

SARS-CoV-2: Origin, Transmission, Prevention and Mitigation

Shekhar Pal¹, Deepak Juyal², Shalabh Jauhari³, Hitendra Singh², Rajat Prakash⁴, Shweta Thaledi⁵

¹Professor & Head, Department of Microbiology, Government Doon Medical College, Dehradun, Uttarakhand, India.

²Assistant Professor, Department of Microbiology, Government Doon Medical College, Dehradun, Uttarakhand, India.

³Associate Professor, Department of Microbiology, Government Doon Medical College, Dehradun, Uttarakhand, India.

⁴Assistant Professor, Department of Microbiology, National Institute of Medical Sciences, Jaipur, Rajasthan, India.

⁵Research Scientist, Viral Research Diagnostic Laboratories, Department of Microbiology, Government Doon Medical College, Dehradun, Uttarakhand, India.

Received: July 2020

Accepted: August 2020

ABSTRACT

Since the outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, coronaviruses have become a major public health concern. In 2012, coronaviruses were again highlighted with the emergence of middle east respiratory syndrome - CoV (MERS-CoV) outbreak. Currently the world is facing yet another outbreak of CoV named as SARS-CoV-2, a causative agent of severe viral pneumonia and respiratory illness similar to SARS and MERS, and the disease has been eventually named as corona virus disease 2019 (COVID-19). Initial cases of COVID-19 were identified in Wuhan, China in December 2019 and the number of cases has been mounting since then. As of 23rd July 2020, the disease has spread worldwide affecting 215 countries with a total of 15,379,943 confirmed cases and 630,313 deaths (overall case fatality 4.2%). Although the fatality rate of SARS-CoV-2 is currently lower than SARS-CoV and MERS-CoV, but it is highly contagious. Lack of timely implementation of the containment policies has resulted such rapid inter-continental transmission of the disease. However, in India the transmission dynamics are slightly different from China, United States of America and European countries particularly with respect to climatological conditions, population densities and age of the patients. This article gives an overview about SARS-CoV-2, its origin, transmission dynamics, overall current scenario, role of critical care medicine, public health response to contain it and the overall Indian perspective of the same. The future of human CoV outbreaks will not only depend on how the viruses will evolve, but will also depend on how efficiently and effectively we implement the prevention and treatment strategies to contain the contagion.

Keywords: Coronavirus, Contagion, COVID-19, Cytokine storm, N-95 mask, Pneumonia, Wuhan.

INTRODUCTION

Human coronaviruses (HCoV) have long been known as a causative agent of common cold in otherwise healthy individuals. However, during the past two decades, 2 highly pathogenic HCoVs – Severe acute respiratory syndrome coronavirus (SARS-CoV; 2002) and Middle east respiratory syndrome coronavirus (MERS-CoV; 2012) emerged from animal reservoirs and caused global epidemics with high morbidity and mortality.^[1,2] More recently in December 2019 a highly pathogenic HCoV, was recognized in Wuhan, capital city of Hubei province, China, causing serious pneumonia like illness and death.^[3] On 12 January 2020 World Health Organization (WHO) named this new CoV as 2019-novel coronavirus (2019-nCoV). As per the International Health Regulations (IHR, 2005) on 30th January 2020, WHO declared the 2019-nCoV

outbreak as a public health emergency of international concern (PHEIC). Later, Coronavirus Study Group (CSG) of the International Committee proposed to name the new coronavirus as SARS-CoV-2 and WHO officially named the disease as corona virus disease-2019 (COVID-19), both issued on 11 February 2020 and on 12th March 2020 WHO declared the COVID-19 outbreak as global pandemic.^[4] This article gives an overview about SARS-CoV-2, its origin, transmission dynamics, overall current scenario, role of critical care medicine, public health response to contain it and the overall Indian perspective of the same. However, the knowledge about this virus is continuously and rapidly evolving and hence the readers are expected to update them on regular basis.

Origin and transmission

Coronaviruses (CoVs) have become the major pathogens of emerging respiratory disease outbreaks and are ecologically diverse group of organisms with the greatest variety seen in bats that are considered as reservoirs for many of these viruses.^[5] Peridomestic animals may serve as intermediate hosts and facilitate recombination and mutation events with expansion of genetic diversity.

Name & Address of Corresponding Author

Deepak Juyal,
Assistant Professor,
Department of Microbiology,
Govt. Doon Medical College, Dehradun, Patelnagar
Dehradun-248001, Uttarakhand, India
E mail: deepakk787@gmail.com

CoVs are a large family of spherical, enveloped, non-segmented, positive sense, single stranded RNA viruses (+ssRNA) characterized by spike proteins projecting from the virion surface and can be divided into four genera; including α - β - γ - δ -CoV, of which α -CoVs and β -CoVs are known to cause human infections [Figure 1].^[3,6,7] Previously, six CoVs have been identified to cause infections in humans, among which α -CoVs: HCoV-229E and HCoV-NL63, and β -CoVs: HCoV-HKU1 and HCoV-OC43 have low pathogenicity and cause mild respiratory symptoms similar to common cold. The other two known β -CoVs: SARS-CoV and MERS-CoV can cause severe and potentially fatal respiratory tract infections.^[7,8] SARS-CoV was identified as a human CoV that caused 2002-2003 outbreak of severe acute respiratory syndrome (SARS) in Guangdong province, China, resulting in 774 deaths out of total 8098 cases that were infected over a period of nine months ($\approx 10\%$ fatality).^[1] Around a decade later in 2012 a new CoV was reported from Saudi Arabia to cause a severe respiratory disease and was named as MERS-CoV.^[2] Since 2012, a total of 2506 infected cases of MERS-CoV have been reported from 27 countries with 862 deaths ($\approx 35\%$ fatality), and has a case fatality three times more than that was seen in SARS-CoV infections.^[9]

SARS-CoV-2 is the third identified HCoV to cause severe respiratory illness named as COVID-19 and has symptoms and incubation period resembling to that of SARS-CoV and MERS-CoV infections.^[3,10] Based on current epidemiological investigations, the incubation period of COVID-19 is 1-14 days, mostly 3-7 days, and is highly contagious during the latency period.^[11] Majority of the adults and children present with mild flu-like symptoms, however around 5% of the infected patients can become critically ill and rapidly develop acute respiratory distress syndrome, respiratory failure, multiple organ failure and even death.^[12] To date the, fatality of SARS-CoV-2 appears to be less than that was observed in SARS-CoV and MERS-CoV infections. However, since new cases are being confirmed everyday, the fatality of the virus keeps changing and cannot be calculated accurately until after the end of this outbreak. As per the data available till date the virus appears to be more fatal in elderly patients or patients with comorbidities.^[13] Table 1 depicts the comparison between SARS-CoV, MERS-CoV and SARS-CoV-2 with respect to their probable receptor usage, hosts (primary and intermediate), incubation period, fatality and basic reproduction number.^[14]

SARS-CoV-2 belongs to genera β -CoV (subgenus sarbecovirus, subfamily Orthocoronavirinae), and preliminary analyses indicates that its genomic sequence is 96.2% identical to a bat CoV RaTG13 and 79.5% identical to SARS-CoV.^[15,16] Its genome contains 2981 nucleotides, encoding for 9860 amino acids. Although its origins are not entirely

understood, the genomic analyses suggests that SARS-CoV-2 probably evolved from a strain found in bats and an alternative intermediate reservoir such as turtles, pangolins and snakes are thought to be involved in its transmission to humans.^[16-19] However it is still not certain that this intermediary exists. As the first cases of COVID-19 disease were linked to direct exposure to the wholesale seafood market of Wuhan, capital city of Hubei province, China, where live animals are sold, mostly for food and medicinal use (folk remedies) as per the Traditional Chinese Medicine,^[3,20] the animal to human transmission was presumed as the main mechanism. The practice of eating raw meat and the close contact between humans and animals are both considered as risk factors for the initiation of new HCoV outbreak and thus like SARS, COVID-19 can also be considered as a zoonotic disease. Similar to SARS-CoV and unlike MERS-CoV, human to human transmission has been confirmed and was evidenced by the infection of healthcare professionals in Wuhan hospital, China, suggesting the virus to be highly contagious.^[13] Soon it was apparent that the infection could be transmitted from asymptomatic people and also before any onset of symptoms. As the virus keeps spreading to more individuals, more mutations may arise which can potentially make the virus more virulent. It is not well understood why outbreaks of CoV infections are mostly occurring in China, however, it is speculated that these viruses may be predominantly circulating in animals in China rather than in different parts of the world, and close interactions with live and wild animals that are consumed as food may be one of the reasons for such sudden outbreaks.

Overall current scenario: Global and Indian

Since December 2019, when the initial cases of SARS-CoV-2 were reported from China, the number of cases has been continuously rising in China and later throughout the world.^[20] Over the due course of time cases continued to increase exponentially and the modeling studies reported an epidemic doubling time of 1.8 days.^[21] As of 23rd July 2020, 15,379,943 cases (86,152 cases in mainland China) have been reported worldwide affecting 215 countries. Of those infected, 630,313 have died with an overall case fatality of 4.2%.^[22] It is important to note that while the number of new cases has reduced in China lately, they have increased exponentially in other countries, particularly in United States of America (USA), Brazil, India, Russia, South Africa, Peru, Mexico, Chile, Spain, United Kingdom (UK), Italy, France and Germany [Table 2]. In terms of case fatality, France, Belgium, UK, Italy, Mexico and Spain have emerged as the worst hit countries due to COVID-19 with an overall case fatality of 16.9%, 15.2%, 15.3%, 14.3%, 11.4 and 9.0% respectively [Table 3].

In India the first case of COVID-19 was reported on 30th January 2020, the number increased to 3 by the end of February 2020, by 1st week of March the number increased to 34, thereafter a sudden spurt in cases was seen and by 23rd July 2020 the number increased exponentially to a total of 1,239,684 confirmed cases with 29,890 (2.4%) deaths.^[22] However, the numbers are possibly an underestimate of the infected and deceased, reason being limited testing facilities and resource constraints. It is also important to mention here that when we particularly talk about the Indian subpopulation, we must understand that most of the Indian population belongs to rural area where the quality healthcare and diagnostic facilities either are not available or have limited resources. The known co-morbidities for COVID-19 are not properly controlled in such population, which makes them more vulnerable to SARS-CoV-2 with catastrophic consequences.

The high infectivity, transmissibility and the mortality rate of over 5% is a cause of concern across the globe.^[23] Elderly patients with co-morbid conditions including pulmonary disease, cardiovascular disease, kidney disease, diabetes mellitus and hypertension have been associated with even higher mortality rates, as seen in France, UK, Belgium and Italy where the mortality rate ranges approximately between 14% to 17% and emphasizes the importance of healthcare system's capacity in the care of critically ill patients with COVID-19.^[22,23] The exact cause of death is unclear at this point with progressive hypoxia and multiorgan dysfunction being the presumed causes. ACE2 has been shown to be a co-receptor for viral entry for SARS-CoV-2 with increasing evidence that it has some role in the pathogenesis of COVID-19.^[16] The data so far available seem to indicate that SARS-CoV-2 is capable of producing an excessive immune reaction, which as a whole is called as 'cytokine storm' and leads to extensive tissue damage and multiple organ dysfunction.

Seasonal and climatic influence in disease transmission

Many respiratory viruses show clear seasonal variation in prevalence, the most well known e.g. being seasonal influenza, which peaks every winter in the temperate zone of the Northern hemisphere. After years of research, low temperature and low humidity environment is now generally recognized as the key factor contributing to the transmission of influenza in winter.^[24,25] A correlation exists between observed spread of COVID-19 and climatological temperatures and latitude. Enhanced spread of the disease has been observed between December 2019 to March 2020, along an observed area of 25-55 degrees north latitude and within a climatological band of 4-12°C.^[26] A recent observational study conducted across 100 cities in China also found that high temperatures and high relative humidity was significantly associated with

reductions in reports of COVID-19 cases.^[27] They also concluded that arrival of summer and rainy season in the northern hemisphere could help reduce the spread of SARS-CoV-2.

Most of the cases of COVID-19 linked with local transmission were identified in countries located in northern hemisphere, which were in winter 'flu' season. The 2002-2003 SARS-CoV also did not have any effect in Africa or South America on a large scale, which suggests that the transmission of respiratory viruses occurs more efficiently in winter season and it is speculated that if at all southern hemisphere will be affected it will occur later in the year. Moreover various other factors like climate specific cultural differences, effect of UV light on survival of virus on surfaces, immunological differences of the population affected, pre-exposure with other coronaviruses or the higher temperature may also contribute.

Public health response to COVID-19 and the Indian perspective

As more and more countries report cases, including those with no link to the disease epicenter, it is clear that there may be many more unrecognized cases all around the world and that community transmission has already started in many countries. One important goal of public health response efforts now should be diminishing the speed of spread and to flatten the peak of the epidemic curve. Of note one of the most important public health intervention to slow the spread will be rapid diagnosis and isolation of cases.^[28] In an outbreak of this magnitude, the most important number that public health planning experts will be looking for is the basic reproduction number, also known as the 'R-naught' or simply R₀.^[29] R₀ is used to describe the intensity of an infectious disease outbreak and measures the maximum epidemic potential of a pathogen. It represents the average number of people who will catch disease from one infected person in a population that has never had and is consistent with R₀ estimates for SARS-CoV and MERS-CoV.^[21,30-34] It is also important to note here that R₀ is not an intrinsic property of the virus itself, and R₀ estimates tend to be lower in places where sound infection control practices are routinely followed and vice versa. Moreover, R₀ estimates are highest at the beginning of an outbreak and then gradually subside once the countries become aware of the outbreak and the transmission dynamics of the pathogen, and manage to implement effective control measures to contain the spread. However, at any rate, any R₀ above 1 should be taken seriously, and particularly in reference to SARS-CoV-2, the goal should be to reduce R₀ to a value that is below 1.

During an exposure from prior zoonotic CoV outbreaks, public health authorities have initiated preparedness and response activities. Additionally the biomedical researchers are initiating countermeasure development for SARS-CoV-2,

using SARS-CoV and MERS-CoV as prototypes. The public health response to COVID-19 in China has illustrated that it is possible to contain COVID-19 if government focuses on tried and tested public health outbreak responses.^[23,35] Although, the timely measures like isolation, quarantine, socio-physical distancing and community containment measures were implemented by the government, we in India have entered into the stage of community transmission and containing the virus to spread any further has become challenging, and the entire population of 1.3 billion is at risk. Thus, it calls for interventions that are disruptive not just for viral transmission but also for way we respond as a country.^[36] Having said that, from Indian perspective we need to focus on six major work streams viz. timely laboratory diagnosis and subtyping; surveillance including screening at points of entry and cross border activities; infection prevention and control particularly in health care facilities; clinical treatment of patients with severe COVID-19; risk communication; management of supply chain. Many cities and states in India have ordered socio-physical distancing, including closing schools, altering business operations, instituting curfews and prohibiting large gatherings. Studies suggest that banning large gatherings can significantly diminish the spread of SARS-CoV-2, and some countries have resorted to more aggressive measures, including cordons sanitaire (guarded areas in which individuals may not enter or leave) or large scale ordering of individuals to remain confined in their homes at all the time.^[37]

Role of advanced critical care facilities

Critical care will be an integral component of the global response to this emerging infection. The rapid increase in the number of COVID-19 cases worldwide highlighted how quickly the healthcare systems can be challenged to provide adequate care. Based on assumption that community transmission is already occurring, and despite of the containment measures implemented by health authorities, it is assumed that cases of COVID-19 may shoot up exponentially in coming days, possibly in lakhs or even more. As per the data available till date, even at a 5% ICU admission rate it would not be possible for healthcare facilities to accommodate all critically ill patients and any substantial increase in the number of such patients would rapidly exceed the total ICU capacity,^[38,39] without even considering other critical admissions like trauma, stroke and other emergencies. Clear-cut guidelines should be made at local and regional levels to optimize the critical care resources. If the number of critically ill COVID-19 patients increases and the access to life saving interventions like hospital bed, ventilators, extracorporeal membrane oxygenation or renal replacement therapy is strained, clear resource allocation policies should be determined by the

clinicians, policy makers and ethicists. In the situation of crisis, if at all it arises, the hospitals are expected to do the following:

- Create cohort ICUs for COVID-19 patients (separate from rest of the ICU beds to minimize the risk of hospital transmission)
- Organize and demarcate a triage area where critically ill patients with suspected COVID-19 infection who may require mechanical ventilation can be kept, till their final diagnostic test results are available.
- Formulating local protocols for triage of patients with respiratory symptoms, their rapid testing and to allocate them appropriate cohort as per their diagnostic reports.
- Ensure the availability of PPE for healthcare professionals and to train all the personnel at risk of contagion.
- Ensure Real time reporting of each positive or suspected critically ill COVID-19 patients to the regional health care authorities

Practically speaking, any healthcare system cannot sustain an uncontrolled outbreak, and implementing stern containment measures is the only option to avoid the total collapse of the ICU system. Clinicians need to continuously advise the health care authorities to augment the containment measures.

Protection of patients, healthcare workers and their family

A serious challenge in responding to COVID-19 is protecting healthcare workers (HCWs) and preventing nosocomial infection, which have been a major problem in China. [40] By now it is known that SARS-CoV-2 primarily spreads through the respiratory tract, by droplets, respiratory secretions and direct contact for a low infective dose.^[21,41] Although, it is not principally an airborne virus, but a recently published report emphasizes on the possibility of respiratory transmission of the virus, particularly in health care settings.^[42] Therefore, ensuring routine droplet barrier precaution, environmental hygiene and overall sound infection control practice is indicated. To ensure minimal risk of infection when treating COVID-19 patients, CDC recommends the use of PPE including a gown, gloves and either an N-95 respirator plus a face shield/goggles or a powdered air-purifying respirator. It is worth noting that N-95 respirators are not suitable for people with facial hair.^[43] The widespread use of recommended barrier precautions in the care of all the patients with respiratory symptoms must be of highest priority and becomes more imperative for clinicians involved with aerosol generating procedures such as endotracheal intubation and diagnostic testing using bronchoscopy.

Placing a surgical face-mask on the patient at arrival, supplying tissues, promoting cough etiquette and

providing for hand hygiene and surface decontamination are all important steps. The symptomatic patients with suspected COVID-19 should be rapidly triaged and separated from the general population ideally in a well-ventilated space with a distance of at least 6 feet from others until they can be placed in isolation room. Ensuring the well-trained hospital staff in standard, contact and droplet infection prevention and control precautions, including the use of relevant PPE is very important. Caregivers who encounter any patient with respiratory symptoms should wear a mask and gloves with goggles as recommended. Strict adherence to the guidelines is of elevated importance and enhances the safety of HCWs. It is also important to communicate to the general public that when and how to wash hands correctly, covering coughs and sneezes and staying home if unwell. Hospitals may encounter serious challenge in handling the overwhelming number of patients who do not need acute care, so those who are infected but otherwise well should keep themselves in strict home isolation and should not contribute to hospital demands any further.

In addition to the aforesaid barrier precautions, meticulous hand hygiene and surface decontamination are key to safety. The coronavirus is known to live on surfaces for hours or days but is also effectively killed by available disinfectants (e.g. 1% hypochlorite solution) when properly used.^[44] Clinical staff should clean workspaces and personal item such as stethoscopes, mobile phones, keyboards, landlines, nametags and other similar items with available disinfectants or alcohol based disinfectants.^[45] Commonly touched surfaces like light switches, counter tops, chair arms, escalator railings, elevator buttons, door knobs and handles must be regularly cleaned at least every 2 to 3 hours if not less. Although it is not possible to entirely eliminate the risk, but prudent adjustments can be warranted.

For frontline caregivers the concerns about transmitting the virus to family members will need to be addressed. Protective planning for the home such as separation of living spaces and bathrooms should be implemented. When arriving home after work the person should take off his shoes outside, remove clothes for washing and immediately take a shower. Although long working hours make any additional home preparations and extra home cleaning a significant challenge but still as far as possible should be followed.

COVID-19: Preparation for prevention

Considering the large population, should COVID-19 spreads more rapidly in India, we won't be able to afford large-scale diagnostics. Hence in the absence of testing, triage based on clinical case definitions or presumptive diagnosis should be prioritized. Moreover, as per the trend of disease progression

being observed all over the world, the number of patients is definitely going to increase in coming days and the patients that may require ventilator support will outnumber the available intensive care unit (ICU) beds. Although in majority of the hospitals, OPD's have been shut down and only the flu OPD and emergency OPD are running, but still the general hospitals (private as well as government) will need to be converted to critical care hospitals and additional primary care physicians and nursing staff trained in critical care medicine will need to be mobilized to the most affected areas. However, funding the additional cost of critical care units from the limited health budget allocated may be a cause of concern. In India, the ICU beds and personnel trained in critical care are currently limited only to tertiary care facilities and the mortality associated with COVID-19, may possibly exceed the reported overall case fatality rate of 5%.

The COVID-19 outbreak has demonstrated the importance of basic infection prevention and control measures, and the importance of having these minimum requirements in place. The disruption of supply chains, increased demand and depletion of stock in both high and low resource settings is being reported daily in print and social media. Panic situation in the wake of current COVID-19 outbreak has led to irrational buying and use of personal protective equipment (PPE) including N-95 respirators which consequently has led to inadequate supplies and may not only have potentially devastating consequences from patient as well as health care professional's perspective, but can also undermine the government's efforts to contain the further spread. The rational use of PPE needs to be ensured and we all need to act wisely in order to secure adequate supplies and stocks. Regional production either large or small scale should also be considered to reduce the risk of shortages of PPE at crucial times.

Role of electronic, print and social media

Responsible and sensible role of media is also one of the crucial factor in public health responses particularly in the emergency situation we are currently facing. Be it electronic, print or social media all need to team up with government in providing consistent, simple and clear messages. Various media platforms can use banners, pop ups and other tools to directly message users about hand washing and socio-physical distancing. Moreover at the same time social media should be used to disseminate reliable information about when to get tested, what to do with the results, and where to receive care. For those whose test results are positive for COVID-19, the platform could enable users to inform their contacts about the potential exposure and how to follow up for testing.

It is evident how quickly both negative and positive messages can influence the public hence one should

refrain from sharing any news from unauthentic sources which otherwise can create a panic situation among the general public. Unlike any prior event, WHO has identified that the “2019-nCoV outbreak and response has been accompanied by a massive infodemic – an over abundance of information – some accurate and some not – that makes it hard for people to find trustworthy sources and reliable guidance”.^[46] Crisp, short motivational messages such as daily briefings, if delivered to the public, can improve the public confidence in the government’s efforts to curb down the spread of this virus. While social media cannot replace in-person contact, there may be ways to better use it to support recovery and resilience.

Diagnostic modalities

Timely and efficient diagnostic testing is critical to an effective response to the current COVID-19 outbreak. Real time reverse transcriptase polymerase chain reaction (rRT-PCR) from nasopharyngeal/oropharyngeal swabs typically has been used to confirm the clinical diagnosis.^[40] Considering the presence of number of circulating respiratory viruses, differentiating COVID-19 from other pathogens, particularly influenza becomes imperative and can be done by rRT-PCR. Rapid access to diagnostic testing results is a public health and clinical priority allowing for efficient patient triage and implementation of infection control practices.

The US, FDA has approved a new test by Abbott laboratories that uses isothermal nucleic acid amplification technology instead of PCR.^[47] As it does not require the alternating temperature cycles which otherwise is time consuming, this method can deliver positive results in just five minutes and negative result in 13 minutes. Currently there are about 18,000 of these machines but are not available outside USA.^[48]

Blood antibody testing and viral antigen testing in respiratory samples, similar to the rapid influenza test, are currently being investigated. The clinical value of these tests is not known yet, and challenges such as cross-reactivity with other corona viruses, and that sometimes the test does not detect the virus when it is there, need to be addressed. The serological testing kits can be used to detect infection in individuals after seven days of the onset of symptoms and hence can be useful in population surveillance in hotspot areas.^[49]

Off label and Compassionate drug use

The world is now facing a pandemic of SARS-CoV-2, for which no proven specific therapies are available other than supportive care. In china and now in USA, Italy, Spain and France, a large number of patients have received off label and compassionate use therapies such as chloroquine, hydroxychloroquine, azithromycin, lopinavir-ritonavir, favipiravir, remdesivir, ribavirin, IFN,

convalescent plasma, steroids and anti-IL-6 inhibitors, based on either their in vitro anti-viral and anti-inflammatory properties.^[50-56] Except for the few randomized controlled trials (RCT) started in China and more recently in USA these therapies have been mostly given without controls.^[57,58] Although many of the aforementioned drugs have in vitro activity against different coronaviruses, no clinical evidence currently supports the efficacy and safety of any drug against SARS-CoV-2. Yet there are some published case reports of old and new drugs with in vitro activity against SARS-CoV-2 that have been given to patients but without a concurrent control group.

Administration of any unproven drug as a last resort wrongly assumes that benefit will be more likely than harm. When any such drug with unknown clinical effects is given to patients who have severe illness, there is no way to know whether the patients have benefitted or were harmed particularly in the absence of a concurrent control group. Having said so, a common interpretation of compassionate drug use is that, if the patient died, they died from the disease, but if they survived, they survived because of the drug, which is not true. Compassionate use of drugs that have not been previously approved for clinical use could cause serious adverse effects and without a control group it is not possible to accurately determine the harm of any experimental drug. Chloroquine/ hydroxychloroquine, azithromycin, lopinavir-ritonavir have a variety of adverse effects, including QT prolongation, torsades de pointes, hepatitis, acute pancreatitis, neutropenia and anaphylaxis. Considering that most patients who died of COVID-19 were elderly, had cardiovascular abnormalities and frequent cardiac arrhythmias,^[23,39] chloroquine/hydroxychloroquine, azithromycin and lopinavir-ritonavir could potentially risk the cardiac death. Moreover hepatitis and neutropenia are clinical manifestations of COVID-19 and both hepatic and bone marrow dysfunction could be further worsened by off label use of these drugs, thus it would be impossible to differentiate the drug related adverse effects from the disease manifestation in the absence of a concurrent control group. However it is imperative to discover new therapies, otherwise there will be no proven treatments for future coronavirus pandemic, if any occurs.

Futuristic approach

Integrating social media as an essential tool in preparedness, response and recovery can influence the response to COVID-19 and future public health threats. Data available from various social media platforms about symptoms, interactions, photos at events, travel routes and other digital footprints about human behavior should be analyzed to understand and model the transmission dynamics and trajectory of COVID-19. Various social media platforms like Facebook is providing aggregated and

anonymized data to researchers about the movement of population density maps to better inform how the virus is spreading. Social media data if merged with electronic medical data could also provide insights about individual level risk. Various funding agencies and foundations have funded researchers to sequence

the complete viral genome of SARS-CoV-2 and the data generated can be used to further analyze the genome to study how the virus is affecting different organ functions or have predilection to particular organ(s) if any and can also be helpful in planning the future therapeutics and vaccine development.

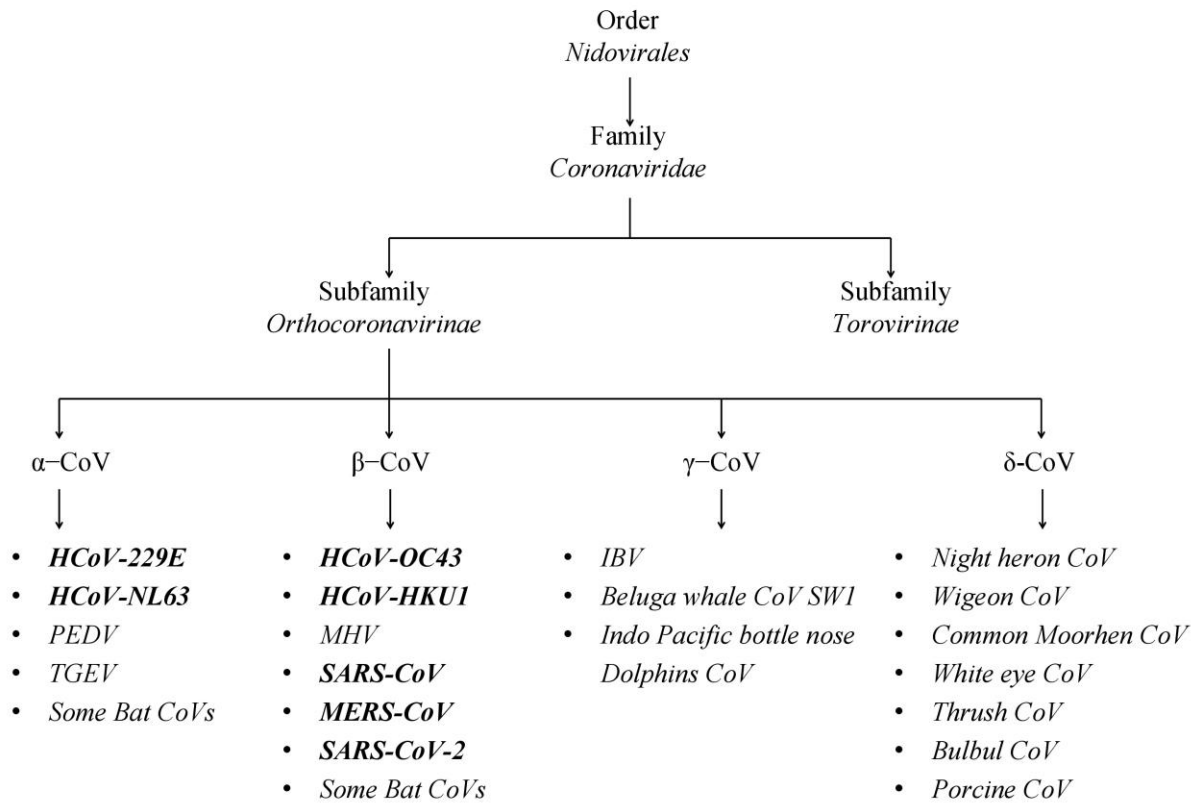


Figure 1: Classification of different types of Coronaviruses (Family: Coronaviridae; Subfamily: Orthocoronavirinae; Genus: α - β - γ - δ -CoV). SARS-CoV-2 belongs to genus β -coronavirus.

Table 1: Comparison between SARS-CoV, MERS-CoV, and the SARS-CoV with reference to their receptor usage, primary and intermediate hosts, incubation period, total number of cases and deaths, and basic reproduction number (R0).^[14]

Virus	Receptor	Primary Host	Intermediate Host	Incubation Period	Total number of cases	Total number of deaths	Fatality	R0
SARS-CoV	ACE2	Bats	Civets and Raccoon dogs	Typically between 2-10 days (upto 14 days)	8098	774	≈10%	2-5
MERS-CoV	DPP4 (CD26)	Bats	Camels	Typically between 2-14 days	2506	862	≈35%	2-5
SARS-CoV-2	Most probably ACE2	Most probably Bats	Not identified (Probably pangolins)	Current estimates between 2-10 days (upto 14 days)	13,56,780 (As of 8th April,2020)	79,385 (As of 8th April,2020)	5.85% (As of 8th April,2020)	2-3.5

SARS-CoV: Severe acute respiratory syndrome coronavirus; MERS-CoV: Middle east respiratory syndrome coronavirus; ACE2: Angiotensin converting enzyme2; DPP4: Dipeptidyl Peptidase 4; CD26: Cluster of differentiation 26; R0: Reproduction number

CONCLUSION

PHEIC is a typical event that constitutes a public health risk and potential for the disease to spread to other countries like it has happened in current COVID-19 outbreak and require coordinated

international response to contain it. During a situation of crisis we are currently facing in the wake of COVID-19, the government has a special responsibility to thoughtfully balance public health protections and civil liberties. Public health officials, local health departments, hospitals, doctors and policy makers should work in a coordinated way to

educate the general public and provide needed supplies to contain the spread of virus. The efficiency with which the virus can cause human-to-human transmission is a cause of concern and necessitates quick development of vaccines, neutralizing antibodies and therapeutics, which can inhibit the viral multiplication and infection. Effective and efficient public health interventions that delay the spread of COVID-19 would allow the time for development and implementation of effective countermeasures and key biomedical technologies, possibly including vaccines. Although the world is hoping to succeed in containing this virus as soon as possible, but even after success, there need to be follow-up with patients who are cured and declared virus free.

Table 2: Situation report of ten countries with maximum number of cases, with reported laboratory-confirmed COVID-19 cases and deaths. (Data as of 23rd July 2020).^[22]

Country	Cases	Total deaths	Case fatality in %
United States of America	4,100,875	146,183	3.6
Brazil	2,231,871	82,890	3.7
India	1,239,684	29,890	2.4
Russia	789,190	12,745	1.6
South Africa	394,948	5,940	1.5
Peru	366,550	17,455	4.8
Mexico	362,274	41,190	11.4
Chile	336,402	8,722	2.6
Spain	314,631	28,426	9.0
United Kingdom	296,377	45,501	15.3

Table 3: Situation report of ten countries in terms of maximum case fatality rate. (Data as of 23rd July 2020).^[22]

Country	Cases	Total deaths	Case fatality in %
France	178,336	30,172	16.9
Belgium	64,627	9,808	15.2
United Kingdom	296,377	45,501	15.3
Italy	245,032	35,082	14.3
Mexico	362,274	41,190	11.4
Spain	314,631	28,426	9.0
Canada	112,240	8,870	7.9
Sweden	78,504	5,667	7.2
Ecuador	77,257	5,418	7.0
Iran	281,413	14,853	5.3

Remember that natural disasters bring people together but epidemics and outbreaks split them apart. The onus lies with governing bodies at varying levels, as well as the healthcare coordinators to better utilize resources to prepare for, mitigate against, respond to and recover from this viral pandemic.

REFERENCES

1. Drosten C, Günther S, Preiser W, van der Werf S, Brodt HR, Becker S, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med.* 2003 May 15;348(20):1967-76

2. Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus AD, Fouchier RA. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. *N Engl J Med.* 2012 Nov 8;367(19):1814-20
3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020 Feb 20;382(8):727-733
4. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available at: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020> [Last accessed on 13 Mar 2020]
5. de Wit E, van Doremalen N, Falzarano D, Munster VJ. SARS and MERS: recent insights into emerging coronaviruses. *Nat Rev Microbiol.* 2016;14(8):523-534
6. de Wilde AH, Snijder EJ, Kikkert M, van Hemert MJ. Host Factors in Coronavirus Replication. *Curr Top Microbiol Immunol.* 2018;419:1-42
7. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. *Respirology.* 2018;23(2):130-137
8. Verma S, Manjunath SM, Ettishree, Singh A, Srivastava M, Sahoo KK, et al. Coronavirus: An emergency for healthcare professionals. *J Family Med Prim Care* 2020;9:1815-9
9. Killerby ME, Biggs HM, Midgley CM, Gerber SI, Watson JT. Middle East Respiratory Syndrome Coronavirus Transmission. *Emerg Infect Dis.* 2020;26(2):191-198
10. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, et al. Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *N Engl J Med.* 2020;382(10):970-971
11. Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res.* 2020;7(1):4
12. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506
13. Gralinski LE, Menachery VD. Return of the Coronavirus: 2019-nCoV. *Viruses.* 2020;12(2):135
14. Ashour HM, Elkhatib WF, Rahman MM, Elshabrawy HA. Insights into the Recent 2019 Novel Coronavirus (SARS-CoV-2) in Light of Past Human Coronavirus Outbreaks. *Pathogens.* 2020;9(3). pii: E186
15. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect.* 2020;9(1):221-236
16. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020;579(7798):270-273
17. Giovanetti M, Benvenuto D, Angeletti S, Ciccozzi M. The first two cases of 2019-nCoV in Italy: Where they come from? *J Med Virol.* 2020;92(5):518-521
18. Paraskevis D, Kostaki EG, Magiorkinis G, Panayiotakopoulos G, Sourvinos G, Tsiodras S. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. *Infect Genet Evol.* 2020;79:104212
19. Zhang T, Wu Q, Zhang Z. Probable Pangolin Origin of SARS-CoV-2 Associated with the COVID-19 Outbreak. *Curr Biol.* 2020;30(7):1346-1351
20. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet.* 2020;395(10224):565-574
21. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel

- Coronavirus-Infected Pneumonia. *N Engl J Med.* 2020;382(13):1199-1207
22. Worldometer: COVID 19 Coronavirus Pandemic. Available at: <https://www.worldometers.info/coronavirus/#countries>. [Last accessed on 23 July 2020]
 23. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA.* 2020;323(13):1239-1242
 24. Shaman J, Kohn M. Absolute humidity modulates influenza survival, transmission, and seasonality. *Proc Natl Acad Sci U S A.* 2009;106(9):3243-8
 25. Shaman J, Pitzer VE, Viboud C, Grenfell BT, Lipsitch M. Absolute humidity and the seasonal onset of influenza in the continental United States. *PLoS Biol.* 2010;8(2):e1000316
 26. Logan P. Seasonal Influences On The Spread Of SARS-CoV-2 (COVID19), Causality, and Forecastability. Available at: <https://ssrn.com/abstract=3554746> [Last accessed on 08 Apr 2020]
 27. Luo W, Majumder MS, Liu D, Poirier C, Mandl KD, Lipsitch M, et al. The role of absolute humidity on transmission rates of the COVID-19 outbreak. *medRxiv* 2020.02.12.20022467
 28. Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *Lancet Glob Health.* 2020;8(4):e488-e496
 29. Delamater PL, Street EJ, Leslie TF, Yang YT, Jacobsen KH. Complexity of the Basic Reproduction Number (R(0)). *Emerg Infect Dis.* 2019 Jan;25(1):1-4
 30. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. *Int J Infect Dis.* 2020;92:214-217
 31. Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020. *Euro Surveill.* 2020 Jan;25(4)
 32. Wu JT, Leung K, Leung GM. Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet.* 2020;395(10225):689-697
 33. Lipsitch M, Cohen T, Cooper B, Robins JM, Ma S, James L, et al. Transmission dynamics and control of severe acute respiratory syndrome. *Science.* 2003 Jun 20;300(5627):1966-70
 34. Lin Q, Chiu AP, Zhao S, He D. Modeling the spread of Middle East respiratory syndrome coronavirus in Saudi Arabia. *Stat Methods Med Res.* 2018 Jul;27(7):1968-1978
 35. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). World Health Organization; 2020. Available at: <https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>. [Last accessed on 11 June 2020]
 36. Mishra S, Mohapatra A, Kumar R, Singh A, Bhadoria AS, Kant R. Restricting rural-urban connect to combat infectious disease epidemic as India fights COVID-19. *J Family Med Prim Care* 2020;9:1792-4
 37. Gostin LO, Hodge JG Jr. US Emergency Legal Responses to Novel Coronavirus: Balancing Public Health and Civil Liberties. *JAMA.* 2020 Mar 24;323(12):1131-1132
 38. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020 Feb 28. doi: 10.1056/NEJMoa2002032
 39. Young BE, Ong SWX, Kalimuddin S, Low JG, Tan SY, Loh J, et al. Epidemiologic Features and Clinical Course of Patients Infected With SARS-CoV-2 in Singapore. *JAMA.* 2020 Mar 3. doi: 10.1001/jama.2020.3204
 40. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. *JAMA.* 2020 Feb 7. doi: 10.1001/jama.2020.1585
 41. Lee PI, Hsueh PR. Emerging threats from zoonotic coronaviruses-from SARS and MERS to 2019-nCoV. *J Microbiol Immunol Infect.* 2020 Feb 4. pii: S1684-1182(20)30011-6
 42. Bourouiba L. Turbulent Gas Clouds and Respiratory Pathogen Emissions: Potential Implications for Reducing Transmission of COVID-19. *JAMA.* 2020 Mar 26. doi: 10.1001/jama.2020.4756
 43. Sandaradura I, Goeman E, Pontivivo G, Fine E, Gray H, Kerr S, et al. A close shave? Performance of P2/N95 respirators in healthcare workers with facial hair: results of the BEARDS (BENchmarking Adequate Respiratory Defences) study. *J Hosp Infect.* 2020 Jan 21. pii: S0195-6701(20)30008-6. doi: 10.1016/j.jhin.2020.01.006
 44. Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, et al. Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient. *JAMA.* 2020 Mar 4. doi: 10.1001/jama.2020.3227
 45. Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for patients with confirmed coronavirus disease 2019 (COVID-19) or persons under investigation for COVID-19 in healthcare settings. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/infection-control/control-recommendations.html> [Last Accessed on 28 April 2020]
 46. World Health Organization. Novelcoronavirus (2019-nCoV): situation report-13. Published February 2, 2020. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/> [Last Accessed on 18 Mar 2020]
 47. A game changer: FDA authorizes Abbott Labs' portable, 5-minute coronavirus test the size of a toaster. Available at: <https://www.usatoday.com/story/news/health/2020/03/28/coronavirus-fda-authorizes-abbott-labs-fast-portable-covid-test/2932766001/> [Last Accessed on 01 May 2020]
 48. Abbott launches molecular point-of-care test to detect novel coronavirus in as little as five minutes. Available at: <https://abbott.mediaroom.com/2020-03-27-Abbott-Launches-Molecular-Point-of-Care-Test-to-Detect-Novel-Coronavirus-in-as-Little-as-Five-Minutes> [Last Accessed on 01 May 2020]
 49. Revised strategy for COVID19 testing in India (Version 5, dated 18/05/2020) Available at:
 1. https://icmr.nic.in/sites/default/files/upload_documents/Strategy_for_COVID19_Test_v4_09042020.pdf [Last Accessed on 12 June 2020]
 50. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D. Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents.* 2020 Mar 4:105932. doi: 10.1016/j.ijantimicag.2020.105932
 51. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents.* 2020 Mar 20:105949. doi: 10.1016/j.ijantimicag.2020.105949
 52. Bhatnagar T, Murhekar MV, Soneja M, Gupta N, Giri S, Wig N, et al. Lopinavir/ritonavir combination therapy amongst symptomatic coronavirus disease 2019 patients in India: Protocol for restricted public health emergency use. *Indian J Med Res.* 2020 Mar 11. doi: 10.4103/ijmr.IJMR_502_20.
 53. Cao B, Wang Y, Wen D, Liu W, Wang J, Fan G, et al. A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19. *N Engl J Med.* 2020 Mar 18 doi: 10.1056/NEJMoa2001282

54. Du YX, Chen XP. Favipiravir: pharmacokinetics and concerns about clinical trials for 2019-nCoV infection. *Clin Pharmacol Ther.* 2020 Apr 4 doi: 10.1002/cpt.1844
55. Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res.* 2020 Mar;30(3):269-271
56. Shen C, Wang Z, Zhao F, Yang Y, Li J, Yuan J, et al. Treatment of 5 Critically Ill Patients With COVID-19 With Convalescent Plasma. *JAMA.* 2020 Mar 27. doi: 10.1001/jama.2020.4783
57. Adaptive COVID-19 Treatment Trial. *ClinicalTrials.gov* identifier: NCT04280705. Posted February 21, 2020. Available at: <https://clinicaltrials.gov/ct2/show/NCT04280705?term=remdesivir&cond=covid-19&draw=2&rank=5> [Last accessed on 19 March 2020]
58. Gao J, Tian Z, Yang X. Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends.* 2020;14(1):72-73

Copyright: © Annals of International Medical and Dental Research. It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Pal S, Juyal D, Jauhari S, Singh H, Prakash R, Thaledi S. SARS-CoV-2: Origin, Transmission, Prevention and Mitigation. *Ann. Int. Med. Den. Res.* 2020; 6(5): MB01-MB10.

Source of Support: Nil, **Conflict of Interest:** None declared