavirus was first isolated on January 7, 2020 (*WHO, Coronavirus disease 2019, Situation Report-01*, 2020). On January 13, 2020, the first incidence of the disease outside mainland China was confirmed in Thailand, which was the imported case from Wuhan, China. Further, imported cases were reported in two neighboring countries of China i.e., Japan and the Republic of Korea on 15 January 2020 and 20 January 2020, respectively (*WHO, Coronavirus disease 2019, Situation Report-01*, 2020). After 7736 confirmed cases and 170 deaths in China (Figure. 1), with very high risk in China and high risk at the regional and global scale, WHO officially declared a "public health emergency of international concern" on January 30, 2020 (*WHO, Coronavirus disease 2019, Situation Report-10*, 2020). On February 11, 2020, an official name was purposed by the World Health Organization for the disease i.e., COVID-19, which is an acronym that stands for coronavirus disease 2019 (*WHO, Coronavirus disease 2019, Situation Report-22*, 2020).

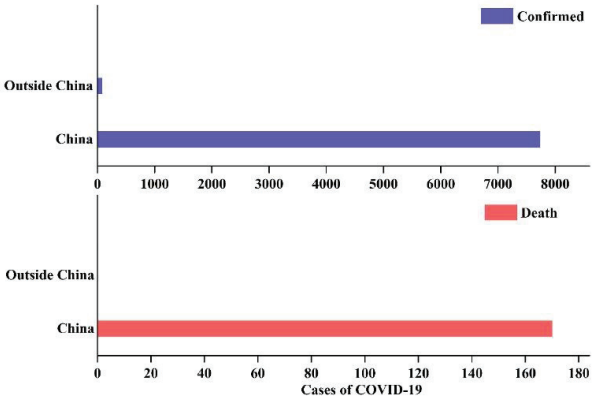

Figure 1. Incidence of COVID-19 infections and death cases when WHO declared a public health emergency of international concern (January 30, 2020)

With 118,319 confirmed cases from 114 countries and 4,292 deaths though mostly from epicenter China, the regional and global level

risk was very high. Considering the rapidly spreading coronavirus outbreak, WHO declared it a pandemic on March 11, 2020 (*WHO, Coronavirus disease 2019, Situation Report-51*, 2020). Based on the chronological order of case data published by WHO, confirmed and death cases of COVID-19 were higher in China till March 15, 2020, meanwhile, both confirmed cases and death cases peaked outside China from March 16 onwards (Figure. 2).

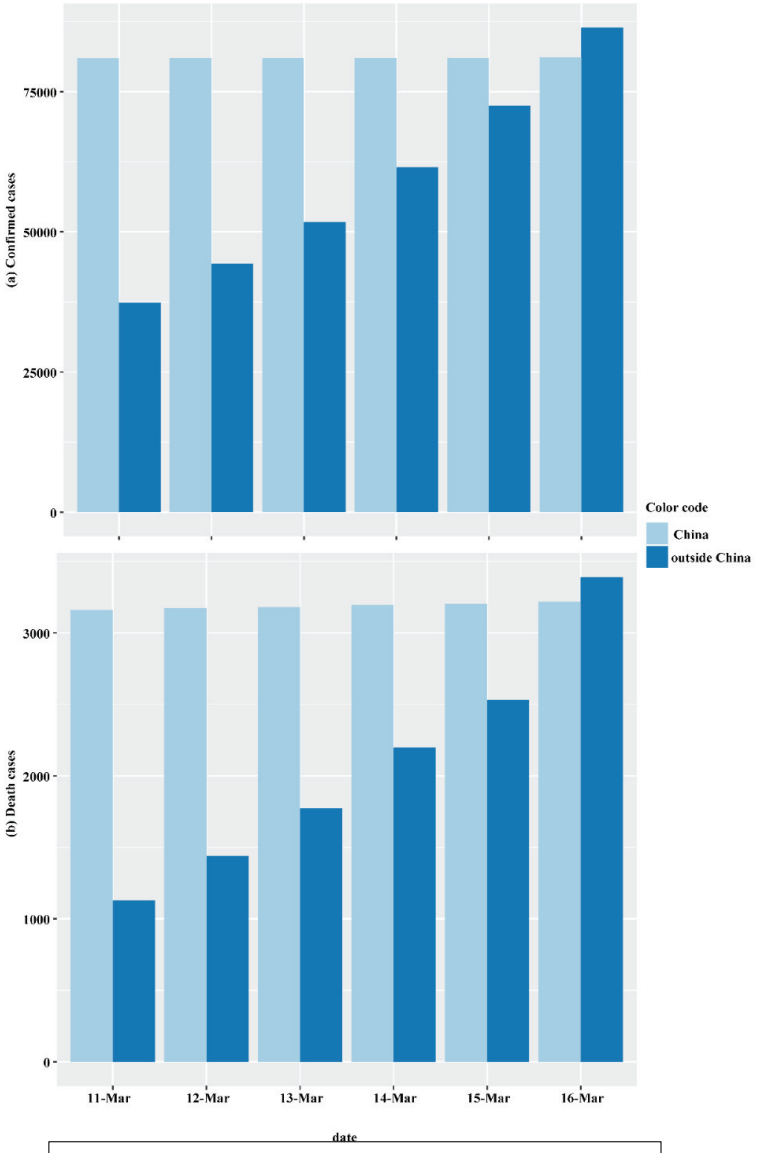

Figure 2 Chronological order (March 11-16) of confirmed (a) and death (b) cases of COVID-19 infections in China and outside China after the declaration of a pandemic by WHO. Data were extracted from the situation reports of WHO

Currently, both confirmed and death cases have been increasing in all regions of WHO i.e. African Region, Region of the Americas, South-East Asia Region, European Region, Eastern Mediterranean Region, and Western Pacific Region. Chronological incidence of COVID-19 infections (Figure. 3) with the highest-burden in the Americas and European Region. As of November 22, 2020, total cases of 57,882,183 and 1,377,395 deaths have been reported globally. Region of the Americas and West Pacific contributed to the highest and lowest confirmed cases and death cases, respectively. Region of the Americas alone contributed for 42% and 51% of total cases and deaths due to COVID-19 infection, respectively (*WHO, COVID-19 Weekly Epidemiological Update- November 24*, 2020). Based on trend analysis using Kendall's tau-b test (Adhikari et al., 2019), the monthly confirmed and death cases showed a significant increasing trend in all regions of WHO (P<0.01). The case fatality rate (CFR) i.e., deaths in COVID-19 patients divided by the total number of COVID-19 cases is different in different

countries, which may be due to the variation in the population of elderly people, population density as well as available health facilities in the selected region. The highest case fatality rate (CFR) was reported in Italy (Iype & Gulati, 2020), probably due to a larger proportion of elderly people.

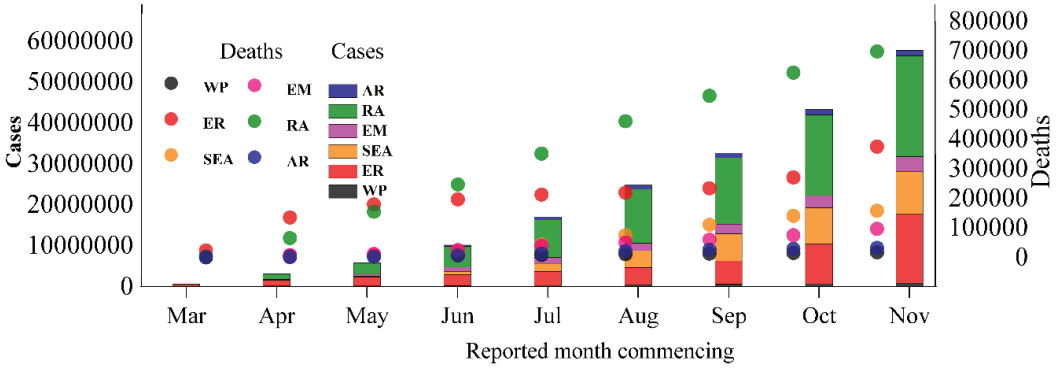

Figure 3 Chronological incidence of COVID-19 infections in different regions of WHO. Data were extracted on monthly basis from the situation reports of WHO. AR: African Region, RA: Region of Americas, EMR: Eastern Mediterranean Region, SEA: South-East Asia, ER: European Region, WPR: Western Pacific Region.

PATHOGENESIS OF COVID-19

Virus transmission occurs during close contact through respiratory droplets released from coughing or sneezing of infected individuals (Rothan & Byrareddy, 2020) or by fomites (*WHO, Coronavirus disease 2019 Situation Report-66*, 2020). Viral particles reach alveolar epithelial cells (the suspected primary target cells) by either of the ways. Envelope, the structural protein of the virus plays an important role in the pathogenesis of this virus. The entry of Coronavirus into host cells is mediated by spikes on their envelope, which then fuses into host cell membranes to release viral nucleocapsid into the host cell cytoplasm (Figure. 4). Viral spikes comprise S1 and S2 subunits. The S2- subunit of spike protein is the receptor-binding domain of the virus, which docks with the angiotensin-converting enzyme 2 (ACE2) in the host receptor (Rothan & Byrareddy, 2020; Wan, Shang, Graham, Baric, & Li, 2020). ACE-2 is a membrane-bound aminopeptidase expressed in the respiratory system, gut, heart, kidney as well as arterial and venous endothelial cells (Albini, Di Guardo, Noonan, & Lombardo, 2020). The expression of ACE-2 is comparatively higher in the lungs and heart (Zheng, Ma, Zhang, & Xie, 2020).

As soon as the viral nucleocapsids are released in the host cell cytosol, they use their own RNA Dependent RNA Polymerase (RdRP) and encode various structural and non-structural polypeptides that facilitate the adaptation of the virus into the human host. Matured virions are released from the infected cells via a process called exocytosis and form the main sign and symptoms. Virions disseminate to other body parts i.e., liver, kidney, intestines as well as T-lymphocytes (Sahin, 2020) (Figure. 4). Proliferated viruses activate immune cells and induce the secretion of pro-inflammatory and inflammatory cytokines as well as chemokines (Rothan & Byrareddy, 2020).

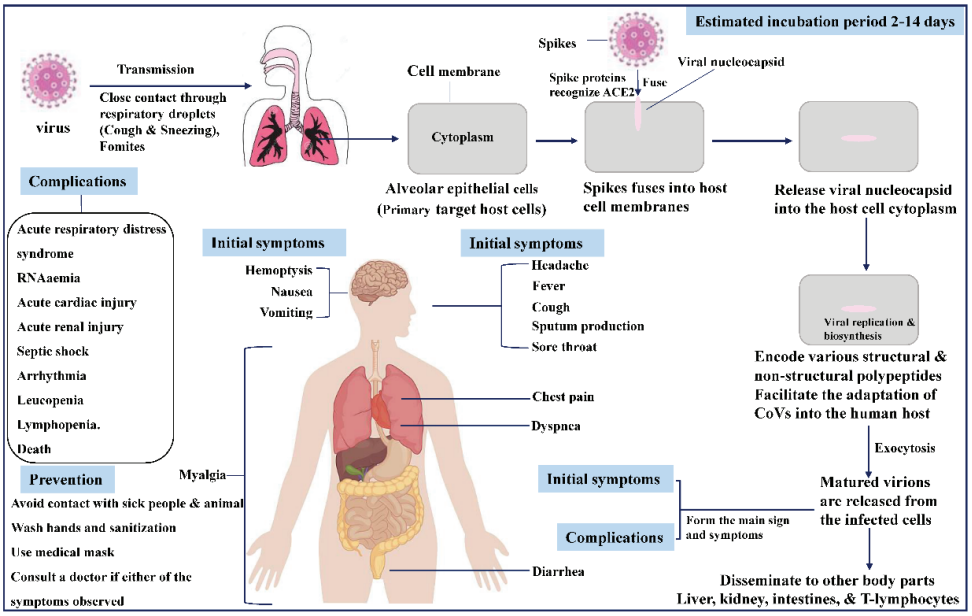

Figure. 4 General diagrammatic sketches showing the transmission, pathogenesis, and clinical manifestations of COVID-19 infection

CLINICAL MANIFESTATIONS

Based on the study including 425 COVID-19 subjects in Wuhan, the mean incubation period was 5.2 days, with the 95th percentile of the distribution at 12.5 days (Q. Li et al., 2020). A similar study on 88 subjects revealed an average incubation period of 6.4 days (Backer, Klinkenberg, & Wallinga, 2020). Though an unusual case showed 19 days incubation period, experts proposed 14 days quarantine period, considering a maximum incubation period of 14 days (Rockx et al., 2020). Clinical signs and symptoms are the consequences of viral replication in human cells. Initial symptoms reported in hospitalized COVID-19 patients are fever, cough, myalgia, dyspnea, headache, sore throat, chest pain, hemoptysis, sputum production, diarrhea, nausea, and vomiting (Albini et al., 2020; Jiang et al., 2020; *WHO, Coronavirus disease 2019 Situation Report-66*, 2020; Zheng et al., 2020). Complications of initial symptoms lead to acute respiratory distress syndrome, RNAaemia, acute cardiac injury, acute renal injury, septic shock, Arrhythmia, and death (Jiang et al., 2020) (Figure. 4). The progression of viruses in multiple organs leads to leucopenia and lymphopenia. Host immune cells also respond to the viral infection by producing various cytokines and chemokines i.e., IL1B, IL1RA, IL7, IL8, IL9, IL10, basic FGF, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1A, MIP1B, PDGF, TNFα (Huang et al., 2020).

DIAGNOSIS OF COVID-19

The primary diagnosis of COVID-19 is based on epidemiological data i.e., history of exposure to the infected area or infected individuals, signs and symptoms, as well as ancillary examinations like molecular tests, radiographic imaging, and serological tests, were conducted in pioneer treatments (Albini et al., 2020; Chen et al., 2020; Fengxiang et al., 2020; Jiang et al., 2020; X. Li, Geng, Peng, Meng, & Lu, 2020; Zheng et al., 2020). Throat swabs, bronchoalveolar lavage, sputum, blood, and feces can be potential specimens for laboratory diagnosis. The nucleic acid test (RT-PCR) is considered the gold standard for the authorized identification of viruses (X. Li et al., 2020). However, due to the huge gap between the number of contracted individuals and laboratory capacities to perform RT-PCR promptly, antigen-based rapid diagnostic tests (RDT) are also for COVID-19 diagnosis (Porte et al., 2020). Chest CT of a hospitalized patient in Wuhan revealed ground-glass opacity lesions were observed in the peripheral and posterior lungs. In addition to molecular and radiographic tools, histological tests are applicable in the diagnosis of COVID-19 as hospitalized patients had leucopenia and lymphopenia. Development and commercial production of more sensitive immunological detection kits targeting viral antigens or antibodies are being high demand in the recent scenario.

PREVENTION AND CONTROL

The first and foremost way to prevent this disease is vaccination. Till now, Pfizer-BioNTech COVID-19 vaccine and Moderna's COVID-19 vaccine are authorized and recommended to use for preventing Covid-19 by the Centers for Disease Control and Prevention (CDC) (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html). Also, several candidate vaccines are in clinical and preclinical evaluations. The vaccines use inactivated virus particle, DNA plasmid, RNA, protein subunit, replicating, and non-replicating viral vectors as a platform (*Draft landscape of COVID-19 candidate vaccines*, 2020). However, the best way to get rid of illness is to be aware of activities that may lead to exposure to the virus. CDC has recommended some preventive measures to minimize exposure to the causative agent. They are self-isolation to avoid person-to-person transmission, minimizing unnecessary travels, washing hands with soap-water or hand sanitizer, cleaning, and disinfecting frequently touched surfaces. Contact isolation wearing masks, gowns, and gloves is essential. Similarly, eye protection is also recommended to avoid possible ocular transmission.

Some broad-spectrum antiviral drugs have been experimented with and found to be successful for the treatment of COVID-19 infection. Some of the drugs used during the early outbreak of the disease in China, Japan, and South Korea are IFN-α, lopinavir/ritonavir, and ribavirin, Arbidol, Chloroquine phosphate, Favipiravir (Dong, Hu, & Gao, 2020). A study revealed that the combination of hydroxychloroquine and azithromycin resulted in viral load reduction/disappearance in COVID-19 patients (Gautret et al., 2020). Though, there is a great effort of scientists and experts for finding a suitable drug specific to COVID-19, neither of the drugs has been officially confirmed for usage yet.

CONCLUSION AND FUTURE PERSPECTIVES

There is a history of recurrent outbreaks of Coronavirus-associated diseases, and most of them are zoonotic in origin. The emergence of such diseases leads to the death of a large number of people and also causes great economic loss. COVID-19 cases and deaths are increasing globally, implying a serious global health problem. Thus, in this unprecedented situation, everyone should strictly follow the guidelines and preventive measures published by the WHO CDC, and national public health authorities. Reduction of person-to-person contact, and prohibition of traveling, and unnecessary gathering would be crucial to control the current pandemic. Special precautions and care should be applied in the susceptible population to prevent transmission. Intergovernmental and inter-continental cooperation is essential in the current situation. Detailed information on the epidemiological outbreak at global, regional, and country levels should be displayed out to develop strategies for future management. A controlling framework in the joint effort following one health approach is necessary following the WHO guideline in global, regional, and local communities to prevent future outbreaks. This might assist in structuring the specific and comprehensive public health measures.

COMPETING INTEREST

The authors declare that no competing interest exists.

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