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## Review

# Epidemiology and Pathogenesis of COVID-19: A Pandemic Novel Coronavirus Disease

Paudel Adhikari Namita<sup>1,2,\*</sup>, Bhusal Bhattarai Januka<sup>3,4,\*</sup>, , Adhikari Subash<sup>2,5</sup>

<sup>1</sup>Key Laboratory of Alpine Ecology and Biodiversity, Institute of Tibetan Plateau Research, Chinese Academy of Sciences, Beijing, China; <sup>2</sup>University of Chinese Academy of Sciences, Beijing, China; <sup>3</sup>Yangtze University, School of Medicine, Jingzhou, Hubei, China; <sup>4</sup>Departments of Obstetrics and Gynecology, Jingzhou Central Hospital, Jingzhou, Hubei, China; <sup>5</sup>Department of Microbiology, Janapriya Multiple Campus, Tribhuvan University, Pokhara 33700, Nepal.

\* These authors contributed equally.

### Correspondence

Bhusal Bhattarai Januka, Department of Obstetrics & Gynecology, Central Hospital of Jingzhou, College of Clinical Medicine, Yangtze university, Jingzhou city, Hubei-Province, PR China . Email: [j\\_bhusal@yahoo.com](mailto:j_bhusal@yahoo.com). Telephone number: 15272324894.

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## Abstract

COVID-19 is being an emerging public health issue, and WHO has already declared a pandemic with very high risk at a global level. This mini-review summarizes the information regarding the virology of the etiological agent, epidemiology, pathogenesis, clinical manifestation, and lab diagnosis from recent papers as well as situation reports of WHO. The chronological incidence of COVID-19 revealed that infections and death cases are rapidly increasing in all regions of WHO. Both local transmission and imported cases are reported in the global scenario. Reduction of person to person contact, traveling, and gathering is the best way to control the current pandemic situation as specific vaccines and antiviral drugs are not available for prophylaxis and treatment, respectively. To combat the underlying serious global health problem caused by COVID-19, a controlling framework in the joint effort is essential following the WHO guidelines at the global and regional levels.

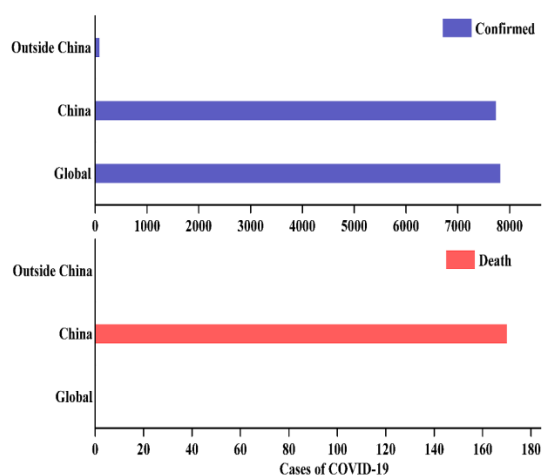
**Key words:** COVID-19; Coronavirus; Epidemiology; Pathogenesis; WHO; Pandemic

## Introduction

Taxonomically, Coronaviruses belong to genus *Coronavirus* within the family Coronaviridae, subfamily Coronavirinae, and order Nidovirales, which comprises of single-strand, positive-sense

RNA viruses [1]. Morphologically, they are enveloped with size 120-160 nm in diameter, containing crown-shaped peplomers, from which the name ‘Corona’ was derived [2]. They are remarkable among all RNA viruses due to the largest genome size, ranging from 26 to 32 kb in

length. Coronaviruses can rapidly replicate in a wide range of hosts, such as humans, pigs, turkey, guinea fowls, bats, cats, dogs, camels, whales, ducks, and avian hosts [3,4]. Till now, there are seven types of Coronaviruses reported to cause human diseases, 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 [5]. As the antigenic structure of Coronaviruses infecting animals, avian species, and humans are similar; there is a chance of shift between the hosts [1]. Previous epidemiological incidences caused by Coronaviruses 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 is causing severe infections and thousands of deaths worldwide. WHO has purposed the name COVID-19 for the new disease caused by a novel strain of coronavirus.

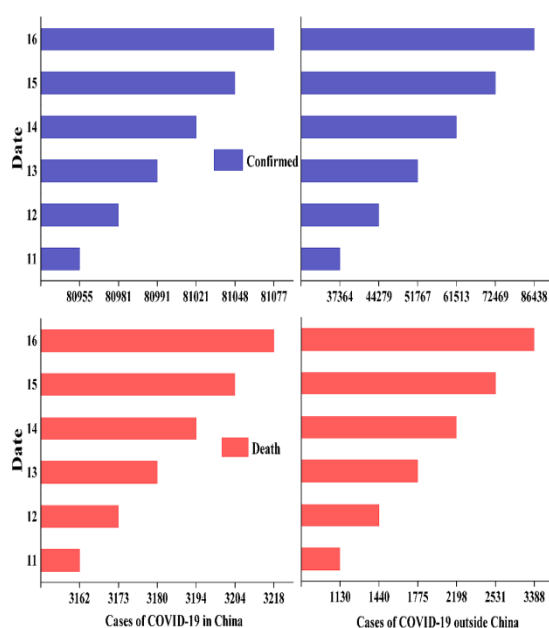


**Figure 1 Incidence of COVID-19 infections and death cases when WHO declared a public health emergency of international concern (January 30, 2020).**

### Epidemiology of COVID-19

Incidences of pneumonia cases caused by 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, a new type of Coronavirus was first isolated on January 7, 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, Japan and the Republic of Korea on 15 January 2020 and 20 January 2020, respectively [6]. 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 [7]. On February 11, 2020, an official name was purposed by the World Health Organization for the disease, COVID-19, which is an acronym that stands for coronavirus disease 2019 [8]. Having reported 118,319 contracted individuals, and 4,292 deaths from 114 countries and very high risk at local (epicenter-China), regional, and global level, WHO declared the rapidly spreading coronavirus outbreak a pandemic on March 11, 2020, which became the first pandemic caused by Coronavirus [9]. 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). In the current situation, both confirmed, and death cases have been reported from all regions of WHO. such as 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) and death cases (Figure 4) revealed that the number of infections and death is rapidly increasing in all regions of WHO with

Region of Americas and European Region being the most. Meanwhile, both confirmed, and death cases are comparatively more stable in Western Pacific Region. In the global scenario, transmission means are local transmission and imported cases. Till the date (15 June), highest and lowest confirmed cases are from Region of Americas and African Region, respectively. The case fatality rate (CFR), number of deaths in COVID-19 positive patients divided by number of COVID-19 positive cases is different in different countries, which is due to the variation in the population of elderly people, population density as well as available health facilities in the selected region. Highest CFR was reported in Italy [10], probably due to a large population of elderly people.



**Figure 2 Chronological order (March 11-16) of confirmed and death 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.**

### Pathogenesis of COVID-19

Viral transmission occurs during close contact through respiratory droplets released from coughing or sneezing of infected individuals [11]

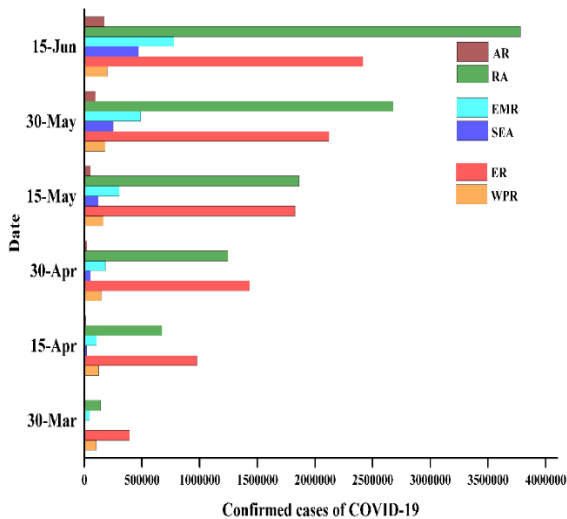
or by fomites [12]. Viral particles reach to alveolar epithelial cells (the suspected primary target cells) by either of the ways. Envelope, the structural protein of the virus plays an important role in the pathogenesis of this virus. The entry of Coronavirus into host cells is mediated by spikes on their envelope, which then fuses into host cell membranes to release viral nucleocapsid into the host cell cytoplasm. Viral spikes comprise of S1 and S2 subunits. The S1- 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 [11,13]. ACE-2 is a membrane-bound aminopeptidase expressed in the respiratory system, gut, heart, kidney as well as arterial and venous endothelial cells [14]. The expression of ACE-2 is comparatively higher in the lungs and heart [15].

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 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, such as liver, kidney, intestines as well as T-lymphocytes [1] (Figure 5). Proliferated viruses activate immune cells and induce the secretion of pro-inflammatory and inflammatory cytokines as well as chemokines [11].

### Clinical manifestations

Based on the study including 425 COVID-19 subjects in Wuhan, the mean incubation period was 5.2 days, with the 95<sup>th</sup> percentile of the distribution at 12.5 days [16]. A similar study on 88 subjects revealed an average incubation period of 6.4 days [17]. Though an unusual case showed 19 days incubation period, experts purposed 14 days quarantine period, considering a maximum incubation period of 14 days [18]. 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 [12,14,15,19]. Complications of initial symptoms lead to acute respiratory distress syndrome, RNAemia, acute cardiac injury, acute renal injury, septic shock, Arrhythmia, and death [19] (Figure 5). 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, such as IL-1B, IL-1RA, IL-7, IL-8, IL-9, IL-10, basic FGF, GCSF, GMCSF, IFN- $\gamma$ , IP-10, MCP-1, MIP-1A, MIP-1B, PDGF, TNF- $\alpha$  [20].

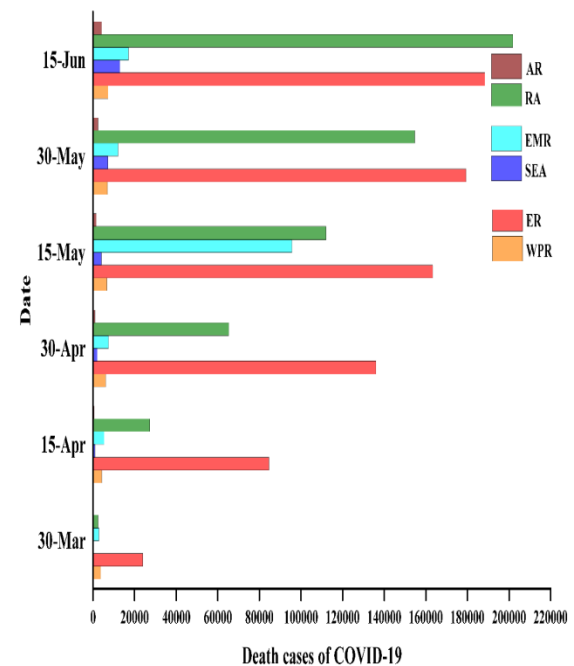


**Figure 3 Chronological incidence of COVID-19 infections in different regions of WHO. Data were extracted on a biweekly basis from the situation reports of WHO. AR: African Region, RA: Region of Americas, EMR: Eastern Mediterranean Region, SEA: South-East Asia, ER: European Region, WPR: Western Pacific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

**Diagnosis of COVID-19**

The primary diagnosis of COVID-19 is based on epidemiological data, such as 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 [14,15,19,21–23]. Throat swab, bronchoalveolar lavage, sputum, blood, and feces can be potential specimens for the laboratory diagnosis. Rapid diagnostic tool (RDT) is a potentially important tool for rapid antigen detection in the early stages, though nucleic acid test (RT-PCR) is considered as the gold standard for the authorized identification of viruses [23]. However, due to the huge gap between the number of contracted individuals and laboratory capacities to perform RT-PCR promptly, RDT is preferred in low and middle-income countries [24]. 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 a high demand in the recent scenario.



**Figure 4 Chronological incidence of COVID-19 death cases in different regions of WHO. Data were extracted on a biweekly 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.

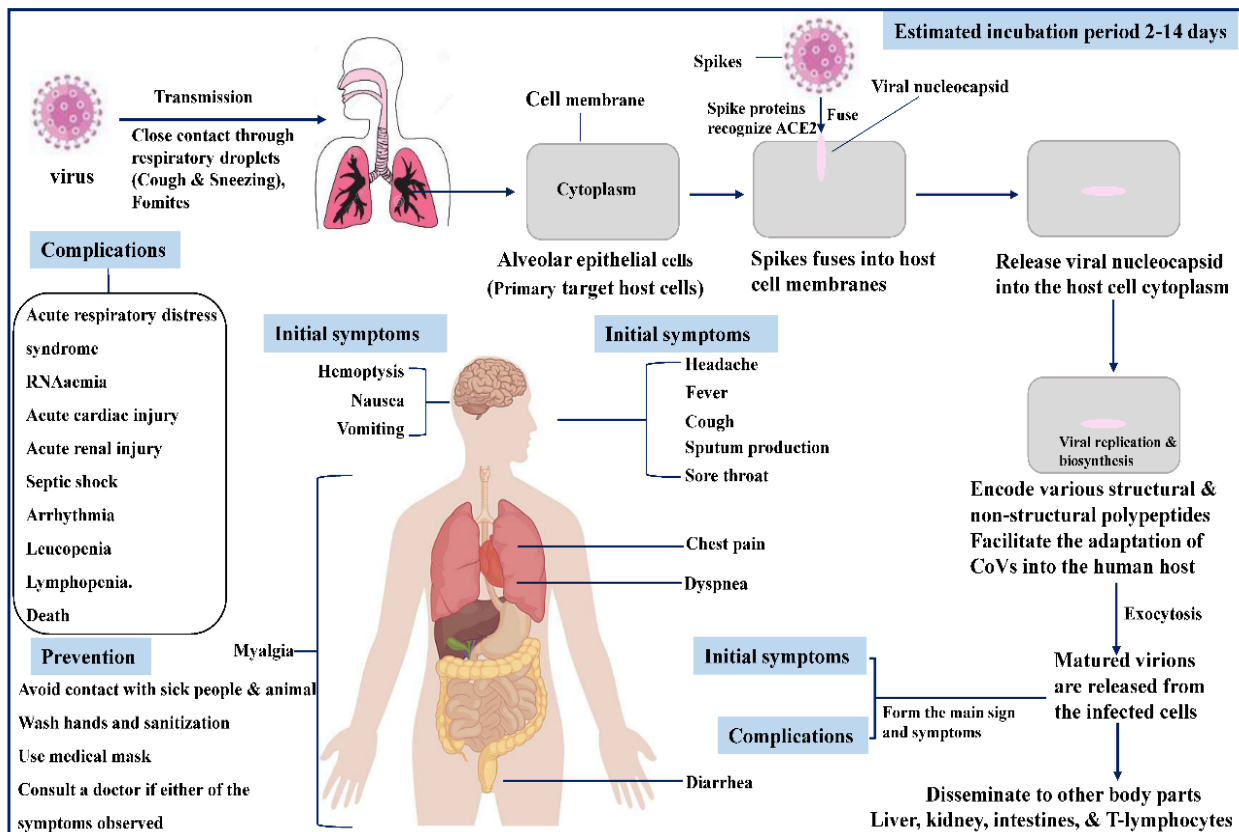
**Prevention and control**

Since vaccines against COVID-19 are not available yet, the best way to get rid of illness is being aware of activities that may lead to exposure to the virus. Center for disease control and prevention (CDC) has recommended some preventive measures to minimize the exposure with 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 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- $\alpha$ , lopinavir/ritonavir, and ribavirin, Arbidol, Chloroquine phosphate, Favipiravir [25]. A study revealed that the combination of hydroxychloroquine and azithromycin resulted in viral load reduction/disappearance in COVID-19 patients [26].

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 the usage yet!.



**Figure 5** General diagrammatic sketch showing the transmission, pathogenesis and clinical manifestations of COVID-19 infection

### 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 many people and great economic loss. COVID-19 cases are increasing globally, implying a serious global health problem. Thus, in this harsh situation, everyone should strictly follow the guidelines and preventive measures published by the WHO and CDC. Reduction of person to person contact, traveling, and gathering should be prohibited to control the current pandemic situation. 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 in global, regional, and country levels should be displayed out to develop strategies for future management. A controlling framework in the joint effort 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.

### Declarations

#### 1) *Consent to publication*

We declare that we all authors agreed to publish the manuscript at this journal based on the signed Copyright Transfer Agreement and followed publication ethics.

#### 2) *Ethical approval and consent to participants*

We declare that our research protocols involving humans or animals were approved by their Institutional Ethics Committee and we obtained Informed Consent from Participants enrolled in our study.

#### 3) *Disclosure of conflict of interests*

We declare that no conflict of interest exists.

#### 4) *Funding*

None

#### 5) *Availability of data and material*

We declare that the data supporting the results reported in the article are available in the published article.

#### 6) *Authors' Contributions*

7) Authors contributed to this paper with the design (NPA), literature search (NPA and SA), drafting (NPA), revision (NPA, SA, and JBB), editing (JB and SA) and final approval (NPA). **Acknowledgement**

None

#### 8) *Authors' biography*

None

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