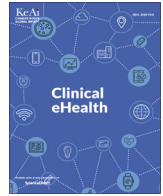




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Coronavirus disease-2019 and its current scenario – A review

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ABSTRACT

Coronaviruses are enveloped non-segmented positive-sense RNA viruses belonging to the family Coronaviridae. The human coronavirus infections are mild; the epidemics of the two β -coronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have caused more than ten thousand cumulative cases in the past twodecades. There is a new public health crisis threatening the world with the emergence and spread of 2019 novel coronavirus (2019-nCoV). The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province in China during the month of December 2019. Till date around 7,823,289 reported cases of coronavirus disease 2019 (COVID-2019) and 431,541 reported deaths till date. The disease is transmitted by inhalation or contact with infected droplets with incubation period of 2–14 days. The symptoms are usually fever, sore throat, dry cough, breathlessness, fatigue while many people are asymptomatic. Coronavirus (2019-nCoV) may progress to pneumonia, acute respiratory distress syndrome (ARDS) and can cause multi-organ dysfunction. Currently diagnosis is done by demonstration of the virus in respiratory secretions by special molecular tests like real-time reverse-transcription-polymerase-chain-reaction (RT-PCR), Radiological examinations (chest CT). Common laboratory tests like white cell counts and C-reactive protein (CRP) and measure symptoms can be used as preliminary screening at large scale after lock down the area or country. Treatment is essentially supportive; role of antiviral agents is yet to be established. It is paramount to implement infection control practices by infection source controlling, transmission route blocking, and susceptible population protection. Early preventive measures can be home isolation of suspected cases and those with mild illnesses and strict infection control measures at hospitals that include contact and droplet precautions. The world-wide impact of this Coronavirus new epidemic is yet uncertain.

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Introduction

Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases. Coronaviruses cause acute and chronic respiratory, enteric, and central nervous system (CNS) diseases in many species of animals, including humans. Human coronaviruses, including hCoV-229E, OC43, NL63, and HKU1, cause mild respiratory diseases. Fatal coronavirus infections that have emerged in the past two decades are severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV).

Coronavirus disease (COVID-19) is a new strain that was discovered in 2019 and has not been previously identified in humans.¹ Till date around 7,823,289 reported cases of coronavirus disease 2019 (COVID-2019) and 431,541 reported deaths till date.² India has reported 29 cases till date. Fortunately so far, children have been frequently affected with no deaths. But the future course of this virus is unknown and what will be happen if measure precautions will not be taken by whole world collectively.

History

The clinical spectrum of COVID-19 varies from asymptomatic or paucisymptomatic forms to clinical conditions characterized by respiratory failure that necessitates mechanical ventilation and support in an intensive care unit (ICU), to multi-organ and systemic manifestations in terms of sepsis, septic shock, and multiple-organ dysfunction syndromes (MODS). In one of the first reports in China on the disease, Huang et al. illustrated that forty one patients showed sighns and symptoms of fever, malaise, dry cough, and dyspnea and chest computerized tomography (CT) scans showed pneumonia with abnormal findings in all forty cases. Concerning is that about a third of those (13, 32%) required ICU care, which is impossible to provide such facility to the required percentage of patients and there were 6 (15%) fatal cases in this number.^{3,4}

Coronaviruses are enveloped positive sense RNA viruses under the electron microscope examination and ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance, hence the name coronavirus.⁵ Four corona viruses namely HKU1, NL63, 229E and OC43 have been in circulation in humans, and generally cause mild respiratory disease. There have been two events in the past two decades where in crossover of animal β -corona viruses to humans have resulted in severe disease. The first such instance was in 2002– 2003 when a new coronavirus of the β -gene RA and with origin in bats crossed over to humans via the intermediary host of palm civet cats in the Guangdong province of China. This virus, designated as severe acute respiratory syndrome corona virus affected 8422 people mostly in China and Hong Kong and caused 916 deaths (mortality rate 11%) before being contained.⁶ Almost a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%).⁷

Early detection and spread of COVID-19

Adults in Wuhan, capital city of Hubei province In December 2019 and a major transportation hub of China started presenting to local hospitals having severe pneumonia with unknown cause. Maximum number of the initial cases had a common exposure to the Huanan wholesale seafood market where trade of animals is going on.^{1,2} 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.^{1,8} On 7th January the virus was identified as a coronavirus that had >95% homology with the bat coronavirus and >70% similarity with the SARSCoV.^{2,8} Environmental samples from the Huanan sea food market also tested positive, signifying that the virus originated from there.⁹ 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.¹⁰ The first fatal case was reported on 11th Jan 2020. The massive migration of Chinese during the Chinese New Year fuelled 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.¹¹ 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 d and tested them for the virus.

Cases continued to increase exponentially and modelling studies reported an epidemic doubling time of 1.8 d.¹² 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.⁸ 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 as of 05/03/2020.² The measure threat is that while the number of new cases has reduced in China lately, they have increased exponentially in other countries including South Korea, Italy, Iran, Spain, Germany, UK, netherlands, India. Of those infected, 20% are in critical condition, 25% have recovered, and 3310 (3013 in China and 297 in other countries) have died.² India, which had reported only 1100 cases till date, has also seen a sudden

increase in cases. 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.^{12,13}

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. Data obtainable from reports allow dividing the clinical manifestations of the disease according to the severity of the clinical pictures. The COVID-19 may present with mild, moderate, or severe illness. Among the severe clinical manifestations, there are severe pneumonia, ARDS, sepsis, and septic shock. The clinical course of the disease seems to predict a favorable trend in the majority of patients. In a percentage still to be defined of cases, after about a week there is a sudden worsening of clinical conditions with rapidly worsening respiratory failure and MOD/MOF. As a reference, the criteria of the severity of respiratory insufficiency and the diagnostic criteria of sepsis and septic shock can be used.¹⁴

These patients usually present with symptoms of an upper respiratory tract viral infection, including mild fever, cough (dry), sore throat, nasal congestion, malaise, headache, muscle pain, or malaise. Signs and symptoms of a more serious disease, such as dyspnea, are not present. Compared to previous HCoV infections, non-respiratory symptoms such as diarrhea are challenging to find.

Respiratory symptoms such as cough and shortness of breath (or tachypnea in children) are present without signs of severe pneumonia.

Fever is associated with severe dyspnea, respiratory distress, tachypnea (>30 breaths/min), and hypoxia ($SpO_2 < 90\%$ on room air). However, the fever symptom must be interpreted carefully as even in severe forms of the disease, it can be moderate or even absent. Cyanosis can occur in children. In this definition, the diagnosis is clinical, and radiologic imaging is used for excluding complications.

The diagnosis requires clinical and ventilatory criteria. This syndrome is suggestive of a serious new-onset respiratory failure or for worsening of an already identified respiratory picture. Different forms of ARDS are distinguished based on the degree of hypoxia. The reference parameter is the PaO_2/FiO_2 :

- Mild ARDS: $200 \text{ mmHg} < PaO_2/FiO_2 \leq 300 \text{ mmHg}$. In not-ventilated patients or in those managed through non-invasive ventilation (NIV) by using positive end-expiratory pressure (PEEP) or a continuous positive airway pressure (CPAP) $\geq 5 \text{ cmH}_2\text{O}$.
- Moderate ARDS: $100 \text{ mmHg} < PaO_2/FiO_2 \leq 200 \text{ mmHg}$.
- Severe ARDS: $PaO_2/FiO_2 \leq 100 \text{ mmHg}$.

When PaO_2 is not available, a ratio $SpO_2/FiO_2 \leq 315$ is suggestive of ARDS.

Chest imaging utilized includes chest radiograph, CT scan, or lung ultrasound demonstrating bilateral opacities (lung infiltrates greater than 50%), not fully explained by effusions, lobar, or lung collapse. Although in some cases, the clinical scenario and ventilator data could be suggestive for pulmonary edema, the primary respiratory origin of the edema is proven after the exclusion of cardiac failure or other causes such as fluid overload. Echocardiography can be helpful for this purpose.

According to the International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), sepsis represents a life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection, with organ dysfunction.¹⁵ The clinical

pictures of patients with COVID-19 and with sepsis are particularly serious, characterized by a wide range of signs and symptoms of multi-organ involvement. These signs and symptoms include respiratory manifestations such as severe dyspnea and hypoxemia, renal impairment with reduced urine output, tachycardia, altered mental status, and functional alterations of organs expressed as laboratory data of hyperbilirubinemia, acidosis, high lactate, coagulopathy, and thrombocytopenia. The reference for the evaluation of multi-organ damage and the related prognostic significance is the Sequential Organ Failure Assessment (SOFA) score, which predicts ICU mortality based on lab results and clinical data.¹⁶ A pediatric version of the score has also received validation.¹⁷

In this scenario, which is associated with increased mortality, circulatory, and cellular/metabolic abnormalities such as serum lactate level greater than 2 mmol/L (18 mg/dL) are present. Because patients usually suffer from persisting hypotension despite volume resuscitation, the administration of vasopressors is required to maintain a mean arterial pressure (MAP) $\geq 65 \text{ mmHg}$.

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 most susceptible populations included whom who have significant health conditions such as diabetes, hypertension and heart and/or kidney function issues. In comparison during the MERS-CoV outbreak most Susceptible Populations were the smokers and who have a cardiovascular disease, diabetes, hypertension and other chronic illnesses.¹⁸ 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.

Common symptoms

Cold- or flu-like symptoms usually set in from 2 to 4 days after a coronavirus infection and are typically mild. However, symptoms vary from person-to-person, and some forms of the virus can be fatal.

Symptoms may include:

- sneezing
- runny nose
- fatigue
- cough
- fever
- sore throat
- exacerbated asthma

Scientists cannot easily cultivate human coronaviruses in the laboratory unlike the rhinovirus, which is another cause of the common cold. This makes it difficult to gauge the impact of the coronavirus on national economies and public health. There is no cure for coronaviruses that cause symptoms resembling the common cold. Treatments include self-care and over-the-counter (OTC) medication. People can take several steps, including:

- resting and avoiding overexertion

- drinking enough water
- avoiding smoking and smoky areas
- taking acetaminophen for pain and fever
- using a clean humidifier or cool mist vaporizer

Epidemiology and pathogenesis

All ages are susceptible. Infection is transmitted through large droplets generated during coughing and sneezing by symptomatic patients but can also occur from asymptomatic people and before onset of symptoms.¹¹ Studies have shown higher viral loads in the nasal cavity as compared to the throat with no difference in viral burden between symptomatic and asymptomatic people. Patients can be infectious for as long as the symptoms last and even on clinical recovery. Some people may act as super spreaders; a UK citizen who attended a conference in Singapore infected 11 other people while staying in a resort in the French Alps and upon return to the UK.⁸ These infected droplets can spread 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favorable atmospheric conditions but are destroyed in less than a minute by common disinfectants like sodium hypochlorite, hydrogen peroxide etc.¹⁹ Infection is acquired either by inhalation of these droplets or touching surfaces contaminated by them or then touching the nose, mouth and eyes. The virus is also present in the stool and contamination of the water supply and subsequent transmission via aerosolization/ feco oral route is also hypothesized.⁸ As per current information, transplacental transmission from pregnant women to their fetus has not been described.²⁰ However, neonatal disease due to post natal transmission is described.²⁰ The incubation period varies from 2 to 14 d [median 5 d]. Studies have identified angiotensin receptor 2 (ACE2) as the receptor through which the virus enters the respiratory mucosa.¹³ The basic case reproduction rate (BCR) is estimated to range from 2 to 6.47 in various modelling studies.¹³ In comparison, the BCR of SARS was 2 and 1.3 for pandemic flu H1N1 2009.²

Clinical features

The clinical features of COVID-19 are varied, ranging from a symptomatic state to acute respiratory distress syndrome and multi organ dysfunction. The common clinical features include fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis has also been described. Thus, they are indistinguishable from other respiratory infections. In a subset of patients, by the end of the first week the disease can progress to pneumonia, respiratory failure and death. This progression is associated with extreme rise in inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF α .²¹ The median time from onset of symptoms to dyspnea was 5 d, hospitalization 7 d and acute respiratory distress syndrome (ARDS) 8 d. The need for intensive care admission was in 25–30% of affected patients in published series. Complications witnessed included acute lung injury, ARDS, shock and acute kidney injury. Recovery started in the 2nd or 3rd wk. The median duration of hospital stay in those who recovered was 10 d. adverse outcomes and death is more common in the elderly and those with underlying comorbidities (50–75% of fatal cases). Fatality rate in hospitalized adult patients ranged from 4 to 11%. The overall case fatality rate is estimated to range between 2 and 3%.² Interestingly, disease in patients outside Hubei province has been reported to be milder than those from Wuhan.^{22–23} Similarly, the severity and case fatality rate inpatient outside China has been reported to be milder.⁸ This may either be due to selection bias wherein the cases reporting from Wuhan included only the severe cases or due to predisposition of the Asian population to the virus due to higher expression

of ACE2 receptors on the respiratory mucosa.¹³ Disease in neonates, infants and children has been also reported to be significantly milder than their adult counterparts. In a series of 34 children admitted to a hospital in Shenzhen, China between January 19th and February 7th, there were 14 males and 20 females. The median age was 8 y 11 mo and in 28 children the infection was linked to a family member and 26 children had history of travel/residence to Hubei province in China. All the patients were either asymptomatic (9%) or had mild disease. No severe or critical cases were seen. The most common symptoms were fever (50%) and cough (38%). All patients recovered with symptomatic therapy and there were no deaths. One case of severe pneumonia and multi-organ dysfunction in a child has also been reported.^{24,25} Similarly the neonatal cases that have been reported have been mild.²⁶

Diagnosis

A suspect case is defined as one with fever, sore throat and cough who has history of travel to China or other areas of persistent local transmission or contact with patients with similar travel history or those with confirmed COVID-19 infection. However cases may be asymptomatic or even without fever. A confirmed case is a suspect case with a positive molecular test. Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates and broncho alveolar lavage). Virus may also be detected in the stool and in severe cases, the blood. It must be remembered that the multiplex PCR panels currently available do not include the COVID-19. Commercial tests are also not available at present. In a suspect case in India, the appropriate sample has to be sent to designated reference labs in India or the National Institute of Virology in Pune. As the epidemic progresses, commercial tests will become available. Other laboratory investigations are usually non specific. The white cell count is usually normal or low. There may be lymphopenia; a lymphocyte count <1000 has been associated with severe disease. The platelet count is usually normal or mildly low. The CRP and ESR are generally elevated but procalcitonin levels are usually normal. A high procalcitonin level may indicate a bacterial co-infection. The ALT/AST, prothrombin time, creatinine, D-dimer, CPK and LDH may be elevated and high levels are associated with severe disease. The chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease. The CT is more sensitive and specific. CT imaging generally shows infiltrates, ground glass opacities and sub segmental consolidation. It is also abnormal in asymptomatic patients/ patients with no clinical evidence of lower respiratory tract involvement. In fact, abnormal CT-scans have been used to diagnose COVID-19 in suspect cases with negative molecular diagnosis; many of these patients had positive molecular tests on repeat testing.^{27–29}

Differential diagnosis

The differential diagnosis includes all types of respiratory viral infections (influenza, parainfluenza, respiratory syncytial COVID-19 coronavirus), atypical organisms (mycoplasma, chlamydia) and bacterial infections. It is not possible to differentiate COVID-19 from these infections clinically or through routine lab tests. Therefore travel history becomes important. However, as the epidemic spreads, the travel history will become irrelevant.²⁷

Treatment

Treatment is essentially supportive and symptomatic. The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers.

Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough. In hypoxic patients, provision of oxygen through nasal prongs, face mask, high flow nasal cannula (HFNC) or non-invasive ventilation is indicated.^{27,30} Mechanical ventilation and even extra corporeal membrane oxygen support may be needed. Renal replacement therapy may be needed in some. Antibiotics and antifungals are required if co-infections are suspected or proven. The role of corticosteroids is unproven; while current international consensus and WHO advocate against their use, Chinese guidelines do recommend short term therapy with low-to-moderate dose corticosteroids in COVID-19 ARDS.^{31–32} Detailed guidelines for critical care management for COVID-19 have been published by the WHO.³³ There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin, lopinavir/ritonavir have been used based on the experience with SARS and MERS. In a historical control study in patients with SARS, patients treated with lopinavir-ritonavir with ribavirin had better outcomes as compared to those given ribavirin alone.²¹ In the case series of 99 hospitalized patients with COVID-19 infection from Wuhan, oxygen was given to 76%, noninvasive ventilation in 13%, mechanical ventilation in 4%, extracorporeal membrane oxygenation (ECMO) in 3%, continuous renal replacement therapy (CRRT) in 9%, antibiotics in 71%, antifungals in 15%, glucocorticoids in 19% and intravenous immunoglobulin therapy in 27%.²¹ Antiviral therapy consisting of oseltamivir, ganciclovir and lopinavir/ritonavir was given to 75% of the patients. The duration of non-invasive ventilation was 4–22 days (median 9 days) and mechanical ventilation for 3–20 d (median 17 days). In the case series of children discussed earlier, all children recovered with basic treatment and did not need intensive care.²³ There is anecdotal experience with use of remdesivir, a broad spectrum anti RNA drug developed for Ebola in management of COVID-19.³⁴ More evidence is needed before these drugs are recommended. Other drugs proposed for therapy are arbidol (an antiviral drug available in Russia and China), intravenous immunoglobulin, interferons, chloroquine and plasma of patients recovered from COVID-19.^{27,35,36} Additionally, recommendations about using traditional Chinese herbs find place in the Chinese guidelines.^{27–28}

Prevention

Since at this time there are no approved treatments for this infection, prevention is crucial. Several properties of this virus make prevention difficult namely, non-specific features of the disease, the infectivity even before onset of symptoms in the incubation period, transmission from asymptomatic people, long incubation period, tropism for mucosal surfaces such as the conjunctiva, prolonged duration of the illness and transmission even after clinical recovery. Isolation of confirmed or suspected cases with mild illness at home is recommended.^{27,37} The ventilation at home should be good with sunlight to allow for destruction of virus. Patients should be asked to wear a simple surgical mask and practice cough hygiene. Caregivers should be asked to wear a surgical mask when in the same room as patient and use hand hygiene every 15–20 min. The greatest risk in COVID-19 is transmission to healthcare workers. In the SARS outbreak of 2002, 21% of those affected were healthcare workers.^{38,28} Till date, almost 1500 healthcare workers in China have been infected with 6 deaths. The doctor who first warned about the virus has died too. It is important to protect healthcare workers to ensure continuity of care and to prevent transmission of infection to other patients. While COVID-19 transmits as a droplet pathogen and is placed in Category B of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission, infection control

measures recommended are those for category A agents (cholera, plague). Patients should be placed in separate rooms or cohorted together. Negative pressure rooms are not generally needed. The rooms and surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite. Healthcare workers should be provided with fit tested N95 respirators and protective suits and goggles. Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. All contacts including healthcare workers should be monitored for development of symptoms of COVID-19. Patients can be discharged from isolation once they are afebrile for at least 3 d and have two consecutive negative molecular tests at 1 d sampling interval. This recommendation is different from pandemic flu where patients were asked to resume work/school once afebrile for 24 h by day 7 of illness. Negative molecular tests were not a prerequisite for discharge. At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission.²⁸ They should be asked to practice cough hygiene by coughing into sleeve/tissue rather than hands and practice hand hygiene frequently every 15–20 min. Patients with respiratory symptoms should be asked to use surgical masks. The use of mask by healthy people in public places has not shown to protect against respiratory viral infections and is currently not recommended by WHO. However, in China, the public has been asked to wear masks in public and especially in crowded places and large scale gatherings are prohibited (entertainment parks etc). China is also considering introducing legislation to prohibit selling and trading of wild animals.^{39,28} The international response has been dramatic. Initially, there were massive travel restrictions to China and people returning from China/evacuated from China are being evaluated for clinical symptoms, isolated and tested for COVID-19 for 2 wks even if asymptomatic. However, now with rapid world wide spread of the virus these travel restrictions have extended to other countries. Whether these efforts will lead to slowing of viral spread is not known. A candidate vaccine is under development.²⁸

Current scenario of disease

The 2019 novel coronavirus (2019-nCoV), officially named as COVID-19 by the WHO, has spread to more than 170 countries including China prompting the WHO to declare the disease as a global pandemic. Confirmed novel coronavirus cases have crossed 7,823,289 while more than 431,541 deaths have been reported across the world as Europe becomes the new epicenter of coronavirus. More than 80% of the global COVID-19 cases are currently outside China.⁴⁰

Cure or vaccines

In general, there are few or no treatment options for viral diseases that occur suddenly.⁴¹ In parallel with this knowledge, today there is no vaccine or effective treatment to prevent COVID-19 infection. Molecules are being tested for COVID-19 in in-vitro and human-based SARS-CoV and MERS-CoV trials. Studies evaluating the antiviral activity of types I and II interferons have reported, interferon-beta (IFN β), as the most potent interferon, was reducing in-vitro MERS-CoV replication.⁴² According to a human MERS-CoV case report from South Korea, the use of the combination of Lopinavir/Ritonavir (LPV/RTV) (Anti-HIV drugs), pegylated interferon and ribavirin provided a successful viral clearance.⁴¹ For this purpose, a randomized control trial (MIRACLE Trial), that aimed to determine whether LPV/RTV-IFN β improved clinical results in MERS-CoV patients, was initiated in 2016 and 76 patients were enrolled.⁴³ Although another antiviral drug, remdesivir was used

in the first case reported from the United States of America, seemed successful, controlled studies with more cases are needed.⁴¹ In-vitro studies have shown that viral RNA transcription was terminated with remdesivir in early stage.^{44,45} There are publications demonstrating that remdesivir has a strong antiviral activity in epithelial cell cultures against SARS-CoV, MERS-CoV and related zoonotic bat CoVs.⁴⁶ Many measures should be taken, such as timely publication of epidemic information for elimination of the source of infection, early diagnosis, reporting, isolation, supportive treatments and for avoiding unnecessary panic. CDC reminds basic measures such as hand washing, using disinfectant solutions, avoiding contact with patients in order to prevent the spread of viruses by droplets. Precautionary actions including the provision of medicines supply chains, personal protective equipment, and hospital supplies should be made in a short time for the protection of the Chinese people and global health, especially in the places with close travel ports to major Chinese ports.⁴⁷ Based on the 2003 SARS-CoV epidemic experience, the Chinese government takes many effective measures including closing public transport, reducing migration and promoting personal protection with masks in Wuhan and other provinces. Hence, there are reported cases of infected hospital personnel, healthcare staff should be informed about taking personal protective measures such as the use of gloves, eye masks and N95 masks during the examination of patients with a suspected history of COVID-19 contact or travel to China.^{48,49}

Several efforts to develop vaccines are underway, but the WHO estimates it will take 18 months for the COVID-19 vaccines to be available.⁵⁰ At present, most treatment is symptomatic and supportive, though anti-inflammatory and antiviral treatments have been employed. Supportive treatment for complicated patients has included continuous renal replacement therapy (CRRT), invasive mechanical ventilation, and even extracorporeal membrane oxygenation (ECMO). No specific antiviral drugs have been confirmed effective. The first reported patient with 2019-nCoV infection in the USA was treated with remdesivir, and others have used antiretrovirals like ritonavir, with trials of both in progress.⁵¹ Baricitinib has been suggested as a potential drug for the treatment in the hope that it might reduce the process of both virus invasion and inflammation.⁵²

Conclusions

This new virus outbreak has challenged the economic, medical and public health infrastructure of China and of other countries especially, its neighbours. Time alone will tell how the virus will impact our lives here in India. More so, future outbreaks of viruses and pathogens of zoonotic origin are likely to continue. Therefore, apart from curbing this outbreak, efforts should be made to devise comprehensive measures to prevent future outbreaks of zoonotic origin.

Common laboratory tests like white cell counts and C-reactive protein (CRP) and measure symptoms can be used as preliminary screening at large scale.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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