

Quick Review on Corona Virus 2019 (COVID-19)

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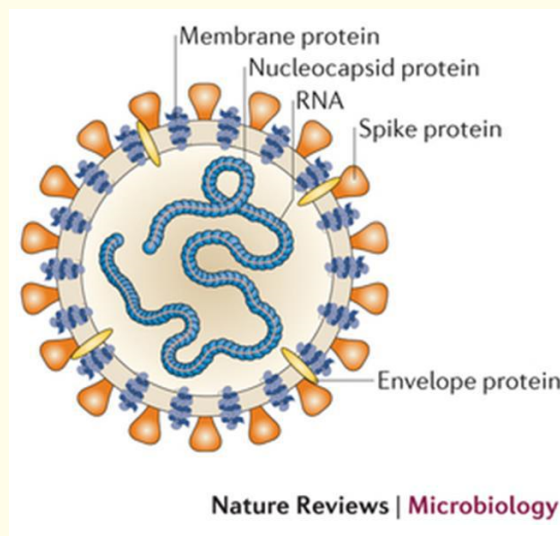
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Abstract

Coronavirus belongs to a large family of enveloped large RNA viruses which infects animal and humans. The name 'corona' is because of the characteristic shape of the envelope which has 20-nm-long club- or petal-shaped projections that are widely spaced on the outer surface of the envelope, looks like solar corona (See figure 1). There are six coronaviruses that can infect humans, the alpha coronaviruses 229E and NL63 and the beta coronaviruses OC43, HKU1, SARS-CoV and MERS-CoV and there are many coronaviruses that can infect animals. In humans, infection is usually limited to upper respiratory tract except for one species which is found to be associated with diarrheal disease. Coronavirus are usually species specific and human coronaviruses are noted to be less virulent causing "common colds," usually mild, afebrile and in adults; and it's the second common cause after rhinovirus to cause common cold. In contrast in the last two decades we have noted emergence of deadly beta coronavirus infection; the first outbreak of SARS-CoV in 2003 and then outbreak of MERS-CoV in 2012. Both were characterized by severe pneumonia and respiratory failure and notably originated in a bats, transmitted from animal to human (SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans) and then propagate from human to human causing major outbreak. A comparison of the current outbreak with the previous coronavirus outbreaks is provided in table 1.

Keywords: *Coronavirus; SARS-CoV; MERS-CoV*



Current 2019 outbreak of coronavirus which started in China is also very similar to these outbreaks. The first cases of COVID -19 were reported from Wuhan City, Hubei Province, China on December 31, 2019. In December 2019, series of viral pneumonia of unclear etiology was reported in Wuhan city, leading to further investigation [1]. Patients presented with fever, myalgia and abnormal CT findings. Deep sequencing analysis of the lower respiratory tract samples showed a novel beta coronavirus which now has been named as 2019-nCoV. WHO announced the official name for the current outbreak of corona virus disease on February 11, 2020 as COVID-19. The aim of this article is to briefly update the current epidemiology, clinical manifestations, steps towards prevention and a glimpse into how the outbreak has affected people across nations and how we are coping with it.

Commencement of the outbreak

In December 2019, several local health facilities in Hubei province of China reported cluster of patients with pneumonia of unknown cause to China National health Commission [1]. On December 31st 2019, the Centre for Health Protection (CHP) of the Department of Health of China reported that they have so far identified 27 cases including 7 critical cases of what seems to be a viral pneumonia of unknown cause. A rapid response team was dispatched by the Chinese center for disease control and prevention to assist the Hubei province and Wuhan city officials. As per subsequent published reports [2] between December 16, 2019 to January 2, 2020 there were 41 confirmed cases with 6 deaths. The initial epidemiological investigation revealed that 27/41 (66%) patients were exposed to “Hua Nan Seafood Wholesale Market”. The local CDC collected bronchoalveolar lavage (BAL) samples, blood and feces and tested for pathogen. A novel beta coronavirus was isolated from the BAL samples by RT-PCR, which was later named as 2019-nCoV. A full genome sequencing and phylogenetic analysis was conducted and viral genome was found to closely resemble SARS corona virus and to bat corona viruses. Given the close proximity to bat coronaviruses, it is postulated that bats might be the primary reservoir for the virus. The intermediate host that led to human infection is unclear at this time. Researchers from China have suggested the virus was spread probably through snakes and through Pangolins [3] though the claims are not proven and still under investigation.

Current global status of the epidemic

As of February 29th 2020, world wide there are 85,403 confirmed cases reported across 53 countries. In China where the epidemic started, there were 79 394 confirmed cases with 2838 deaths [4]. In United States, currently there are 60 confirmed cases and more are being reported everyday. 44 out of these 60 cases were American travelers from Diamond Princess Cruise ship which was docked in Yokohama, Japan. The reported cases were from 8 states: 12 cases from California, cases from Washington state, 2 cases from Illinois, 1 case each from Arizona, Texas, Oregon, Massachusetts and Wisconsin. On February 27th 2020 US reported the first case with no known close exposure to any infected patient, posing a possibility of community acquired case of COVID-19 [5]. Since the report WHO has increased the assessment of the risk of spread and risk of impact of COVID-19 to very high at the global level and CDC has changed the definition for PUI (Person Under Investigation).

Clinical symptoms and natural course

From current published data and from prior experience with coronavirus, it is believed that the incubation period for the disease ranges from 2 to 14 days with majority of the patients developing disease within 5 days. Disease manifestations range from being asymptomatic to development of severe pneumonia, acute respiratory distress syndrome, acute respiratory failure. Dawei Wang, *et al.* reported clinical characteristics of 138 hospitalized patients from Wuhan China [6]. In this case series, reported mortality was 4.3% although 26% of the patients were severe, requiring an intensive care unit admission. Most common clinical symptoms is fever, occurred in 98%, fatigue in 69 %, dry cough in 59 %. Lymphopenia was the leading laboratory abnormality occurring in 70 %, followed by prolonged prothrombin time in 58 %, elevated lactate dehydrogenase in 39%. Chest Imaging showed bilateral ground glass opacities and bilateral patchy infiltrates in all the patients. Though the exact numbers are difficult to estimate at this time the WHO estimated case fatality rate is 2% [7]. Comparison with other similar virus is shown in table 1.

	Novel corona virus	SARS (2002-2003)	MERS (2012)	Influenza (2019 - 2020)
Origin	China	China	Arabian peninsula	South East Asia
Transmission	Person to person	Person to person	Person to person	Person to person
Reservoir	Snakes and Pangolians	Civets	Dromedary camels	Humans, wild birds
Vaccine	In development	No	In development	Yes
Cases	86,013	8,098	8,494	15,000,000 - 21,000,000
Deaths	2,977	774	858	8,200 - 20,200
Case fatality	2%	11%	35%	0.095%

Transmission

The current understanding of the virus is incomplete and primarily comes from our experience of similar beta coronavirus like the SARS and MERS coronaviruses. Transmission is primarily through respiratory droplets. Virus spread between people who are in close contact (within 6 feet of each other) Although transmission can occur through fomites, this is not the principal modality. Spread occurs at the patient’s peak occurrence of symptoms but also occurred from asymptomatic patients. The viral RNA was also isolated from blood and stool specimens of infected patients, but it is not known if it can be transmitted through any other routes other than respiratory secretions [8].

Diagnosis

Diagnosis is achieved by real time PCR. Respiratory specimens including nasopharyngeal, oropharyngeal aspirates or washes, nasopharyngeal or oropharyngeal swabs, bronchoalveolar lavage, tracheal aspirates, sputum and serum can be used. CDC has listed prerequisites for specimen collection, transport, processing [9]. The 2019-nCoV primer and probe sets were designed for universal detection of SARS like Corona viruses (N3 assay) and for specific detection of 2019-nCoV (N1 and N2 assays).

Evaluating and reporting suspected persons

CDC has identified criteria to guide clinicians to identify suspected patients. Currently we have limited knowledge about the complete characteristics of the disease and the criteria have been developed based on our understanding about MERS-CoV and SARS-CoV and available information on this novel COVID 19 virus. The criteria is changing as we know more about the virus. Clinical features and epidemiological risk factors should be taken into account while suspecting a case of coronavirus. Identified suspected case is otherwise called person under investigation (PUI) is identified based on clinical features and their epidemiological risk.

PUI is defined as any person who presents with clinical features of fever or signs/symptoms of lower respiratory illness (e.g. cough or shortness of breath)

AND

- a) has had close contact with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset
- b) has a history of travel from affected geographic areas within 14 days of symptom onset
- c) has no other alternative explanatory diagnosis (e.g., influenza).

Close contact is defined as being within approximately 6 feet (2 meters) of a 2019-nCoV case for a prolonged period of time or in direct contact with respiratory secretions of infected patient. PUI once identified should be placed in airborne isolation and the health care

professionals should then alert infection control personnel at their health institution and also their local and state health department officials. State department officials then contact the CDC's Emergency Operations Center (EOC). At this time diagnostic lab tests for the virus are confined to CDC jurisdiction. To increase the likelihood of detecting the virus, multiple specimens need to be collected. Of note specimens need to be collected from PUI regardless of duration of symptoms [10].

Management of confirmed cases

Severity of illness varies from mild to severe. Patient with mild symptoms may worsen and hence it is advisable to admit them and monitor their respiratory status closely. No antivirals or specific treatments available at this time. Management is basically supportive especially antipyretics, fluid management, antipyretics, management of superimposed bacterial infections and ventilatory support. CDC/WHO recommends against use of steroids based on prior reports of prolonged viral replications in SARS-Cov [11] and MERS-CoV [12].

In conjunction with state or local health department staff, a healthcare professional can assess whether home care setting is adequate and appropriate for COVID-19 cases. This can be accomplished when the patient is stable and there are resources like a separate bedroom where the patient can convalesce and there is access to food and other necessities. The patient and household members should have access to personal protective equipment and should receive education on donning, doffing and appropriate disposal. The patient is stable enough to receive care at home. The decision on home care is made on an individual basis in each case and should take into consideration, presence of household members at increased risk of complications from 2019-nCoV infection such as people > 65 years old, young children, pregnant women, people who are immunocompromised or who have chronic heart, lung, or kidney conditions.

Prevention

With no vaccine or appropriate treatment in sight, prevention of spread of the virus is our major goal at this point. This serves to buy time for science to catch up before COVID-19 becomes pandemic. CDC enumerates preventive measures. Measures should be instituted prior to arrival of the patient, during their hospital stay and post discharge. Standard precautions should be in place and assume that every person is potentially infected. Rapid triage and appropriate isolation in airborne isolation room (AIIR) when available is a key factor. When AIIR is not available in the facility patient should be transferred to a nearby facility that has AIIR. AIIR are single patient rooms at negative pressure relative to the surrounding environment and with a minimum of 6 air changes per hour [13].

The exact duration of the isolation is unclear. Current CDC and WHO guidelines advise to discontinue isolation when at least two consecutive sets of paired nasopharyngeal and throat swabs specimens collected ≥ 24 hours apart are negative for COVID-19 molecular assay and patient is afebrile, with resolution of respiratory symptoms. The decision should be made on case by case basis.

Epidemic response

Since 2003, the Chinese government has improved their response to epidemic outbreaks. In 2002 - 2003 SARS outbreak about 300 cases and 5 deaths already had occurred before WHO was informed about the outbreak [14]. During COVID-19 outbreak only 27 cases with zero fatalities occurred before WHO was notified on January 3rd 2020 [1]. Identified cases were rapidly contained and 2 new hospitals were built in the epicenter of the outbreak to isolate and care for increasing number of cases. The occurrence of the outbreak before the Chinese New Year played a major part in how China has decided to respond to the outbreak. Chinese New Year being a culturally important holiday of the year and in anticipation of billions of person trips made, the Chinese government could visualize how each effected person can infect many close contacts and across many miles. Given that there was no vaccine or treatment available; china resorted to stringent isolation, quarantine and social containment. Although these measures were criticized as excessive by some, whether it is successful or not will remain a debate for years to come. In Japan, Schools have been shut down to prevent spread of the virus [15]. In the US, government has made an emergency request to congress to release 1.25 billion dollars of new funding and another 1.25 billion dollars

from previously allocated budget items be mobilized for corona virus epidemic preparations. Also U.S. government suspended entry of foreign nationals who have been in China, Iran within the past 14 days and U.S. citizens, residents, who have been in Hubei province and other parts of mainland China are allowed to enter the United States, but they are subject to health monitoring and possible quarantine for up to 14 days. Italy has quarantined people in 11 towns at the center of the outbreak along with losing malls, schools have been closed [16]. As many new nations are being affected local governments are resorting to draconian measures to contain the virus. Travel advisories are in place to the effected countries and are being monitored by WHO/CDC. On February 29th, the State department has imposed Level 4 travel restrictions on Italy and South Korea as well [17].

Economic impact of COVID-19

From the examination of the economic impact of SARS epidemic, effects on economy can be classified into two broad categories - direct and indirect. Included direct effects were loss of revenue and output due to death and illness and greater costs of health care. Indirect costs arise because of public's understanding of the outbreak induces cumulative behavior changes. Across every economic environment harmed during the SARS epidemic, greatly impacted sectors were in-house consumption of recreational activities, domestic and international transport and tourism. As of February 29th, Dow has plummeted 3583 points entering correction territory. S&P has dwindled by 7% and US Treasury bond yields slipped to historic lows suggesting investors are expecting a considerable economic damage [18]. The outbreak that shut down businesses and cities again pushed down many Asian economies that were simply pinching back to growth after the negative impacts of the 18 month US China business dispute. Reuter's poll projects that the Chinese economic growth would slow down to 3.5% in the current quarter because of the COVID outbreak as compared to 6% growth rate in the final quarter of 2019 [19].

We are still yet to see what the future holds as the epidemic continues to spread across nations.

What is in the pipe line

Many pharmaceutical companies and research organizations are striving to develop vaccines and drugs against COVID- 19. Favipiravir a viral RNA polymerase inhibitor which was initially being studied for Influenza. It is now being tested against COVID-19 [20]. Similarly, antivirals like Ritonavir, Lopinavir, Hydroxychloroquine are under study at the current time [21]. TNX-1800 by Tonix Pharmaceuticals is a protein-based vaccine that is currently under development [22]. Clover biopharmaceuticals is developing the vaccine based on the trimeric S protein (S-Trimer) of the 2019-nCoV virus, which is responsible for binding with the host cell and causing a viral infection [23]. Many USA based research organizations are also in the process of developing drugs and or vaccines for COVID-19. Remdesivir (GS-5734) by Gilead Sciences is under investigation. Researchers at Columbia University have been awarded a \$2.1m grant to develop a coronavirus cure. First U.S. clinical trial for a coronavirus treatment with Remdesivir has been launched at the University of Nebraska Medical Center (UNMC) in Omaha [24].

Conclusion

As more and more cases are being diagnosed in the US and around the world, we are yet to see that full scale of this disease. Global travel has paved way for easy spreading of infectious disease across the world. There is growing concern that it may become pandemic. So far the case fatality seems to be low and many cases are mild and going for full recovery. Our understanding of the virus is also evolving as well as the scientific research against the virus.

Bibliography

1. Centre for Health Protection of the Hong Kong Special Administrative Region Government. CHP closely monitors cluster of pneumonia cases on Mainland (2019).
2. C Huang, *et al.* "Clinical features of patients infected with 2019 novel coronavirus in Wuhan". *China Lancet* (2020).

3. Wang W., *et al.* "Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China". *Journal of Medical Virology* 202 (2019).
4. CDC. World Map (2020).
5. CDC Announces Additional COVID-19 Presumptive Positive Cases.
6. Dawei Wang., *et al.* "Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China". *JAMA* (2020).
7. World Health Organization. Novel coronavirus (2019-nCoV) situation reports.
8. W Zhang., *et al.* "Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes". *Emerging Microbes and Infections* 9.1 (2019): 386-389.
9. CDC. Information for Laboratories.
10. CDC. Evaluating and Testing Persons for Coronavirus Disease 2019 (COVID-19).
11. Lee N., *et al.* "Effects of early corticosteroid treatment on plasma SARS-associated Coronavirus RNA concentrations in adult patients". *Journal of Clinical Virology* 31 (2004): 304-309.
12. Arabi YM., *et al.* "Saudi Critical Care Trial Group. Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome". *American Journal of Respiratory and Critical Care Medicine* 197.6 (2018): 757-767.
13. CDC. Interim Infection Prevention and Control Recommendations for Patients with Suspected or Confirmed Coronavirus Disease 2019 (COVID-19) in Healthcare Settings.
14. W Cao., *et al.* "What we have learnt from the SARS epidemics in mainland China?" *Global Health Journal* 3.3 (2019): 55-59.
15. All schools in Japan told to close until April over virus outbreak.
16. Coronavirus Spreads Outside of Italy, Prompting Fresh Restrictions.
17. Global Health Advisory: Do Not Travel. Avoid all international travel due to the global impact of COVID-19.
18. 10-year Treasury yield drops below 1.3% for the first time in history.
19. Economic contagion spreads beyond China to other Asian economies: Reuters poll.
20. China's scientists unite in COVID-19 fight.
21. Coronavirus puts drug repurposing on the fast track.
22. Tonix Pharmaceuticals forms alliance to develop Covid-19 vaccine.
23. Clover to use GSK's adjuvant system for Covid-19 vaccine candidate.
24. NIH Clinical Trial of Remdesivir to Treat COVID-19 Begins.

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