The Pharma Innovation Journal 2020; 9(4): 07-10

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2020; 9(4): 07-10

www.thepharmajournal.com
Received: 07-02-2020
Accepted: 09-03-2020

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A review of the 2019 novel coronavirus (COVID-19) based on current evidence

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Abstract
Coronavirus (COVID-19) is an enveloped RNA virus that is diversely found in humans and wild life. A total of six species have been identified to cause disease in humans. They are known to infect the neurological, respiratory, enteric, and hepatic systems. The past few decades have seen endemic outbreaks in the form of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome Related Coronavirus (SARS-CoV). Yet again, we see the emergence of another outbreak due to a new strain called the SARS-CoV-2 virus. The most recent outbreak initially presented as pneumonia of unknown etiology in a cluster of patients in Wuhan, China. The epicenter of infection was linked to seafood and exotic animal wholesale markets in the city. SARS-CoV-2 is highly contagious and has resulted in a rapid pandemic of COVID-19. As the number of cases continues to rise, it is clear that these viruses pose a threat to public health. This review will introduce a general overview of coronavirus and describe the clinical features, evaluation, and treatment of COVID-19 patients. It will also provide a means to raise awareness among primary and secondary healthcare providers during the current pandemic. Furthermore, our review focuses on the most up-to-date clinical information for the effective management, prevention, and counseling of patients worldwide.

Keywords: COVID-19, coronaviruses, respiratory infection, SARS- CoV

Introduction
Coronavirus (CoV) is a large family of positive-sense, single-stranded RNA viruses that belong to the Nidovirales order. The order includes Roniviridae, Arteriviridae, and Coronaviridae families [1]. The Coronaviridae family is subdivided into Torovirinae and Coronavirinae subfamilies [1]. Coronavirinae is further subclassified into alpha-, beta-, gamma-, and delta-COVs [1]. Phylogenetic clustering accounts for the classification of these subtypes of viruses. Their viral RNA genome ranges from 26 to 32 kilobases in length [2]. They can be isolated from different animal species. These include birds, livestock, and mammals such as camels, bats, masked palm civets, mice, dogs, and cats [2]. The widespread distribution and infectivity of COV make it an important pathogen.

Origin and Spread of COVID-19
In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause. Many of the initial cases had a common exposure to the Huanan wholesale seafood market that also traded live animals. The surveillance system (put into place after the SARS outbreak) was activated and respiratory samples of patients were sent to reference labs for etiologic investigations. On December 31st 2019, China notified the outbreak to the World Health Organization and on 1st January the Huanan sea food market was closed. On 7th January the virus was identified as a coronavirus that had >95% homology with the bat coronavirus and > 70% similarity with the SARS- CoV. Environmental samples from the Huanan sea food market also tested positive, signifying that the virus originated from there [5]. The number of cases started increasing exponentially, some of which did not have exposure to the live animal market, suggestive of the fact that human-to-human transmission was occurring [6]. The first fatal case was reported on 11th Jan 2020. The massive migration of Chinese during the Chinese New Year fueled the epidemic. Cases in other provinces of China, other countries (Thailand, Japan and South Korea in quick succession) were reported in people who were returning from Wuhan. Transmission to healthcare workers caring for patients was described on 20th Jan, 2020. By 23rd January, the 11 million population of Wuhan was placed under lock down with restrictions of entry and exit from the region.

Soon this lock down was extended to other cities of Hubei province. Cases of COVID-19 in countries outside China were reported in those with no history of travel to China suggesting that local human-to-human transmission was occurring in these countries [7]. Airports in different countries including India put in screening mechanisms to detect symptomatic people returning from China and placed them in isolation and testing them for COVID-19. Soon it was apparent that the infection could be transmitted from asymptomatic people and also before onset of symptoms. Therefore, countries including India who evacuated their citizens from Wuhan through special flights or had travelers returning from China, placed all people symptomatic or otherwise in isolation for 14 day and tested them for the virus.
Cases continued to increase exponentially and modelling studies reported an epidemic doubling time of 1.8 d [8]. In fact on the 12th of February, China changed its definition of confirmed cases to include patients with negative/ pending molecular tests but with clinical, radiologic and epidemiologic features of COVID-19 leading to an increase in cases by 15,000 in a single day [4]. As of 05/03/2020 96,000 cases worldwide (80,000 in China) and 87 other countries and 1 international conveyance (696, in the cruise ship Diamond Princess parked off the coast of Japan) have been reported [3].
It is important to note that while the number of new cases has reduced in China lately, they have increased exponentially in other countries including South Korea, Italy and Iran. Of those infected, 20% are in critical condition, 25% have recovered, and 3310 (3013 in China and 297 in other countries) have died [3]. India, which had reported only 3 cases till 2/3/2020, has also seen a sudden spurt in cases. By 5/3/2020, 29 cases had been reported; mostly in Delhi, Jaipur and Agra in Italian tourists and their contacts. One case was reported in an Indian who traveled back from Vienna and exposed a large number of school children in a birthday party at a city hotel. Many of the contacts of these cases have been quarantined.
These numbers are possibly an underestimate of the infected and dead due to limitations of surveillance and testing. Though the SARS-CoV-2 originated from bats, the intermediary animal through which it crossed over to humans is uncertain. Pangolins and snakes are the current suspects.

Types
Coronaviruses belong to the subfamily *Coronavirinae* in the family *Coronaviridae*.
Different types of human coronaviruses vary in how severe the resulting disease becomes, and how far they can spread.
Doctors currently recognize seven types of coronavirus that can infect humans.
Common types include:

- 229E (alpha coronavirus)
- NL63 (alpha coronavirus)
- OC43 (beta coronavirus)
- HKU1 (beta coronavirus)

Rarer strains that cause more severe complications include MERS-CoV, which causes Middle East respiratory syndrome (MERS), and SARS-CoV, the virus responsible for severe acute respiratory syndrome (SARS).
In 2019, a new strain called SARS-CoV-2 started circulating, causing the disease COVID-19.

Transmission
Limited research is available on how HCoV spreads from one person to the next.
However, researchers believe that the viruses transmit via fluids in the respiratory system, such as mucus.
Coronaviruses can spread in the following ways:

- Coughing and sneezing without covering the mouth can disperse droplets into the air.
- Touching or shaking hands with a person who has the virus can pass the virus between individuals.
- Making contact with a surface or object that has the virus and then touching the nose, eyes, or mouth.
- Some animal coronaviruses, such as feline coronavirus (FCoV), may spread through contact with feces. However, it is unclear whether this also applies to human coronaviruses.

Coronaviruses will infect most people at some time during their lifetime.
Coronaviruses can mutate effectively, which makes them so contagious.
To prevent transmission, people should stay at home and rest while symptoms are active. They should also avoid close contact with other people.

Covering the mouth when sneezing may help stop the spread of coronaviruses

Symptoms of COVID-19
Symptoms vary from person-to-person with COVID-19. It may produce few or no symptoms. However, it can also lead to severe illness and may be fatal. Common symptoms include:

- fever
- breathlessness
- cough
- potential loss of taste or smell

It may take 2–14 days for a person to notice symptoms after infection.
No vaccine is currently available for COVID-19. However, scientists have now replicated the virus. This could allow for early detection and treatment in people who have the virus but are not yet showing symptoms.
The National Institutes of Health (NIH) suggest that several groups of people have the highest risk of developing complications due to COVID-19. These groups include:

- young children
- people aged 65 years or older
- women who are pregnant

The CDC advise that although there have been reports of complications in young children, these are rare. COVID-19 most commonly produces mild symptoms in children.
Covering the mouth and nose with a tissue or handkerchief while coughing or sneezing can also help prevent transmission. It is important to dispose of any tissues after use and maintain hygiene around the home.

Diagnosis
The U.S. CDC has developed criteria for persons under investigation (PUI) [9]. If a person is deemed a PUI, immediate prevention and infection control measures are undertaken. Epidemiological factors are used to assess the requirement of testing. These include close contact with a laboratory-confirmed patient within 14 days of symptoms or travel history to an infected area within 14 days of symptom onset [9].
The WHO recommends collecting samples from both the upper and lower respiratory tracts. This can be achieved through expectorated sputum, bronchoalveolar lavage, or endotracheal aspirate [9]. These samples are then assessed for viral RNA using polymerase chain reaction (PCR). If a positive test result is achieved, it is recommended to repeat the test for re-verification purposes. A negative test with a strong clinical suspicion also warrants repeat testing.

Prevention
Preventive measures are the current strategy to limit the spread of cases. Because an epidemic will increase as long as R0 is greater than 1 (COVID-19 is 2.2), control measures must focus on reducing the value to less than 1.
Preventive strategies are focused on the isolation of patients and careful infection control, including appropriate measures to be adopted during the diagnosis and the provision of clinical care to an infected patient. For instance, droplet, contact, and airborne precautions should be adopted during specimen collection, and sputum induction should be avoided.
The WHO and other organizations have issued the following general recommendations:

- Avoid close contact with subjects suffering from acute respiratory infections.
- Wash your hands frequently, especially after contact with infected people or their environment.
- Avoid unprotected contact with farm or wild animals.
- People with symptoms of acute airway infection should keep their distance, cover coughs or sneezes with disposable tissues or clothes and wash their hands.
- Strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections.
- Individuals that are immunocompromised should avoid public gatherings.

The most important strategy for the populous to undertake is to frequently wash their hands and use portable hand sanitizer and avoid contact with their face and mouth after interacting with a possibly contaminated environment.
Healthcare workers caring for infected individuals should utilize contact and airborne precautions to include PPE such as N95 or FFP3 masks, eye protection, gowns, and gloves to prevent transmission of the pathogen.
Meanwhile, scientific research is growing to develop a coronavirus vaccine. In recent days, China has announced the first animal tests, and researchers from the University of Queensland in Australia have also announced that, after completing the three-week in vitro study, they are moving on to animal testing. Furthermore, in the U.S., the National Institute for Allergy and Infectious Diseases (NIAID) has announced that a phase 1 trial has begun for a novel coronavirus immunization in Washington state.

Treatment
Remdesivir (GS-5734)
Remdesivir is an investigational monophosphoramidate prodrug of an adenosine analog that was developed by Gilead Sciences, Inc. in response to the Ebola outbreak in West Africa from 2014-2016. In its active triphosphate nucleoside form, remdesivir binds to RNA-dependent RNA polymerase and acts as an RNA-chain terminator. It displays potent in vitro activity against SARS-CoV-2 with an EC50 at 48 hours of 0.77 µM in Vero E6 cells. [10] Similar activity has been demonstrated against other zoonotic coronaviruses with EC50 values of 0.07 µM demonstrated for both SARS-CoV-1 and MERS-CoV. [10-13] Remdesivir is highly selective for viral polymerases and is therefore expected to have a low propensity to cause human toxicity. Accordingly, Sheahan and colleagues demonstrated a wide therapeutic index for remdesivir in a human airway epithelial cell model.6 The drug also displays a high genetic barrier to resistance in coronaviruses and has a long intracellular half-life that allows for once daily dosing. [14, 15] The dose under investigation for treatment of COVID-19 is 200mg intravenously (IV) on day 1 followed by 100mg IV daily for up to 10 days, infused over 30-60 minutes.

Chloroquine and hydroxychloroquine
Chloroquine, an antimalarial agent with anti-inflammatory and immunomodulatory activities, has gained significant interest as a potential therapeutic option for the management of COVID-19. In early February, Wang and colleagues demonstrated potent in vitro activity of chloroquine against SARS-CoV-2 with an EC50 at 48 hours of 1.13 µM in Vero E6 cells [10]. These data were consistent with previous data for chloroquine's inhibitory activity against SARS-CoV-1 and MERS-CoV in various cell lines, where EC50 values of 1 – 8.8 and 3.0 µM were demonstrated, respectively [16]. These findings have supported the clinical use of chloroquine, at a dose of 500 mg by mouth twice daily, in numerous clinical trials in China during this outbreak. While the rationale for this dosing regimen remains unclear, and peer reviewed data from the trials are currently unavailable, it was announced in mid-February that promising early results have been demonstrated. Per Gao and colleagues, "thus far, results from more than 100 patients have demonstrated that chloroquine phosphate is superior to the control treatment in inhibiting the exacerbation of pneumonia, improving lung imaging findings, promoting a virus-negative conversion, and shortening the disease course according to the news briefing. Severe adverse reactions to chloroquine phosphate were not noted in the aforementioned patients" [17].

Conclusions
The COVID-19 pandemic is spreading across the globe at an alarming rate. It has caused more infections and deaths as compared with SARS or MERS. Based on R0 values, it is deemed that SARS-CoV-2 is more infectious than SARS or MERS. Elderly and immunocompromised patients are at the

greatest risk of fatality. The rapid spread of disease warrants intense surveillance and isolation protocols to prevent further transmission. No confirmed medication or vaccine has been developed. Current treatment strategies are aimed at symptomatic care and oxygen therapy. Prophylactic vaccination is required for the future prevention of COV-related epidemic or pandemic.

References

1. Fehr AR, Perlman S: Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 2015, 1282:1-23. 10.1007/978-1-4939-2438-7_1
2. Lu R, Zhao X, Li J, *et al*. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet. 2020, 395:565-574. 10.1016/S0140-6736(20)30251-8
3. Coronavirus Outbreak. Available at: https://www.worldometers.info/coronavirus/. Accessed 23 Feb 2020.
4. World Health Organization. Situation reports. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/. Accessed 22 Feb 2020.
5. Xinhua. China's CDC detects a large number of new coronaviruses in the South China seafood market in Wuhan. Available at: https://www.xinhuanet.com/2020-01/27/c_1125504355.htm. Accessed 20 Feb 2020.
6. 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.
7. Rothe C, Schunk M, Sothmann P *et al*. Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med, 2020. https://doi.org/10.1056/NEJMc2001468.
8. Li Q, Guan X, Wu P *et al*. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
9. Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Napoli RD: Features, Evaluation and Treatment Coronavirus (COVID-19). Stat Pearls Publishing, Treasure Island, FL; 2020.
10. Wang M, Cao R, Zhang L, *et al*. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *in vitro*. Cell research. 2020; 30(3):269-271.
11. Gordon CJ, Tchesnokov EP, Feng JY, Porter DP, Gotte M. The antiviral compound remdesivir potently inhibits RNA-dependent RNA polymerase from Middle East respiratory syndrome coronavirus. The Journal of biological chemistry, 2020.
12. Sheahan TP, Sims AC, Leist SR, *et al*. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nature communications. 2020; 11(1):222.
13. Sheahan TP, Sims AC, Graham RL, *et al*. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. Science translational medicine. 2017; 9(396).
14. Agostini ML, Andres EL, Sims AC, *et al*. Coronavirus Susceptibility to the Antiviral Remdesivir (GS5734) Is Mediated by the Viral Polymerase and the Proofreading Exoribonuclease. mBio. 2018; 9(2).
15. Siegel D, Hui HC, Doerffler E, *et al*. Discovery and Synthesis of a Phosphoramidate Prodrug of a Pyrrolo[2,1-f][triazin-4-amino] Adenine C-Nucleoside (GS-5734) for the Treatment of Ebola and Emerging Viruses. Journal of medicinal chemistry. 2017; 60(5):1648-1661.
16. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. International journal of antimicrobial agents. 2020, 105932.
17. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. Bioscience trends, 2020.