

Coronavirus Disease-19 (Severe Acute Respiratory Syndrome-Coronavirus-2) is not Just Simple Influenza: What have we Learned so Far?

Since December 2019, the world is experiencing a global, rapidly evolving spread of a novel coronavirus (2019-nCoV). Scientists, public health practitioners, clinicians, and health officials are racing to understand more about the nature of this virus. Every day, there is a new discovery, but there are so many inquiries that need to be addressed and unknowns that need to be explored.

2019-nCoV emerged first in Wuhan, Hubei Province, China, which is a major transportation hub with a population of more than 11 million people.^[1] The majority of the initially diagnosed 41 confirmed cases and admitted with pneumonia visited a local fish and wild animal market in the previous month.^[2] The World Health Organization (WHO) named this virus (COVID-19), while the International Committee on Taxonomy of Viruses has renamed as severe acute respiratory syndrome-coronavirus (SARS-CoV-2).^[3] Although calling the virus as “SARS-CoV-2” is probably more accurate, for simplicity, we will use the WHO name (COVID-19) in this editorial.

On January 30, 2020, the WHO declared the COVID-19 outbreak as the sixth public health emergency of international concern due to the fact that this virus is transmitted from human to human through droplets and direct or indirect contact, and carry a great potential to lead to pandemic disease.^[4] Viral shedding of the virus from the upper respiratory tract can continue up to 1–3 weeks in symptomatic patients from the initial onset of symptoms.^[5,6] This virus can be shed in the stool of the asymptomatic patients up to 17 days of last exposure to the virus.^[7] Asymptomatic patients or a presymptomatic carriers have the potential to transmit SARS-CoV-2 to others.^[8] Contaminated inanimate surfaces surrounding the patients with COVID-19 in the hospital should not be overlooked as a major source of transmission of infection.^[9]

At the time of writing this editorial, SARS CoV-2 has spread in 168 countries and the number of confirmed cases exceeded 270,000; more than 69.4% were outside China, and 30.6% of the cases were in China, with approximately 12,000 (4.2%) recorded deaths globally. The documented deaths in Italy secondary to COVID-19 infection were 4032, exceeding China with 3,261 deaths. Italy as well reported the highest number of confirmed cases outside China ($n = 47,021$) followed by Spain ($n = 19,980$), and then Iran ($n = 19,644$).^[10] These countries outside China with ongoing local transmission are documented to be a new focus on transmission of COVID-19 to neighboring countries in the Arabian Gulf countries, the

Middle East, and Europe. The WHO, on March 11, 2020, stated that “after making the necessary assessment COVID-19 can be characterized as a pandemic.”

COVID-19 was found to be a positive-sense, single-stranded RNA virus belonging to the genus Betacoronavirus.^[11] Several coronaviruses are known to cause human respiratory diseases like coronavirus 229E/NL63/OC43, which causes mainly mild upper respiratory tract infection in normal hosts. In contrast, others like SARS-CoV-1 and MERS-CoV can cause severe lower respiratory tract infection and acute respiratory distress syndrome (ARDS) as well as outbreaks similar to SARS CoV-2.^[11] A recent genomic study of COVID-19 proposed bat or bat excreta as the source of the COVID-19 that contaminated food in markets^[12] and rejected the other hypothesis of emergence as a result of a recent recombination event.^[13] COVID-19 genomic sequence showed more than 80% similar identity of this virus to SARS-CoV-1 and only 50% identity to MERS-CoV.^[11,14]

Clinically, in a recent review of 1099 of laboratory-confirmed cases in China, fever was documented in 43% of the patients on admission and 93% during hospitalization, and cough in 67.8%, while only 3.8% had diarrhea.^[15] The median incubation period was 4 days (interquartile range, 2–7); however, it may extend up to 14 days. Therefore, isolation of contacts of patients with COVID-19 should be put on quarantine for 14 days.

Ground glass appearance on chest CT scan was found reported in 56.4% of the patients and lymphopenia was the major hematological finding (83.2%).^[15] Among all patients presented, mild disease was seen in 81%, severe in 14%, and only 5% had critically severe illness.^[16] Another study reported the following organs function failure, ARDS (17%), acute respiratory injury (8%), acute renal injury (3%), and septic shock (4%).^[17] The patients admitted to the intensive care units (ICUs) were more likely to be elderly patients with underlying comorbid chronic medical disorders.^[18] Children can be infected with COVID-19, and they usually present with a milder disease; however, they might act as carriers and spread the infection to close contacts.^[19]

The reported mortality rate of patients with COVID-19 pneumonia ranges from 4.3%–14.6%.^[18,20] The fatality rate reported by the Chinese Center for Disease Control and Prevention among all patients with COVID-19 was 2.3%, which is much lower than the rate of previous studies from Wuhan that reported a fatality rate of 3.28%, and higher than the recently reported fatality rate from Beijing 0.9%.^[16,17,20–22]

The possible explanation for the high fatality in initial studies from Wuhan is the inclusion of only sick patients presented to the health-care facilities, rather than including all cases confirmed with COVID-19 infection. The WHO on March 4, 2020, estimated that the global COVID-19 death rate is 3.4%. It has been proven that mortality rate varies significantly with highest mortality rate among patients ≥ 80 years of age 14.8%, 70-79 years (8%), 60-69 years 3.6%, 50-59 years 1.3%, < 50 years 0.4%.^[16]

Furthermore, the investigators suggested that the development of a new variation in the functional sites in the receptor-binding domain (RBD) of the spike seen in COVID-19 due the viral evolution as a result of mutation, selection and recombination evolve into two major types (L-type and S-type), each has different (Single Nucleotides Polymorphisms) SNPs. The L-type is the one that spread quickly initially during the outbreak in Wuhan (70%) and was associated with more severe disease, and decreased in early January, while Type S is the ancestral version (30%) that spreads afterward and is less aggressive. Some patients have been found to be infected by both types.^[23]

All suspected cases of COVID-19 should be tested using the recommended molecular method recommended by the WHO.^[24] A negative nasopharyngeal/oropharyngeal sample result should not be used to rule out COVID-19 infection. It is known that the target functional receptor of these viruses is angiotensin-converting enzyme 2 (ACE2) that is mainly located on Type 1 and Type 2 alveolar cells.^[25] It is recommended that all results be interpreted in concordance with the clinical suspicion and epidemiological link.^[26]

Serological tests for COVID-19 may detect the infection in patients with symptoms or asymptomatic patients. The fact that these tests (IgM, IgG) might take from few days to a couple of weeks after the development of symptoms in order to be detected, and the issue of cross-reactivity with other viruses make their clinical utility in the management of acutely ill patients surrounded by limitation and skepticism. However, serological tests, in general, have superior value in epidemiological studies in the hospital setting and the community for contact tracing and to estimate the burden of the disease.^[27,28] Currently, there are no approved specific antiviral treatments or vaccination for COVID-19.^[29] However, several treatment options have recently been used for the treatment of patients with COVID-19 pneumonia in Wuhan, China, including; ganciclovir, oseltamivir, and lopinavir/ritonavir, twice a day for a duration ranging from 3 to 14 days in 75% of the patients.^[17,18,20] Other promising drugs are remdesivir, chloroquine, and tocilizumab, and clinical trials on these medications are going on in the USA, Europe, and China.^[30,31]

Recently, studies demonstrated clinical and virologic benefits of chloroquine and hydroxychloroquine in patients with COVID-19 compared to controls.^[30,31] Based on limited in-vitro and anecdotal data, chloroquine and hydroxychloroquine are currently recommended for the treatment of hospitalized

COVID-19 patients in several countries. Both drugs have known safety profiles; the main side effect is cardiotoxicity (prolonged QT syndrome) after prolonged use in patients with hepatic or renal impairment and those who are immunosuppressed. However, both drugs were reportedly well-tolerated in COVID-19 patients. Hydroxychloroquine is currently under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of COVID-19 infection, and treatment of patients with mild, moderate, and severe infection. A randomized, controlled, non-blinded study in hospitalized patients with severe COVID-19 showed no benefits of treatment lopinavir/ritonavir beyond the standard care.^[32-34] Several academic centers and many biopharmaceutical companies are currently working to develop a vaccine for COVID-19. Several potential targets, including DNA, mRNA, proteins, and adenovirus vectors, have been identified. We hope that with global collaboration among all international medical centers and sharing the knowledge and expertise, a new development of an effective vaccine for COVID-19 will evolve soon.^[35] Recently, the US National Institute of Allergy and Infectious Diseases announced phase I human trial to develop (mRNA-1273 to express viral spike protein) vaccine for COVID-19.^[36]

Urgent collaboration and cooperation among all health care sectors, public health, and governments are required globally.^[37] It is very important to communicate the epidemiological and clinical data and the risk of COVID-19 infection to health-care workers and the general population, and to activate public health education based on evidence sound scientific information to prevent misinformation that might lead to distress and anxiety of the public.^[38] The effective approach to the control of COVID-19 is to limit human-to-human transmission through practicing evidence-based community measures, i.e., rigorous hand hygiene with alcohol based or water and soap, cough etiquette, and face masks only for persons with upper respiratory tract infection.^[39] Additionally, distant social measures and international travel based following the country recommendation based on the risk assessment to minimize the social and economic impact of these measures.^[40] Infection prevention and control (IPC) measures should be implemented strictly in all health-care facilities to prevent the spread of the infection to vulnerable patients and to protect the health-care workers. Clear protocols for all IPC measures should be in place, i.e., early identification of the suspected cases, early and proper isolation, wearing the appropriate personal protective equipment (PPE), effective terminal cleaning of the room after each COVID-19 patient transfer, educational campaigns, and audits as well as efficient communication with public health.^[41]

There is a misconception among some practitioners and the general public that COVID-19 infection will diminish and disappear during summer. However, there are no data to support that COVID-19 is a seasonal infection. Therefore, all recommended prevented measures should continue during summer until the WHO or other national and international health authorities announce information about the behavior of COVID-19 during summertime.

In summary, COVID-19 is an emerging virus considered as a global public health emergency, which requires a collaborative higher level of responsive measures from all countries. Efficient communication, collaboration, and cooperation in implementing scientific evidence-based measures on the personal, national, and international levels are crucial. Urgent clinical trials on potential drugs for COVID-19 are required, and the development of an efficient and safe vaccine is a public health priority. More research is urgently needed to better understand the epidemiology, transmission, pathogenesis, and clinical severity of the COVID-19 infection.

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