

SARS-CoV-2 / COVID-19: Salient Facts and Strategies to Combat Ongoing Pandemic

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Abstract

Severe acute respiratory syndrome coronavirus – 2 (SARS-CoV-2), an emerging novel coronavirus causing coronavirus disease 2019 (COVID-19) pandemic, has now rapidly spread to more than 215 countries and has killed nearly 0.75 million people out of more than 20 million confirmed cases as of 10th August, 2020. Apart from affecting respiratory system, the virus has shown multiple manifestations with neurological affections and damaging kidneys. SARS-CoV-2 transmission mainly occurs through close contact of COVID-19 affected person, however air-borne route is also now considered as dominant route of virus spread. The virus has been implicated to have originated from animals. Apart from bats, pangolins and others being investigated to play role in transmitting SARS-CoV-2 as intermediate hosts, the recent reports of this virus infection in other animals (cats, dogs, tigers, lions, mink) suggest one health approach implementation along with adopting appropriate mitigation strategies. Researchers are pacing to develop effective vaccines and drugs, few reached to clinical trials also, however these may take time to reach the mass population, and so till then adopting appropriate prevention and control is the best option to avoid SARS-CoV-2 infection. This article presents an overview on this pandemic virus and the disease it causes, with few recent concepts and advances.

Keywords: SARS-CoV-2, COVID-19, pandemic, prevention, control

INTRODUCTION

In December 2019, the wet market in the city of Wuhan, China saw the beginning of a deadly outbreak with an unexpected new strain of beta-coronavirus, severe acute respiratory syndrome coronavirus - 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19). Beginning as an outbreak within China, this virus rapidly spread across many nations and continents making it a pandemic that is now posing the worst situation after the 1918 Spanish flu virus pandemic which killed millions of people. Presently, SARS-CoV-2 has very quickly affected more than 215 countries while accounting for nearly 0.75 million deaths out of more than 20 million positive cases as of 10th August, 2020. In addition to a very severe global health concerns it also led to very high social and economic instability and huge panic and fear to the public^{1,2}. In order to attempt to stop it from rapidly spreading, many countries followed locked down, halted their social and business activities, causing significant damages to their economy, GDP and share markets³⁻⁶.

Among previously known coronaviruses, this strain was unique in its nature since it had not been previously identified in humans. Preliminary research indicates bat as the primary reservoir of virus suggesting close similarity of SARS-CoV-2 to bat coronavirus⁷. This virus is said to mutate

twice a month and is easily transmitted through respiratory secretions of an infected person to a susceptible person in close contact approximately within 6 feet or more⁸. Air-borne transmission has also been reported to be a dominant route of transmission. Although factors such as humidity and temperature have shown to affect the survival of the pathogen, numerous studies have claimed the infectious nature of the virus on inanimate objects and surfaces at room temperature for up to 9 days⁹. The abundance of the susceptible host is a promising factor deciding the invasion and spread of a new pathogen. This susceptibility is difficult to explain because of prior cross-protective immunity in population recently exposed to similar antigenic pathogens. Epidemiological information of the co-circulating viruses provides an understanding of the immune potential, virus-virus interactions and population susceptibility¹⁰. No particular antiviral treatments and vaccines are available for COVID-19, and this endeavors to create antivirals and vaccines at an early time to counter ongoing pandemic. The present article highlights main features SARS-CoV-2 / COVID-19 and recent advances to counter it.

Transmission and Spread

Coronaviruses (CoVs) including SARS-CoV-2 spread mainly via respiratory droplets released from the mucus secretions and saliva

from the nose and mouth during the act of sneezing, coughing, talking, laughing, singing and breathing. These droplets containing the virus may gain access to the body mainly through the eyes, nose and mouth but not through intact skin. Droplets fall on the ground or settle on the surfaces if they do not hit any inanimate object, while on their trajectory to settling down; thereby serving as a mode of self-inoculation among healthy individuals. In addition, CoVs may remain infective on metal, glass and plastic surfaces for a period of 2 hours to 9 days. In contrast to this, SARS-CoV-2 may persist in air from 3 hours to an average of 2-3 days in steel and plastic surfaces¹¹. Application of a simple disinfectant including soap and diluted solution of sodium hypochlorite or a diluted household bleach over contaminated surfaces may consider them safe as the delicate envelope of the virus gets easily destroyed by disinfectants. Although CoVs are not transmitted sexually but kissing could definitely transmit the disease. In addition, SARSCoV-2 has been reported in feces, although its significant role in feco-oral transmission has not been determined¹². Therefore, the role of hand sanitization after using toilet plays a pivotal role in preventing the spread of the COVID-19 after the evidence of passage of virus in feces and urine.

For an infection to occur, patients found positive with SARS-CoV-2 must be in close contact (within 6 feet) with a susceptible host for at least 15 minutes or should be in a closed environment, where an infected patient has the ability to spread the virus in an area with a pre-existing low viral load in air¹³. For e.g., in a case scenario, the chances of a taxi driver getting infected with the pathogen while carrying a diseased passenger to a 5 minute airport ride is less. In contrast, if a health care personnel examining a suspected case of COVID-19, showing typical features of acute respiratory illness, coughing for more than 15 minutes, without taking any protective measures or maintaining adequate respiratory etiquette is more likely to get infected with the virus. Meanwhile another health care professional entering the same room where the suspected case is being examined can get infected easily due to the presence of pre-existing viral particles present in the air.

COVID-19: Clinicopathology

SARS-CoV-2 is closely related to SARS virus with respect to sharing of the same receptor viz. ACE-2 receptor for entry into the host cells. In contrast to previous two coronavirus epidemics with SARS and MERS, the SARS-CoV-2 is found less lethal but highly contagious. Death related to COVID-19 is mainly attributed to respiratory failure because of cytokine storm due to overstimulation of immune system¹⁴. The clinical symptoms manifested by SARS-CoV-2 patients depend upon the disease severity and immune status of the individuals. Moreover, on the basis of clinical symptoms the COVID-19 is stratified into critical/severe, moderate, mild and asymptomatic forms¹⁵. Among all the forms, the severe form is particularly observed in elderly and immune-compromised persons with known comorbidities^{16,17}. COVID-19 incubation period is variable, mean value of 5.2 days has been observed, and mainly depends on disease severity^{16,18}. The clinical symptoms include fever, muscle ache, generalized weakness, dyspnoea, rhinorrhoea, dry cough, pleuritic chest pain, dry and less commonly hemoptysis, headache, diarrhoea, nausea and vomiting^{15,19-23}. Moreover, fever and cough are the most common clinical signs of COVID-19.²⁴ The current evidence suggests multiple organ systems may be affected by hyperinflammation in SARS-CoV-2 infection²⁵. In this context, neurodegeneration, neuroinflammation, and delirium in some COVID-19 cases might be attributed to inflammatory response in central nervous system (CNS)²⁶. In addition, neurological manifestations such as anosmia and ageusia have been observed as salient symptoms during SARS-CoV-2 infection²⁷.

The virus has also been reported to cause neurological manifestations as well as affect other organs including kidneys. Pregnancy related immune-suppression is found to be beneficial as far as severity of the disease is concerned. The presence of viral RNA in all body fluids, respiratory secretions and feces of infected individuals has been described in scientific literatures. Young children are also affected with the SARS COV-2 and most of them recover without any major disease associated events. It has been observed that some young children diagnosed with COVID-19 had classic Kawasaki disease (KD) or a KD-like disease,

that may be a significant clinical manifestation of pediatric COVID-19²⁸. Vertical transmission from infected mother to neonates as per the studies suggest the implementation of robust neonatal healthcare monitoring systems²⁹.

Liang et al. (2020) showed COVID-19 mortality rate to be negatively related to the test numbers³⁰. The higher mortality is related to lower test number, ageing population, fewer hospital or beds and better infrastructure. However, the test number and population screening for reducing mortality are under debate. Few studies also reported the old age and different comorbidities for higher mortality^{21,31}.

Biosafety measures, Quarantine and Isolation

Since, the physical social distance to be maintained from a patient is uncertain, the prevention or treatment option relies on non-pharmaceutical approaches, pandemic mitigation strategies until an effective treatment or vaccine becomes available³². Maintaining hand hygiene by regular hand washing plays an important role in breaking chain of transmission. The use of surgical mask is not recommended as it won't prevent the small airborne particles from inhalation. The surgical mask can only filter pathogens above 2 microns. However, this virus is 0.12 microns in size, thereby raising the possibility of viral transmission mainly from hand to the mucous membrane of the aforementioned sites while frequently trying to adjust the mask. A more specialized mask, known as an N95 respirator, is thicker than a surgical mask, which filters almost 95 percent particles of 0.0001 inches (0.3 microns) in diameter^{33,34}. This mask is to be worn specifically by patients and health care professionals handling infected patient, their samples, waste and surroundings³⁵. However the likelihood of prevention of infection by wearing such respirators has not yet been proved.

Since SARS-CoV-2 incubation period is usually 2-14 days³⁶, therefore those who need to be quarantined, should be quarantined for 14 days in an open well-ventilated area. Quarantine in a semi-closed environment (e.g. ships and hotels) may be counter-productive³⁷. In a semi-closed environment, the virus incubates easily and spreads quickly between individuals, leading to widespread transmission as seen in Diamond Princess, a quarantined cruise ship in Japan.

Similar to the inevitable rampant spread of the virus in Diamond Princess Cruise ship, another outbreak occurred in Grand Princess, a voyage ship which was on a 15-day trip from San Francisco to Hawaii. Grand princess tour witnessed the unfortunate outbreak and had difficulty on tracing the source of infection, which eventually found a 71 year old man from California harboring the virus. Prior to sail, he had visited Mexico for a brief period of time from Feb 11th - 21st 2020. He died of the COVID-19 infection during his voyage³⁸. Out of 3,533 people in the trip, only 46 were tested. Amongst them 21 were found to be infected with COVID-19 with 19 of them being staff members. The Cruise has been circling along the coast of California for several days until 9th March 2020, when they finally docked in Oakland. Four different Military bases in California, Texas, and Georgia were prepared for quarantine of passengers on sail. Nearly, 1000 passengers residing in California were taken either to Travis Air Force Base, near Fairfield, or Marine Corps Air Station Miramar, near San Diego and remaining to federal facilities out of states³⁹.

Standard quarantine practices recommend a minimum of two weeks period quarantine before discharging patients, as the pattern of viral shedding of COVID-19 is still unclear.¹⁸ Strict quarantine measures of all known and possible interactions with the infected individual are to be traced. Social distancing along with community quarantine plays a pivotal role in curving the infection and may prove vital in ongoing pandemic.⁴⁰

Standard quarantine practice includes a combination of movement restriction along with clinical care of individuals exposed to close contacts with patients in addition to rapid, comprehensive contact tracing of all confirmed cases. Quarantined individuals must record their temperature followed by assistance of a healthcare team daily. In case of development of the symptoms meeting the case definition of COVID-19, the individual must be investigated and referred to designated hospital. In addition, if a disease develops under quarantine period, it would not spread further, resulting in lowering of reproduction number (R_0) to less than 1. Once contact tracing of infected individuals is

not possible, community-wide containment is then applied to reduce personal contacts like suspension of public gatherings, social distancing and community quarantine⁴¹.

To avoid air-borne route of SARS-CoV-2 transmission, social distancing of 6 feet / 2 meters or more from an infected person along with following personal biosafety measures including wearing face masks and hand washings are required⁴²⁻⁴⁴. Small particles loaded with virus may diffuse up to 10 m distance from source of infection, which is of high concerns in spreading this virus dominantly by air-borne route⁴⁵. SARS-CoV-2 RNA was also detected in sewage and wastewater, hence water-borne route of transmission need to be checked and investigated by wastewater-based epidemiology, sewage surveillance along with emphasis on fecal-oral transmissions, which would aid in prevention and control strategies to check spread of this pandemic virus⁴⁶⁻⁵⁰. There was no significant relation between temperature, humidity, and the virus distribution⁵¹.

Why elderly people have more mortality rate than children and adult?

Elder people generally over 60 years of age are at larger risk of COVID-19, with increased mortality in individuals above the age of 80 years. Likely explanation to this observation may be due to the presence of other chronic diseases like high blood pressure, diabetes, kidney disease, cancer, frail immune conditions and overall poor health increasing the mortality among the elderly⁵². In contrast; stronger immune system with fewer/no co-morbid conditions, likely exposure to other coronaviruses may reduce the predisposition to infection as in children and younger people⁵³. Researches showed that men were more affected than women due to increased travel patterns exposing them to asymptomatic or pre-symptomatic carriers. So far there are no proven inherent biological differences among the two genders⁵².

Pregnancy and birth outcomes in COVID 19

Maternal viral infections can adversely affect pregnancy outcome and preliminary research being done in developed countries hinted towards COVID-19 association with increased events of miscarriage, preterm birth and respiratory distress during pregnancy. Previous

studies have shown high rates of spontaneous abortion and preterm birth among mothers infected with SARS during pregnancy. Although no evidence is there that foetal growth retardation (FGR) occurs due to COVID-19, two-thirds of pregnancies with SARS showed FGR, so ultrasound need to be carried out. Impact of the infection on infants born to infected mothers has not been looked into and for a country like India where such data is scarce it is important to understand long term impacts on the children. Currently, the effect of COVID19 on pregnancy outcome in developing nations is unclear.

Clinically, SARS-CoV-2 infection characteristically induces cytokine storm, with elevated plasma levels of inflammatory cytokines such as MIP-1 α , TNF-A etc. In the context of pregnancy, maternal inflammation is known to affect fetal brain development leading to various behavioural disorders later in life. For example, increased maternal inflammatory cytokine IL-17a is known to induce autism spectrum like disorder in children. Cytokine storm and hyper-inflammation in pregnant women having SARS-CoV infection can elevate risks for neurodevelopmental disorders in the newborns⁵⁴. Malaria induced increased inflammatory cytokines such as TNF-A, IFN-G in maternal circulation is correlated with poor birth outcome. Therefore, there is a need to evaluate the load of pro-inflammatory cytokines among SARS-CoV-2 infected pregnant women and their correlation with birth outcome.

A probable passage of virus from the SARS-CoV-2 infected pregnant mother to the amniotic fluid has not been evidenced as well as vertical transmission of SARS-CoV-2 has also not been evidenced during late stages of pregnancy and vaginal delivery^{55,56}.

COVID-19 pandemic has elevated anxiety levels and few mental health illnesses in pregnant women as pregnancy period has delicate uncertainties. Lockdown along with financial issues can add to the anxiety. There is also a higher risk of domestic abuse during pregnancy, which has skyrocketed in this ongoing COVID-19 pandemic⁵⁷. Treatment regimen of COVID-19 in pregnancy also has to be looked at carefully. Although clinical studies on chloroquine and hydroxy-chloroquine in pregnant women are assuring when used against

malaria, however these drugs are genotoxic⁵⁸. There is a need to have studies of their impact during COVID-19 treatment.

Why is there a variation in transmission rate amongst countries with many showing a widespread increase in cases while some such as Turkmenistan, Bhutan, and Burundi etc. are reporting their first few cases or no cases?

Countries like Turkmenistan and Democratic People's Republic of Korea have no confirmed cases till July 26, 2020, whereas countries like Bhutan, Falkland Islands (Malvinas) and Papua New Guinea have less than 100 cases. Few of the individuals were suspected due to travel history from COVID-19 affected areas with mild symptoms but were all tested negative. Some countries have initiated strict social distancing measures mandating individuals on a 14-day self-quarantine practices among their fellow citizens returning from abroad⁵⁹. The government of Singapore cancelled all public events and installed medical booths to measure the core body temperature to screen and detect cases at their earliest for isolation and clinical management. Papua New Guinea has imposed travel restrictions to affected areas as well as prevented cruise ships and tourists from entering their nation. Italy's preparedness to tackle COVID-19 pandemic included shutting down educational institutions, executing travel restrictions and prohibition to mass gatherings.

Animal linkages and cross-species jumping

The virus is reported to have emerged from bats but the search for an intermediate host still remains obscure. Reptiles and endangered animals such as snakes, pangolins, and other mammals are suspected to be the intermediate host, however in-depth studies are required to reach to any conclusion. SARS-CoV-2 has been documented to be of animal origin, jump the cross-species barrier and possess zoonotic concerns⁶⁰. SARS-CoV-2 infection has been identified in pet, farmed and zoo animals (cats, dogs, tigers, lions and minks), while ferrets and primates also reported to be susceptible⁶¹⁻⁶⁵. The concept of reverse zoonosis has been stated in studies where a dog was found to be infected from its owner. Surveillance and monitoring of SARS-CoV-2 in animals must be undertaken via rapid detection,

using geographical information system (GIS) and tracking tools along with implementing one health approach and other necessary mitigation measures^{61,66-68}.

Developing vaccines, drugs and a global cure to fight COVID-19 pandemic

Researchers across the world are making very high efforts to develop vaccines, prophylactics, drugs/medicines and therapies to combat COVID-19, halt SARS-CoV-2 spread and safeguard health of mass population, few of which have reached clinical trials but may take time of few more months to reach to the market⁶⁹⁻⁷⁴. Vaccine candidates being explored include mRNA vaccine, DNA vaccine, vectored vaccine, virus like particles (VLPs) vaccine along with attempts for developing inactivated and attenuated SARS-CoV-2 vaccines. Antiviral drugs like remdesivir, favipiravir, umifenovir, oseltamivir, lopinavir/ritonavir and anti-malarial drugs chloroquine and hydroxychloroquine have shown fruitful results in treating COVID-19 patients. The modern upcoming tools of artificial intelligence (AI) and CRISPR are also being utilized to design effective vaccines and therapeutics against SARS-CoV-2^{75,76}. The fields of bioinformatics, cheminformatics, structure-based drug development, network-based techniques predicting drug-target interactions, AI and machine learning could aid for designing anti-SARS-CoV-2 drugs⁷⁷. Apart from developing vaccines and antiviral drugs, few of the potent therapeutics showing promising results in treating COVID-19 patients comprise of neutralizing antibodies, monoclonal antibodies, intravenous immunoglobulin (IVIg), natural killer (NK) cell based immunotherapies, convalescent plasma therapy and different kind of immunomodulatory agents⁷⁸⁻⁸². Dietary intake of balanced and nutritious foods along with supplementation of nutraceuticals, probiotics, plant-based molecules / phytochemicals, herbs and traditional medicines, Ayurvedic products, zinc and vitamins (A, C, E, B6 and B12) have been suggested to regulate and enhance immunity of the body to fight against SARS-CoV-2 infection developing into disease (COVID-19), as were found effective against other viral diseases^{83,84,92,85-89,89-91}. Besides, doing daily exercises and yoga activities also help in maintaining the biological function and boost immunity to safeguard from this pandemic

virus. In the current situation where no effective vaccine or drug is still available, boosting of the immune system with a holistic approach following different regimens as discussed, having synergistic effects, could protect, provide probable cure and would aid in flattening of the COVID-19 rising pandemic curves⁹³⁻⁹⁷.

The targeted repurposing strategies provide a fast method for approved treatment. Large scale screening of known drugs can provide a better pre-clinical and clinical evaluation. A high-throughput reprofiling screen using the ReFRAME (Repurposing, Focused Rescue, and Accelerated Medchem) provide access to a large number of drugs in clinical or pre-clinical trials and help in characterizing drugs for SARS-CoV-2⁹⁸.

The COVID-19 outbreak could judge preparation of countries for major medical health emergencies. It also provides an opportunity to develop and safeguard world with preparations to counter future health emergencies and pandemics. Increasing the test number and better infrastructure facility can reduce mortality. Also, the estimation of physical distancing will help in developing guidelines for control of COVID-19. To assess the health care burden of COVID-19 on population, continuous monitoring of co-circulating viruses is required for developing guidelines and research priorities in the susceptible population. Further studies are required to know the modes of interactions between CoVs and severity of COVID-19.

CONCLUSION AND FUTURE PROSPECTS

In spite of strengthening of healthcare system with increased testing, contact tracing, and implementation of strict control measures such as lock down, travel restrictions, masks, and social distancing, the virus found its way to spread rapidly among the people in different countries when such measures are relaxed or removed. The economic activities are severely affected in many countries and it is on the verge of collapse in many countries affecting the livelihood of millions of people in several low- and middle-income countries. Such measures could not be implemented for prolonged time as the economic activities need to be reviewed with extreme precautions. While doing so, we need to

protect the highly vulnerable elderly population who are severely affected by this virus and the young people should be allowed to resume their work with precautionary preventive measures. As this virus spreads through aerosol⁹⁹, wearing masks, maintaining social distance, following hand hygiene, avoiding any gatherings, avoid meetings in closed rooms with poor ventilation, avoid serving food or drink during the office meetings, etc need to be strictly followed to stop the chain of transmission¹⁰⁰. Though the virus is detected in stool samples, fecal-oral route of transmission may not play an important role^{29,101}. However, it may play significant role while people use common toilets in public places.

People with any sign of sickness should self-isolate and stay at home. A false sense of complete protection from virus while wearing masks need to be discouraged as mask can only reduce the risk of acquiring an infection and it does not provide complete protection against virus. It is becoming clear now that the virus is not going to disappear anytime soon. During the initial phase of the pandemic, it was perceived that an effective control measure such as lockdown can prevent the virus spread. Though it worked till the lockdown was strictly implemented. However, when the lockdown was removed and people activities have started, a massive increase in the cases were observed in several countries. It appears that the virus will be circulating in human population for prolonged period of time.

A successful vaccine could change the natural course of this disease. Until then, people need to learn to live with this virus following strict preventive measures as mentioned above. A behavioral change is much needed to improve the personal hygiene and mask hygiene. A dirty and reused mask is more dangerous than not wearing mask. Thus, everyone needs to ensure the mask it clean and it should be washed or disinfected and used appropriately.

The control of COVID-19 pandemic appears to be more complicated than previously thought. The spread of SARS-CoV-2 from asymptomatic persons, persistence of virus in contaminated surfaces, air-borne transmission, variation among susceptibility of people to viral infection, severity of disease and rapidly

increasing pandemic waves and highly rising cases continuously have altogether also made several limitations and lacunae in the prevention and control strategies^{51,102}. The natural course of reduced virulence of the virus, our improved ability to manage the patients with better health systems, availability of specific treatments and vaccine can significantly boost our ability to control ongoing COVID-19 pandemic. Some of these factors are already contributing to the reduced case fatality rate worldwide.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

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