Unusual routes for transmission of coronavirus disease (COVID-19): Recommendations to interrupt the vicious cycle of infection

ABSTRACT
The outbreak of the novel COVID-19, which began silently in Wuhan City, China, has now taken the form of a pandemic, with its claws spreading rapidly in many countries, with new and new cases emerging rapidly. The COVID-19-associated CoV is a beta coronavirus, which spreads at such a deadly rate that the World Health Organization (WHO) has to declare it a Public Health Emergency of International Concern (PHEIC). The objective of the narrative review is to describe what is COVID-19-related coronavirus (CoV), its structure and particle size, potential transmission routes, the risk of infection in patients undergoing blood transfusion or in patients with diabetes and cancer, and recommendations to prevent its spread in office settings, travel / recreation settings, residential and health facilities. This paper also discusses several groundbreaking approaches that are used to counter COVID-19. With this narrative review, we hope to raise awareness of the usual and unusual pathways of transmission and prevent the spread of this pandemic disease.

Key words: Coronavirus; disease outbreaks; emergencies; pandemics; public health; viruses

Introduction

On Dec 31st 2019, China reported the world health organization (WHO) of their citizen experiencing flu-like symptoms from an unknown pathogen in the Wuhan city of China, which they termed as “pneumonia of unknown etiology.”[1] This not only posed a threat to the world of a new pandemic disease but also to economic crises. On the verge of a new pandemic disease, WHO on Jan 5, 2020, advised against travel restriction.[2]

In recent decades, China has faced the emergence of many viral disease-like avian influenzas, severe acute respiratory symptom (SARS), and severe fever with thrombocytopenia syndrome (SFTS), which emerged in 1997, 2002-03, and 2010, respectively.[3-6]

Moreover, the identical outbreak of Middle East Respiratory Syndrome (MERS) occurred in 2012, which led to an understanding of the possibility of transmission of coronaviruses from animals to humans, which are now

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considered deadly pathogens to vertebrates as well as humans. These coronaviruses are linked to infecting respiratory, gastrointestinal, hepatic, and central nervous systems of humans, livestock, avian, bat, mouse, and many other wild animals.\[^7\]

The aim of the narrative review is to describe what is COVID-19-related coronavirus (CoV), its structure and particle size, potential transmission routes, the risk of infection in patients undergoing blood transfusion or in patients with diabetes and cancer, and recommendations to prevent its spread in office settings, travel/recreation settings, residential and health facilities. This paper also discusses several groundbreaking approaches that are used to counter COVID-19.

**What is Coronavirus (CoV) Associated with COVID-19**

Coronavirus is the virus of the family Coronaviridae and subfamily Coronavirinae and belongs to the suborder of Nidovirales. The subfamily of Coronavirus contains four genera named: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus. The sequence analysis of the genome of currently spreading CoV associated with COVID-19 in Wuhan city of China shows that it belongs to the cluster of beta coronaviruses and shows much resemblance to Bat-SARS-like (SL)-ZC45, Bat-SL ZXC21, and snakes coronaviruses.\[^8\]

**Structure of Coronavirus (CoV) Associated with COVID-19**

Coronaviruses are dependent on four structural proteins for their assembly and infection. The main component, i.e., the spikes on the surface of the virus particles, consists of S protein homotrimers divided into two functional units, S1 and S2.\[^9\] Not only do these spikes give the virus a characteristic appearance but they also play a crucial role in the viral attachment to host cells. Therefore, these viruses are known as corona viruses, because when seen under a microscope, they are seen with spikes protruding like a crown from the surface.\[^10\] M protein which is also a structural unit consists of three transmembrane domains that maintain the shape and curvature of the virion and bind to the nucleocapsid.\[^11,12\] Coronavirus also contains E proteins, which are essential for its assembly and release and ultimately contribute to pathogenesis. The protein of the COVID-19 virus is 90% amino acid similar to that of the SARS-CoV N protein.\[^13\]

**The Morphological Particle Size of Coronavirus (CoV) Associated with COVID-19**

A study published by Kim *et al.* in 2020 reveals that the particle size of CoV associated with COVID-19 measures 70–90 nm in cytoplasm of a wide variety of organelles and is specially located in vesicles.\[^15\]

**Mode of Transmission of Coronavirus (CoV) Associated with COVID-19 as Evident from Literature**

**The first case or “Patient Zero”**

Although first cases of human exposure to COVID-19-associated CoV have occurred in the Huanan Seafood Wholesale Market, where the first human may have been exposed to the virus through zoonotic or environmental exposures, the subsequent increase in the number of infected individuals shows evidence of human-to-human transmission at a later stage.\[^16\]

**Droplet transmission**

Human to human transmission is mainly carried out by symptomatic patients suffering from COVID-19. Symptomatic individuals transmit CoV through the expulsion of respiratory droplets, which are relatively smaller in size, resulting from coughing or sneezing similar to what seen in the case of normal flu and other rhino-virus infections. Due to the higher amount of aerosol present in closed environments such as homerooms, this human-to-human transmission generally occurs in people who are in close contact with these infected...
individuals (e.g., family members, visiting peers, and health care professionals). [17]

As estimated, coughing and sneezing activities can rapidly spread approximately 710 to 40,000 particle counts per cough or sneeze. The other factors that also play an important role in airborne transmission are temperature and relative humidity. As temperature increases, the chances of survival of the virus particle in the aerosol are lower and therefore lower temperatures increase the chances of the virus in suspended aerosols. Similarly, wet and humid conditions make the aerosol particle heavier and, as a result, these aerosols suspended in the air tend to settle on the surface. [18]

**Surface transmission**

Although the transmission of droplets can spread the disease from human to human, this type of transmission is seen only when the infected person is in close contact, especially within three feet. Surface transmission occurs when virus particles in the suspended aerosol tend to settle down on surfaces like table, chairs, furniture, and other materials made up of cardboard, wood or stainless steel. These surface deposited virus particles may tend to secondary infect other persons who are not in close contact with the primary cases. [19]

**Other possible routes of transmission**

When inanimate objects and fomites are in close contact with the saliva, mucus, nasal secretions of a person infected with CoV related to COVID-19, inanimate objects and fomites may become one of the most potential reservoirs for transmission of pathogens such as virus and bacteria either by direct means, surface-to-mouth contact, or indirectly, by contamination of fingers or hands. [19]

van Doremalen *et al.*, in 2020 conducted a study to assess the aerosol and surface stability of SARS related CoV revealed that CoV related to COVID-19 being similar to SARS related CoV is more stable on plastic and stainless steel as compared to copper and cardboard and can survive up to 48-72 hours after application, while in case of copper and cardboard the viable virus can be found from 4 to 24 hours. These cases are similar to contamination of inanimate objects and fomites by the infected person in real scenarios. These inanimate can be anything ranging from door handles, pen, mobile phone, wallet, computer keyboards or mouse, and even in worst-case national currency in case of manual transaction. [20]

**Risk of COVID-19 in patient undergoing blood transfusion**

Blood transfusion is a commonly used technique during treatment of multiple life-threatening conditions. According to studies carried out, CoV associated with COVID-19 may not only shield itself during the incubation time in the plasma of the infected individuals but may also multiply within lymphocytes, thus rendering the blood transmission procedure risky for the recipient. While there is still very little evidence of COVID-19 transmission in hospital settings by blood transfusion of blood products, it is still worth considering in the case of blood products containing higher lymphocytes. [21]

**Risk of COVID-19 in patient suffering from diabetes**

Diabetes which has not only emerged as a global chronic pandemic disease with detrimental effects on the various functions of the body, had also proved itself as a major risk factor for unfavorable outcomes for those undergoing treatment for COVID-19. A study conducted by Wang *et al.*, in 2020 stated that eight patients had underlying diabetes out of 41 confirmed COVID-19 patients. Hence, diabetes not only unfavorably affects the recovery of patients but can also impose a greater risk of death. [22-25]

**Risk of COVID-19 in patient undergoing cancer treatment**

It is well known that patients receiving cancer treatment, i.e., chemotherapy and radiotherapy, are in constant danger of nosocomial infections and other airborne infections as both the treatment protocols are immunosuppressive in nature. [26,27]

Patients with cancer who need regular hospital visits for their ongoing care and weakened immunity are at greater risk of acquiring these viruses, both in hospital settings as well as in any community settings. An interesting research reported by Wang *et al.* in 2020 shows that out of 138 hospitalized patients with the confirmed novel coronavirus (2019-nCoV)-infected pneumonia (NCIP) in Wuhan city of China, 41% were anticipated to be linked to hospital-based transmission, with 26% receiving ICU treatment and mortality rates being 4.3%. [24]

The CoV associated with COVID-19 has been linked to evolve from CoV associated with severe adult respiratory syndrome coronavirus 2 (SARS-CoV-2) which makes it much more dangerous for patients receiving lung cancer treatment as the symptoms can resemble those of lung cancer which can lead to false provisional diagnosis and delay in specialized care. [28]

A research report released by Dong *et al.* in 2020 on 2143 pediatric patients with COVID-19 shows that children of all ages are susceptible to this disease. Although the disease is less serious in children than adults, still poses a significant threat to young children and adults, particularly those under or equal to 5 years of age. [29]

Therefore, chemotherapy and radiotherapy patients are more vulnerable to this COVID-19 viral outbreak. Considerable steps should be taken to limit these patient visits to hospital
facilities, and those who need the visit must be kept in strict isolation to prevent them from acquiring the infection in hospital settings, particularly those belonging to an older age group or infants/children younger than five years.

Recommendations for preventing CoV spread among workers in the office setting
- Installations of heating, ventilation, and air conditioning (HVAC) system.[18]
- A minimum of 3-6 feet distance in sitting arrangements.[18]
- Use of a proper three-ply surgical mask or N-95 mask.
- Use of disposable paper, plastic, and latex gloves.
- Regular disinfection of surface by fumigation or use of surface disinfectants.

Recommendations for preventing CoV spread in a travel/leisure setting
A closed cabin of an air-conditioned bus, trains, airplanes, and cruise ships creates a favorable environment for the secure transmission of airborne pathogens.
- Provision for proper cabin ventilation through windows, in case of airplanes provisions, should be made for proper filtration of recirculated air through high-efficiency particulate air (HEPA) filters.[30]
- Proper disinfection of door handles, windows, and chair rest arms by alcohol-based disinfectants.
- Use of fumigators for disinfecting air inside the cabin after every flight before the each boarding.[18,31]

Recommendations for preventing CoV spread in residential premises
- The well-known method to prevent CoV related to COVID-19 is social distancing. In the case of people taking care of family members suspected of infection with CoV, appropriate hand hygiene measures and personal protective equipment like mouth mask, gloves, head cap, and protective eye-wear should be used.
- The isolation room for an infected person should be devoid of tables, cupboard, TV remote, or in case of presence, should be disinfected at a regular interval wearing gloves.
- Suspected infected individuals should be encouraged not to touch TV, or AC remotes or cell phones, which are the most common reservoir and common mode of transmission of the virus to other family members or, in other cases, can be disinfected by recommended disinfecting agents after every use.[20,32]
- As much as possible, payments should be made by digital transactions, in case of use of paper money and coins, handling should be done using proper disposable gloves and should not be manhandled again without gloves for another 24 h.[33,34]
- All the groceries and food packets purchased from the local market should be disinfected and processed using proper protocols.[33]

Recommendations for preventing CoV spread in healthcare facility setting
Healthcare facilities experience similar threats by sharing a similar characteristic of environment like office and commercial buildings; in addition, they possess a threat of nosocomial infection also.
- Care should be taken for thorough cleaning and sterilization of the instruments or equipment for minimizing spread of the virus from infected instruments or equipment used in infectious patient.[36]
- Separate seating arrangements should be made in closed waiting rooms with a provision of disposable mouth masks for all patients and an absolute patient quarantine is a must in case a positive patient is encountered.[36]
- Awareness must be created for strict infection control protocol, hand hygiene, and personal protection through personal protective equipment (PPE) in the event of encountering such cases.[36]

Some Innovative Technology in Fighting COVID-19

Mylab PathoDetect COVID-19 qualitative PCR kit
This is a kit developed by Mylab Discovery Solutions Pvt Ltd in collaboration with Serum Institute of India Pvt. Ltd. for the rapid and cost-effective detection of COVID-19. This is the only kit that has been approved by the Food and Drug Administration (FDA)/Central Drugs Standard Control Organization (CDSCO) of India after an in-depth evaluation by the Indian Council of Medical Research (ICMR). When in the market, this kit will reduce testing time by 65% or, in other words, will deliver results within 2.5 h as compared to 7 h or more when tested by the currently available method.[37]
COVID-19 sample collection mobile booth
This mobile booth for COVID-19 sample collection, which was first innovated in South Korean, is now being rapidly introduced in Indian scenarios also. This Phone style mobile booth helps the doctors in the collection of samples safely and efficiently and reduces the requirement of personal protective equipment (PPE) kits.\(^{[38]}\)

Image 3: A COVID-19 sample collection mobile booth in South Korea.\(^{[39]}\)

Decontamination and Sanitizing tunnel
In the battle against COVID-19, the engineers and technical personnel of different countries are not behind scientists. A recent breakthrough in equipping hospitals and health workers with coronavirus-fighting devices in India known as the "Decontamination and Sanitizing Tunnel" has demonstrated its efficacy in decontaminating and sanitizing the public and doctors from the COVID-19 virus.\(^{[40]}\)

Image 4: A prototype of decontamination and sanitizing tunnel for fighting against COVID-19 in Srinagar, India.\(^{[40]}\)

Conclusion
Since the outbreak of COVID-19, it had infected a more significant number of people both in China and around the world, with the death toll rising each and every day. As of now, no effective treatment or vaccine has been available for the same. The best way to tackle this problem is to isolate and quarantine infected people and to follow the rules of social distancing. This narrative review addresses emerging insights regarding structure, particle size, source of infection, mode of transmission therefore suggesting measures that can be implemented in workplace settings, travel/leisure settings, residential settings and health care facilities to contain the deadly virus and break the vicious cycle of infection. It is evident from the research that the risk of infection with COVID-19 is much higher in patients undergoing blood transfusion and those suffering from cancer and undergoing treatment for the same. Diabetes that kills many people around the globe is a major factor in compromising the immune system and poses a serious risk of COVID-19 infection. At the personal and community level, awareness should be created to adopt strict infection control measures and to ensure good personal hygiene by the use of masks and protective gloves, and to avoid crowded environments to safeguard themselves. Frontline staff such as doctors and nurses should be fitted with the PPE kits to avoid infection. In the scenario of a patient undergoing cancer treatment or suffering from diabetes, extensive steps should be taken to limit the visits of these patients to hospital facilities, and those who need to be visited must be kept in strict isolation to prevent them from becoming infected in hospital settings, especially in the elderly, or in infants and children younger than five years of age. This review also highlights some groundbreaking technology that can help prevent spread and aid in the early detection of this pandemic disease in a very simple and cost-effective way, and thus should be used worldwide. With this review, we're hoping to build necessary awareness to contain the deadly virus and tackle this disease more efficiently.

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Conflicts of interest
There are no conflicts of interest.

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