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Epidemiology and clinical features, transmission, origin and treatments of COVID-19 (SARS-CoV-2): Review of literature

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ABSTRACT: This review summarizes the emerging and critical aspects of the novel coronavirus (COVID-19) with reference to epidemiological and clinical features, origin of the virus, transmission and present available treatments and the need for effective response to prevent and control further spreading of COVID-19 disease and any kind of future emerging infectious diseases which may pose threat to the public health.

Key words: Coronaviruses, SARS-CoV-2, COVID-19, pandemic, epidemiology, transmission, treatment.

I. INTRODUCTION

Coronaviruses of the family Coronaviridae are enveloped single stranded, non-segmented positive sense RNA genome ranging from 26-32 kilo bases in length.[1-4] Coronaviruses have been identified in avian hosts.[2,5,6] and various mammalian hosts including bats, camels, masked palm civets, pangolins and raccoon dogs and are previously considered as pathogens that causes only mild diseases in human until the recent emergence of the coronaviruses that caused severe acute respiratory syndrome (SARS-CoV) in 2002-2003 in Guangdong Province, China.[7-9] and the middle east respiratory syndrome (MERS-CoV) that caused severe respiratory disease in the Middle East in 2012.[10,11] The four human coronaviruses, HCoV-OC43, HCoV-HKU1 (Betacoronavirus), HCoV-229E and HCoV-NL63 (Alphacoronavirus) are known to cause only typical common cold symptoms in immunocompetent persons.[1-3] Evident of its high prevalence and wide distribution, the large genetic diversity and frequent genomic recombination and increasing human-animal interface incidences, the coronaviruses are periodically emerging and may re-emerge in humans on account of frequent cross-species infections and occasional spill-over events.[12,13]

After almost a decade, a novel coronavirus was detected in Wuhan, Hubei Province, China in the later part of 2019 which was reported from patients with unknown cause of pneumonia and was linked to the Hunan local seafood wholesale market.[2-4,14-18] On January 7, 2020 the China Center for Disease Control (China CDC) reported that a novel coronavirus was identified based on the samples collected from patients.[17,19,20] It was on January 10, 2020, that a novel coronavirus genome sequence was shared in the public domain by The Shanghai Public Health Clinical Center & School of Public Health, in collaboration with the Central Hospital of Wuhan, Huazhong University of Science and Technology, the Wuhan CDC, the National Institute for Communicable Disease Control and Prevention, the China CDC and the University of Sydney, Australia.[21] The isolated sequence was deposited in the Gene Bank database (accession number MN908947) and was uploaded to the Global Initiative on Sharing all Influenza Data (GISAID).[22] The novel coronavirus was subsequently given the interim name 2019-nCoV.[19] The outbreak of the novel coronavirus (SARS-CoV-2) was declared a public health emergency of international concern (PHEIC) on 31 January 2020.[23] On 11 February 2020, the novel coronavirus was given a new name; COVID-19 as mandated by the WHO guidelines citing that the disease nomenclature cannot refer to a particular geographical location or an animal or an individual or group of people.[24]

The spread of COVID-19 was declared a pandemic on 11 March 2020.[25] As of 04 October 2020, 10 am CEST, the cumulative total of COVID-19 cases have crossed 34.8 million with over 1 million deaths spread across 235 countries, areas or territories, of which the majority were reported in the Region of the Americas (55%) followed by Europe (23%).[26]

Our review analyses the current state of COVID-19 disease with regard to epidemiology and clinical aspects, origin, transmission and treatment with a view that this work might

enlighten and give insight towards better understanding of the COVID-19 disease and other likely future re-emerging epidemic events. The review concludes with identification of important key areas where research and investigation on emerging and re-emerging pathogens need to be pressed on.

Epidemiology and clinical features

Since December 2019, multiple cases of unexplainable pneumonia were reported at different hospital facilities in Wuhan city in Hubei Province, China. All the reports were initially linked to Hunan seafood wholesale market in Wuhan where fishes and live animals of different species were sold.[2-4, 14-18, 27] Notably, besides fishes, shellfishes and fresh meat with animal carcasses, variety of wild live animals including hedgehogs, badges, palm civets, Malayan pangolins and birds (turtledoves) were sold in the Wuhan market.[3,14] At that early stage, the investigation by China's mainland has not identified any evidence of definite human-to-human transmission and no healthcare workers were infected and the early investigation has ruled out respiratory pathogens including influenza viruses, avian influenza viruses, adenovirus, Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV) as the causative pathogen and cause of infection and all the patients are isolated and transferred to designated hospital and given symptom based treatment.[14,17]

The first identified cases were 27 hospital patients as of 31 Dec. 2019, out of which 24 (88%) were directly related to the Wuhan seafood market, with 7 serious cases and the rest are stated to be stable.[27] Other early studies reported 49% to 66% patients had contact history to the Wuhan seafood wholesale market.[15,17] The World Health Organization (WHO) stated that, the environmental samples from Hunan seafood wholesale market had tested positive for the novel coronavirus (2019-nCoV).[28] The first laboratory confirmed case of COVID-19 outside China was reported on 13 January 2020 from Thailand. It was followed by Japan on 15 January 2020, and the Republic of Korea on 20 January 2020. All these cases are confirmed to be exported from the Wuhan City, China.[15,20,29] At present (10 am CEST, 04 Oct. 2020), the cumulative global COVID-19 cases has crossed 34.8 million with 1 million deaths across 235 countries, areas or territories.[26]

Transmission

Transmissibility of a disease is one of the key factors in understanding and determining the severity of an epidemic.[30] Human to human transmission and to other geographical regions of the COVID-19 disease has already been confirmed based on the study of cluster of patients who did not have any direct contact to the Wuhan seafood market.[15,31] Tracing the contact history of virologically documented patient with COVID-19 has revealed the possibility of acquired infection from hospital set up (Nosocomial).[31,32] Evidence from virology and epidemiological studies that COVID-19 was primarily transmitted from symptomatic patients to other close contact persons through respiratory droplets from coughing or sneezing, by direct contact with the infected person or by contact with contaminated objects and surfaces (fomites).[2,4,15,17,31,33-40]

Data from samples collected from COVID-19 patients were clinically and virologically studied and have provided enough evidence that virus shedding is highest in the upper respiratory tract (nose and throat) at the early stages of the disease and it happens particularly during the first 3 days from the onset of the symptom.[39-44] Preliminary data also suggests that virus transmission may be more contagious at the time of symptom onset as compared to the later stage of the disease.[40] Reports are available in regard to the laboratory-confirmed cases that are truly asymptomatic (asymptomatic means a person who is infected with COVID-19 but does not develop symptoms) and are still able to transmit to other persons, but to date, there has been no documented asymptomatic transmission. Asymptomatic cases have been reported as part of contact tracing efforts in some countries.[38,40]

The mean incubation period (The time between exposure to the virus and symptom onset) for COVID-19 was 5.2 days (95% CI, 4.1 to 7.0) in a study of 425 case cohorts.[34] The median incubation period was 3.0 days in a study of 1099 cases and 4.0 days in 62 case cohorts and the longest reported incubation period was 24 days.[45,46] During the "pre-symptomatic" period, some infected persons can be contagious, and thus, transmission from a pre-symptomatic case can occur even before symptom onset.[47,48] There are several reports from studies on cluster of patients that pre-symptomatic transmission has been documented through contact tracing and enhanced investigation of confirmed COVID-19 cases.[47-50] Data supports are available suggesting that some people can test positive for COVID-19 from 1-3 days before they develop symptoms and is possible to transmit the virus to other close contacts even before significant symptoms are developed.[38,40,48] In another study of viral shedding in patients with

mild and more severe infections, it has revealed that the viral shedding seems to be greatest in the early phase of disease.[51,52]

The common symptoms of COVID-19 are mostly fever (83% to 98%), cough (76% to 82%), dyspnoea (31% to 55%) and myalgia or fatigue (11% to 44%); less common symptoms are sputum production (28%), headache (8%), haemoptysis (5%), sore throat (5%), diarrhea (2% to 3%), rhinorrhoea (4%), chest pain (2%) and nausea or vomiting (1%).[15,17,27] In addition, the United States Centers for Disease Control and Prevention (CDC) has recently added three new symptoms to its ongoing list - congestion or runny nose, nausea and diarrhea joining the federal agency's list of recently added new symptoms such as loss of taste or smell and sore throat. Symptoms may appear from 2-14 days after exposure to the SARS-CoV-2 virus.[53] Further complications developed in patients and included acute respiratory distress syndrome (ARDS), RNAaemia, acute cardiac injury and secondary infections.[15,17] Several studies reported that, most of the infected patients are male (56% to 73%), and the median age was 49, 55.5 and 59 years in 41, 99 and 425 case cohorts respectively.[15,17,34] It was reported that the COVID-19 disease may have adverse affect on the elderly with underlying comorbidities, like cardiovascular disease, diabetes, respiratory disease and hypertension. The common laboratory abnormalities exhibit similarity with the SARS-CoV and MERS-CoV infections with more adverse affect on males than females.[17,54-56] In this connection, the role of X-chromosome and sex hormones may be attributed for the lesser susceptibility of females to viral infections, but this projection need further detailed investigation.[17] SARS-CoV-2, SARS-CoV and MERS-CoV infections seems to share many similar clinical symptoms including fever, cough, myalgia and dyspnoea.[57] They are the most severe type of coronaviruses that infects the lower respiratory tract and causes acute respiratory distress syndrome (ARDS), which lead to patient deaths.[58,59]

The pathogen and its origin

The novel coronavirus SARS-CoV-2 responsible for COVID-19 disease belongs to the genus Betacoronavirus, subgenus Sarbecovirus of the family Coronaviridae, order Nidovirale.[2,3,16,31] The virion (SARS-CoV-2) is spherical in shape measuring about 125nm in diameter and has spike protein measuring about 9 to 12 nm on its surface and gave the virions the appearance of a solar corona.[16] The genome sequence was 29 kbs and contains two untranslated regions (UTRs): 5'-cap structure and 3'-poly-A tail, with a single open reading frame (ORF) encoding a polyprotein, similar to that of the SARS-CoV and MERS-CoV.[4,31,60-62] Genome structure is in the order of 5'- the viral replicase (ORF1a and ORF1b)-structural proteins [Spike(S)-Envelope(E)-Membrane(M)-Nucleocapsid(N)] -3' and some genes of accessory proteins.[2,3,16,31,60,61,63]

The pathogenesis of SARSCoV-2 being inspired by that of SARS-CoV, was known to infect the human cells by spike glycoprotein binding to its cellular receptor, angiotensin converting enzyme 2 (ACE2).[4,64] Current evidence from studies supports this idea. The spike protein of SARS-CoV-2 contains two regions or subunits i.e., S1 and S2, which consists of 1253 amino acids.[61,62,65] The amino acid identity of spike protein of SARS-CoV and SARS-CoV-2 is about 75%.[28,62,66] Analysis of the virus genome indicates that some genes of the SARS-CoV-2 share less than 80% nucleotide sequence identity with SARS-CoV. But, the amino acid sequences of the seven conserved replicase domains in ORF1ab has 94.4% sequence identity between SARS-CoV-2 and SARS-CoV, suggesting that they belong to the same species - SARSr-CoV.[4] There is a sequence homology of 79% between SARS-CoV-2 and SARS-CoV, while it is 50% between SARS-CoV-2 and MERS-CoV.[2,67] Basing on these evidences, it is thus, reasonable to suspect bats as the natural host of SARS-CoV-2 since it highly resembles the SARS-CoV. SARS-CoV-2 also shows about 85% - 89% overall genome sequence similarity to that of SARS-CoV and bat SARSr-CoVs and phylogenetically clusters with them.[2,16,31] Previous reports are also available with regard to the origin of human coronaviruses isolated from horse shoe bats implicating them (bats) as natural reservoirs of SARS-CoVs with masked palm civets as the intermediate host.[68-71]

Current evidences are also projecting that bats are the probable evolutionary origin of SARS-CoV-2 with high genome sequence identity between the SARS-CoV-2 and bat-CoVs.[2-4,72] In a Simplot analysis carried out by Zhou and colleagues[4], the overall genome sequence identity between SARS-CoV-2 and bat coronavirus (BatCoVRaTG13) showed 96.2% identity throughout the genome. However, there might exists an intermediate host between bats and human since there were no bats sold or found in Wuhan wet market during the outbreak and bats usually hibernate in the winter season. Besides, there was always an existence of an intermediate host for other previously known human infecting coronaviruses as in the case of SARS-CoV and

MERS-CoV with the masked palm civets and dromedary camels as the intermediate hosts respectively, and bats as their natural host for both the coronaviruses.[72,73] In this connection, pangolin might be the probable intermediate host for SARS-CoV-2 since the coronavirus isolated from Malayan pangolins showed 100%, 98.2%, 96.7% and 90.4% amino acid identity with SARS-CoV-2 in E, M, N and S genes respectively, and particularly the RBD of the S protein of the pangolin-CoV was virtually identical to SARS-CoV-2 with only one amino acid difference.[74,75,76] However, the role of bats and pangolins as the natural and intermediate hosts respectively for SARS-CoV-2 require further investigation.

Treatments

According to the statement issued by the World Health Organization (WHO), the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH) and the Infectious Diseases Society of America (IDSA), there are currently no proven specific medications or vaccines which are effective for the treatment or prevention of the SARS-CoV-2.[77-81] Several therapeutic agents are being used on clinical trials, and compassionate protocols based on in vitro activity but the efficacy of drugs for SARS-CoV-2 have not been established.[82] However, in the early stages of treatment for COVID-19 patients, certain drugs showed substantial clinical benefits but fewer adverse clinical outcomes.[15] Therapeutic strategies for COVID-19 patients included antiviral treatment, empirical antibiotic treatment, corticosteroid therapy, intravenous immunoglobulin therapy, oxygen support (nasal cannula, mask oxygen inhalation, non-invasive ventilation and invasive mechanical ventilation), continuous renal replacement therapy (CRRT) and extra corporeal membrane oxygenation (ECMO)[15,17,32,45,46] Case report of the COVID-19 infected hospitalized patients indicated that a combination of lopinavir and ritonavir therapy in a randomized controlled trial may be beneficial for COVID-19 cases.[15,83,84] Lopinavir and ritonavir may bind to M^{pro} which is a key enzyme for the replication of coronaviruses and this binding suppresses the virus activity.[85] However, in a retrospective cohort study of 29 hospitalized COVID-19 infected patients, reviewing clinical course and risk factors for mortality showed no difference in the duration of viral shedding after treatment with lopinavir and ritonavir.[86] The European Society of Intensive Care Medicine (ESICM) and Society of Critical Care Medicine (SCCM) recommendations on "Surviving sepsis" campaign suggest against the routine use of lopinavir and ritonavir in critically ill adults infected with COVID-19.[87] Similarly, the NIH COVID19 treatment guidelines recommend against the use of lopinavir and ritonavir or other HIV protease inhibitors outside of clinical trials due to unfavorable pharmacodynamic and negative clinical trial data.[80]

Remdesivir (a broad-spectrum antiviral nucleotide pro-drug) was found to be highly effective against the SARS-CoV-2 virus and other coronaviruses activity in vitro.[88-95] It was reported that the first confirmed COVID-19 case of the United States of America was successfully treated by intravenous remdesivir and other supportive care.[96] Remdesivir, despite of been not an FDA-approved, has been made available through an Emergency Use Authorization (EUA).[97] Other nations have similarly issued restricted market authorizations.[98,99] Under the EUA, remdesivir was used to treat several severe hospitalized patients infected with COVID-19 disease in the United States, Europe and Japan.[100] Besides, in August 2020, the use of remdesivir under EUA was expanded to hospitalized adults and children with suspected or lab confirmed COVID-19 infection irrespective of their severity.[97] Currently, several clinical trials evaluating the efficacy of remdesivir in patients infected with COVID-19 disease are being conducted.[100]

Several reports have stated that chloroquine and hydroxychloroquine has in vitro activity against SARS-CoV-2 and may have immunomodulating properties.[101-103] Chloroquine and hydroxychloroquine may be effective in the inhibition of viral enzymes, viral DNA and RNA polymerase, viral protein glycosylation, virus assembly and new virus particle transport and virus release. Chloroquine and hydroxychloroquine may also be involved in ACE2 cellular receptor inhibition, acidification at the surface of the cell membrane inhibiting fusion of the virus and immunomodulation of cytokine release.[101,104-108] Chloroquine and hydroxychloroquine are not FDA-approved for treating SARS-CoV-2 but based on the EUA directive that treatment was permitted for adult and adolescent patients with body weight above 50 kg. However, on June 15, 2020, the FDA revoked the EUA statement for chloroquine and hydroxychloroquine stating that it may not be effective in treating COVID-19 disease. Also, the known and potential benefits of chloroquine and hydroxychloroquine no longer qualify the risk for the authorized use in light of ongoing serious cardiac adverse events and other serious side

effects.[109-112] Due to the potential risk for serious adverse events and drug interactions, the use of chloroquine and hydroxychloroquine in COVID-19 patients outside of clinical trials or in a non-hospital setting is not recommended by the NIH[80] and FDA.[113] WHO on June 17, 2020, stopped the use of hydroxychloroquine in the treatment of COVID-19 stating that the data from solidarity trial of French Discovery and the results announced from the UK's Recovery trial both showed that the use of hydroxycholroquine do not reduce the mortality of the hospitalized COVID-19 patients.[114]

Another broad-spectrum antiviral drug with in vitro activity against RNA viruses is favipiravir, an investigational RNA dependent RNA polymerase (RdRp) inhibitor that inhibits viral RNA synthesis.[115,116] On February 15, 2020, favipiravir was approved for treatment of novel influenza in China and it is currently undergoing clinical trials for the treatment of COVID-19 disease. Favipiravir has anti-influenza virus activity and is also capable of blocking the replication of flavi-, alpha-, filo-, bunya-, arena-, noro- and other RNA viruses.[117] Currently, additional data on the clinical efficacy of favipiravir along with chloroquine and hydroxychloroquine for the treatment of COVID-19 disease are being evaluated.[100]

Azithromycin, a broad-spectrum antibiotic macrolide may prevent bacterial superinfection and may have immunomodulatory properties to work as adjunctive therapy.[118-122] The immunomodulatory properties of azithromycin may include reducing chemotaxis of neutrophil to the lungs by inhibiting cytokines, inhibition of mucus hypersecretion, decreased production of reactive oxygen species, fastening neutrophil apoptosis and blocking the activation of nuclear transcription factor. Macrolides are used to down-regulate inflammatory responses and reduce the excessive cytokine production associated with respiratory viral infections, but it is not certain about its direct effects on viral clearance.[118-121] Preclinical data on the use of azithromycin from small trials and trials outside COVID-19 are available but are limited and inconclusive.[122-124] The NIH COVID-19 treatment guidelines recommend against the use of azithromycin in combination with hydroxyl chloroquine outside of clinical trials due to the risks of having potential toxicity.[80]

Corticosteroids are extensively used for the treatment of acute respiratory distress syndrome (ARDS) in patients with severe lung injury based on their ability to reduce the inflammatory and pulmonary fibrotic phenomena. However, there are some side effects such as, delay in viral clearance and risk of secondary infections, and evidence of its use in the treatment of COVID-19 are also limited and some controversies still exist with regard to its therapeutic efficacy despite of its administering popularity.[125-127] Despite of the existing controversies, a recent retrospective study of 201 COVID-19 case in China by Russell and colleagues stated that corticosteroids are effective for COVID-19 patients who developed acute respiratory distress syndrome and was associated with lower risk of death.[128] WHO recommend the administering of systemic corticosteroids to COVID-19 patients who are critically ill but suggest against the use in patients who are less severely ill since the treatment prove no benefit, and might rather be harmful.[129] A rapid advice guidelines for diagnosis and treatment for COVID-19 recommend against corticosteroid therapy for viral pneumonia, however corticosteroids may be considered for COVID-19 patients with refractory shock or with severe acute respiratory distress syndrome.[18,77,87]

Another therapeutic option currently under clinical trial is the COVID-19 Convalescent Plasma therapy (a type of passive immunotherapy). The convalescent plasma therapy uses plasma that contains antibodies to SARS-CoV-2 from persons who have recovered from COVID-19 disease but it is not intended for prevention from COVID-19 infection.[130] Although, convalescent plasma for the treatment of COVID-19 has not yet been approved by the FDA for use, it has been made available under emergency use authorization (EUA) or an investigational new drug application (IND) and currently, clinical trials are being conducted to evaluate its use on patients with severe or immediately life-threatening COVID-19 infections, and to participate in these trials, investigators should get the approval from the FDA for investigational use under the traditional investigational new drug application (IND) regulatory pathway.[130-133] A study by Rojas and colleagues[134] reported that the convalescent sera or immunoglobulin from donor was found to be highly effective in SARS-CoV-2 infected patients by gaining immediate immune response and was able to neutralize the viral particles in the host system. Previous evidences have shown the use of passive immunotherapy for the treatment of other infectious outbreaks, including SARS-CoV (2002-2003), H1N1 influenza (2009-2010), MERS-CoV (2012) and Ebola (2014).[135-138] Phase II multicentre randomized controlled trial of convalescent plasma therapy treatment in India (PLACID) (the first RCT for plasma in COVID-19 patients to be completed in the world) showed that

the use of convalescent plasma did not translate into reduction in 28-day mortality, or progression to severe disease in moderate COVID-19 patients.[139] Moreover, convalescent plasma therapy had some safety concerns since the recipients experienced transfusion-related adverse events including transmitting infection, allergic or anaphylactic reaction, febrile nonhemolytic reactions, hemolytic reactions, transfusion-associated circulatory overload (TACO), transfusion-related acute lung injury (TRALI), post-transfusion purpura, hypothermia, and metabolic complications.[132] Despite the wide use of convalescent plasma therapy, the NIH COVID-19 treatment guidelines recommends against the use of convalescent plasma due to lack of clinical data.[80]

According to WHO, as of October 02, 2020 there are 42 vaccine candidates for COVID-19 that are in clinical evaluation and out of which 10 are already in Phase III trials (Table 1). Besides, 151 vaccine candidates are undergoing preclinical evaluation. All top vaccine candidates are for intra-muscular injection and are designed for a two-dose schedule except AstraZeneca and CanSino vaccines which are single dose schedule.[140]

Table 1. List of candidate vaccines in phase III clinical evaluation.

Candidate vaccines in phase III clinical evaluation	**Vaccine platform**	**Location of studies**
Sinovac	Inactivated virus	Brazil
Sinopharm / Wuhan Institute of Biological Products	Inactivated virus	United Arab Emirates
Sinopharm / Beijing Institute of Biological Products	Inactivated virus	China
Sputnik V / Gamaleya National Research Institute of Epidemiology and Microbiology	Viral vector	Russia
Janssen Pharmaceutical Companies	Viral vector	USA, Brazil, Colombia, Peru, Mexico, Philippines, South Africa
AstraZeneca / University of Oxford	Viral vector*	USA
CanSino Biological Inc. / Beijing Institute of Biotechnology	Viral vector*	Pakistan
Moderna / NIAID	RNA	USA
BioNTech / Fosun Pharma / Pfizer	RNA	USA, Argentina, Brazil
Novavax	Protein subunit	UK

*Single dose schedule.

The first batches of COVID-19 vaccines are expected to gain approval by the end of 2020 or early 2021[141] and an important consideration is the vaccine allocation strategy. First preference would be to allocate supplies to people at high risk of severe morbidity and mortality. This theoretical inference was supported by the preliminary model-informed analyses.[142] It is important to look into vaccine allocation perspectives in addition to utilitarian considerations. Preliminary Framework for Equitable Allocation of COVID-19 Vaccines by the US National Academy of Medicine has identified other foundational criteria; equal regard, fairness, mitigation of health inequities, and transparency to determine vaccine allocation.[143]

II. CONCLUSION

The emergent outbreak of the COVID-19 pandemic caused by the novel coronavirus (SARS-CoV-2) has changed the world's perspective in its outlook on global health. SARS-CoV-2 being a novel coronavirus, there are still many things which are not known about them. However, much work has been accomplished in understanding the cause and prophylaxis, especially on its symptoms, prevention, testing, preparedness etc., but, a remedy or immunity in the form of vaccines, are still some way off. Today, the general assumptions about COVID-19 vaccines are that these vaccines will provide herd immunity that can reduce SARS-CoV-2 transmission and lead to normalcy as in pre-COVID-19 days. This notion that COVID-19 vaccine induced population immunity will allow a return to pre-COVID-19 "normalcy" might be based on illusory assumptions.[141] The question still lies, whether the efficacy of the vaccines will be effective to all the persons having different immunity as claimed by the potential vaccine producing agencies.

Nevertheless, COVID-19 vaccines are the need of the hour, no matter how minimal an impact they may have on the transmission and vaccine allocation challenges. Moreover, these vaccines would have an important role if they show acceptable effectiveness in reducing morbidity and mortality in COVID-19 high-risk groups, irrespective of its impact on transmission and population immunity. Finally, it will be critically important to communicate to the policy makers and the general public that first-generation vaccines are actually only one tool in the overall public health response to the present COVID-19 pandemic and that it may unlikely be the ultimate solution as expected by many.

Declaration of interest

The authors declare no competing interests.

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