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COVID-19: The Virus, Impact and Future Perspective

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Abstract

The coronavirus disease 2019 (COVID-19), a highly contagious viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has emerged as a public health concern worldwide. The disease is mainly transmitted between humans by respiratory droplets with clinical outcomes ranging from mild respiratory illness to severe conditions in some elderly and people with comorbidities. Currently, there is no approved vaccine or treatment for COVID-19 due to which intensive surveillance and implementation of containment measures are crucial to curb the disease. Besides creating a global health crisis, the virus has a significant impact on life and economy. In this review, an attempt has been made to provide insight into COVID-19 with respect to epidemiology, diagnosis, prevention, treatment and future prospective.

Keywords: COVID-19; Coronavirus; SARS-CoV-2; Pandemic.

Introduction

"The worst pandemic in modern history was the Spanish flu of 1918, which killed tens of millions of people. Today, with how interconnected the world is, it would spread faster". These words by Bill Gates aptly describe the ongoing situation of COVID-19 outbreak. Coronavirus disease 2019 is a severe respiratory illness caused by a newly emergent coronavirus, namely severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is the third from the family of coronaviruses to infect the human beings, after the first outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 and second Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012 [1].

The initial cases of the disease came up in December 2019, when an outbreak of an unusual pneumonia happened in the Huanan Seafood Wholesale Market, in Wuhan, China. The local health authorities of China announced an epidemiologic alert and closed the market on January 1, 2020. However, within a month, thousands of people in China were attacked by the uncontrolled spread of the disease [2]. Initially described as "pneumonia of unknown etiology", was later attributed to be caused by a novel coronavirus and the disease caused by this virus was named as "COVID-19" on 11th February 2020, by WHO. The novel coronavirus outbreak further spread to various countries and was declared as a global public health emergency by World Health Organization (WHO) on 30th January 2020, the sixth time in history and later declared as a pandemic on 11th March, 2020 [2,3]. Due to global spread, severity and high mortality rate of COVID-19, an attempt has been made in this review to highlight the various aspects of the disease i.e. the virus, its epidemiology, diagnosis, preventive strategies, treatment measures and its impact on life. However, the information is still in infancy and detailed information will keep on unfolding in coming future.

Epidemiology

In December 2019, the first case of COVID-19 was reported from Wuhan, China, during an outbreak of mysterious viral pneumonia. Initially a regional epidemic, spread rapidly to different countries like South Korea, Thailand, Japan, Italy, USA due to which WHO issued public health emergencies of international concern (PHEIC) alarm on January 30, 2020. Even with intensified containment and control measures, COVID-19 continued to spread and came up as a pandemic that has affected more than 200 countries, areas or territories with significant

morbidity and mortality. According to WHO COVID-19 situation report-153, there were more than 8.5 million total confirmed cases and 4,61,715 reported deaths globally as on 21st June, 2020 [4]. Countries most affected by COVID-19 include United States of America with more than 2.2 million cases; Brazil with more than 1 million cases, Russian Federation with more than 0.5 million cases; India with more than 4 hundred thousand cases; The United Kingdom with more than 3 hundred thousand cases; Spain, Italy, Peru, Iran with more than 2 hundred thousand cases; Canada, Germany, Turkey, France, Saudi Arabia, Pakistan and Bangladesh with more than 1 hundred thousand cases and China with more than 80 thousand cases as on 21st June, 2020 [4,5]. Further, with increasing number of new cases of coronavirus, South Korea fears possibility of second wave of COVID-19. Also, as situation with COVID-19 pandemic is continuously evolving, number of cases and CFRs continue to vary. The basic reproductive number ("R0"), which refers to the expected number of cases generated from a single case, is estimated to be 2-3.5 for SARS-CoV-2, as compared to 0.5-1.0 and 1.5-4.0 with MERS-CoV-2 and SARS, respectively [6,7].

Coronavirus

Coronaviruses (CoVs) are a family of enveloped, RNA viruses, belonging to *Coronaviridae* family and are the members of subfamily *Coronavirinae*, order *Nidovirales* that are characterized by "crown like" glycoprotein on their surface [8,9,10]. Based on serological analysis and genetic studies coronaviruses are classified into four different genera i.e. alpha, beta, gamma and delta-CoV [11]. Among them, alpha and beta coronaviruses infect mammals, gamma coronaviruses infect avian species while delta coronaviruses infect both avian and mammalian species. CoVs have a high frequency of recombination and mutation allowing them to acclimatize and infect new hosts. Earlier, six CoVs have been identified as human-susceptible virus, i.e. 229E, NL63, OC43, HKU1 but had low pathogenicity, causing mild respiratory tract infections e.g., common cold, pneumonia, bronchiolitis, rhinitis, pharyngitis and sinusitis. However, the other two known CoVs, SARS-CoV and MERS-CoV lead to severe and potentially lethal respiratory illness [8].

Among all RNA viruses, CoV has one of the largest genome in the range of 26.2 and 31.7 kb [9]. The single stranded genome RNA is linked with the basic nucleocapsid protein and is enclosed within the envelope. Viral envelope is associated with important structural proteins like the membrane protein (M) and the envelope protein (E) which are involved in virus assembly and spike protein (S) that mediates the virus entry into host cells and also determines viral host range and induces host immune response [11]. Some coronaviruses additionally encode an envelope associated glycoprotein, hemagglutinin-esterase (HE). Besides these main structural proteins, different CoVs also encode special nonstructural and accessory proteins, which are responsible for replication of virus inside the host cells and for maintaining its genome [9,12]

Novel coronavirus

SARS-CoV-2 is an enveloped, positive single-strand RNA virus belonging to *Orthocoronavirinae* subfamily, genus beta-coronavirus and subgenus *sarbecovirus* (**Figure 1**). Electron microscopy images revealed that the virus has a diameter ranging from 60 to 140 nm, with overall structure similar to other viruses of *Coronaviridae* family. SARS-CoV-2 was identified in early January, 2020 and its genetic sequence shared publicly on 11-12 January [13]. The genome sequence of SARS-CoV-2 is 96.2% identical to a bat CoV RaTG13 and shares 79.5% identity to SARS-CoV [12]. The genome of novel coronavirus is approximately 30kb in length and encodes polyproteins, nucleoproteins, and membrane proteins, such as RNA polymerase, papain-like protease, 3- chymotrypsin-like protease, helicase, glycoprotein and accessory proteins [14]. The S glycoprotein of virus has two subunits, S1 and S2 where S1 determines the virus-host range and facilitates the virus binding to host receptor while S2 mediates the fusion of virus with host cell membrane [12].

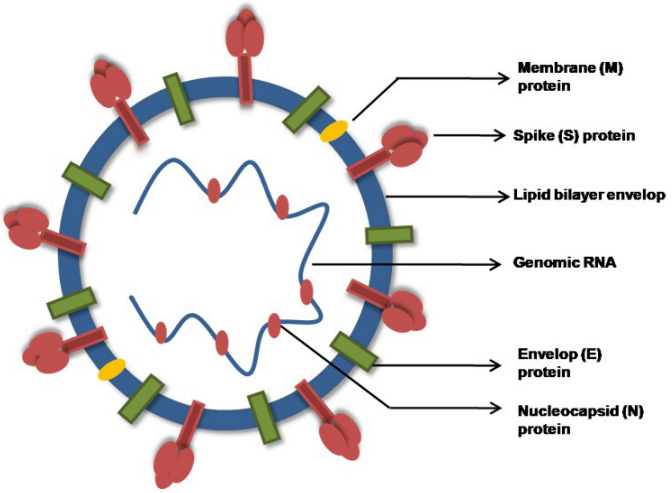

Figure 1: Structure of SARS-CoV-2 virus.

Initially called 2019-nCoV, the new virus was subsequently termed as the SARS-CoV-2 virus, by the experts of the International Committee on Taxonomy of Viruses (ICTV) as it is very similar to the virus that caused the SARS outbreak (SARS-CoVs). Due to the sequence identity, it is a general belief that the virus originated from bats and all evidences suggest that the virus has a zoonotic origin [12,13]. Recently, National Institute of Biomedical Genomics India, conducted a global study using 3636 coronavirus RNA sequences from 55 countries and reported that the virus has mutated into 10 different types i.e. B, B1, B2, B4, A3, A6, A7, A1a, A2 and A2a from ancestral 'O' type of which type A2a dominates across all geographical regions. The A2a mutation has made the virus transmission more efficient due to which COVID-19 has emerged as a pandemic [15].

Mode of transmission

The COVID-19 virus, a zoonotic virus, can be transmitted between animals and humans [16,13]. However, as there is limited close contact between humans and bats, it is more probable that transmission of the virus to humans occurred through some intermediate animal host or zoonotic source which could be a domestic or a wild animal, but has not been identified yet [13]. The COVID-19 virus spreads between people mainly via inhalation of respiratory droplets due to coughing or sneezing, but can also be passed through aerosol and fomites as the virus can remain viable and infectious in aerosols for hours and on surfaces up to days [17]. Besides these, nosocomial transmission is also possible if adequate Infection Prevention and Control (IPC) measures are not followed by health care workers [18]. However, the role of asymptomatic carrier in the transmission of disease is still not clear, but has been found to play an important role in human to human transmissions [18,19,20]. Besides these, the isolation of the virus from fecal swabs and blood of patients, also suggests the possibility of multiple transmission routes [12,21,22]. Some reports also indicate the transmission of virus from humans to animals in certain situations.

As per the Centers for Disease Control and Prevention (CDC), the first case of an animal testing positive for COVID-19 in the United States was a tiger that had a respiratory illness at Bronx zoo in New York City. CDC has also reported a small number of animals, including cats, dogs and minks to be infected with the virus mostly after close contact with COVID-19 people [23].

The incubation period ranges between 1-14 days and varies from person to person depending upon immunity with median incubation period of about 5–6 days with high virus levels being detected in the upper respiratory tract early in the disease course. Further, it has been observed that virus load is still detected in the upper as well as lower respiratory tract by molecular assay for several days after symptoms have resolved [18].

High risk individual

As per currently available information, susceptible hosts for COVID-19 illness are people over 65 years and people of all ages with underlying medical conditions, including people with chronic lung disease or asthma, serious heart conditions, obesity (body mass index of 40 or higher), diabetes, hypertension, cancer, liver disease and chronic kidney disease including kidney transplant and those undergoing dialysis and immune compromised individuals [24]. However, frontline workers i.e. doctors, nurses and people living in nursing home or long-term care facility are also at high risk. It has been observed that females are less susceptible than males.

Clinical features

Clinical features vary from person to person that ranges from mild acute respiratory illness to severe conditions like progressive organ dysfunction, sepsis (10-20%) and acute respiratory distress syndrome in 3–5% of infected individuals [18]. Common clinical manifestations included fever, cough, sore throat, malaise, sputum, shortness of breath and headache along with gastrointestinal symptoms like diarrhea and vomiting in certain individuals [25]. Recently, CDC included additional information pertaining to symptoms of COVID-19 that includes chills, repeated shaking with chills, muscle pain, headache and loss of taste or smell. The Case Fatality Ratios (CFR) of 1-6% has been reported from some countries [18]. Higher CFRs have been seen in the elderly (over 60 years) and those with underlying chronic conditions like hypertension, diabetes, pulmonary diseases and cardiovascular diseases [25,26]. Children normally suffer from mild disease. Chest-X-ray and CT imaging generally indicate bilateral infiltrates and ground-glass opacity [12,18]. Further, blood tests of COVID-19 patients frequently illustrate lymphopenia [25]. The disease progression is also found to be associated with increased secretion of inflammatory cytokines including IL-1β, IL-4, IL-10, IFN-γ, IP-10 and MCP-1 [26,27].

Viral life cycle and pathogenesis

The life cycle of SARS-CoV-2 in host cells begins when its spike protein (S glycoprotein) binds to the angiotensin converting enzyme 2 (ACE2) receptor on the surface of host cells, that facilitates the virus entry with the help of transmembrane protease serine 2 (TMPRSS2) [28-31]. After the fusion, virus uncoats and releases its genomic RNA in the host cell and once the RNA is released, it utilizes the host cell ribosome machinery to translate its genomic RNA into viral replicase polyproteins pp1a and pp1ab [14]. These are further cleaved into small active products by viral proteases and form replication-transcription complex (RTC) in double-membrane vesicle. RTC replicates continuously and produces a series of subgenomic RNAs, which in turn encode accessory proteins and structural proteins [12, 14]. Viral proteins and genomic RNA are subsequently assembled into virions in the ER and Golgi and then transported via vesicles and released out of the cell by exophagocytosis (**Figure 2**) [32].

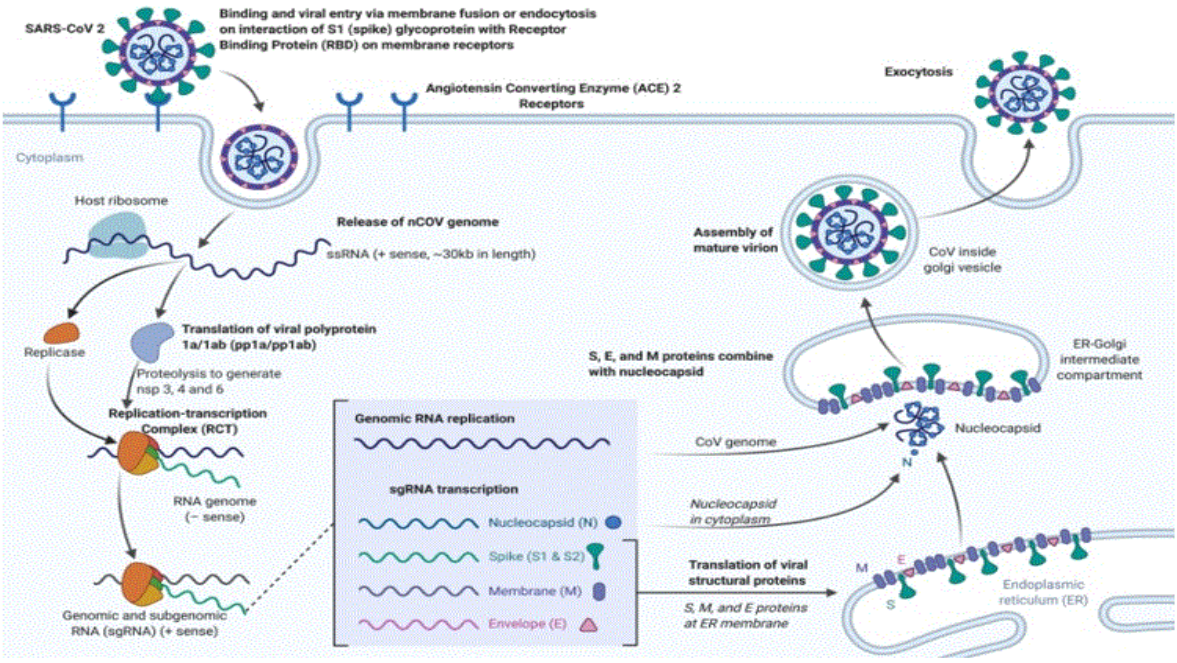

Figure 2: Life cycle of SARS-CoV-2 virus inside host cell. The spike protein (S) binds to the ACE2 receptor on the surface of host cells and facilitates the virus entry followed by uncoating of virus thereby releasing genomic RNA in the cytoplasm that utilizes the host cell ribosome machinery to translate the RNA into viral replicase polyproteins. These are cleaved into small active products by viral proteases and form replication-transcription complex (RTC) in double-membrane vesicle. RTC replicates continuously and produces a series of subgenomic RNAs, which encode accessory and structural proteins that are subsequently assembled into virions in the Endoplasmic reticulum- Golgi intermediate compartment and releasing the virions by exocytosis [32].

The mechanism of coronavirus replication and pathogenesis provide answers to various outcomes of the disease. Firstly, as ACE 2 receptor is expressed in various tissues i.e. lungs, Gastrointestinal (GI) tract, kidney, and cardiovascular system in the human body that accounts for the systemic manifestations, including GI symptoms, renal problems, cardiovascular dysfunction and multiple organ failure in some SARS-CoV-2 cases [3]. As ACE 2 is also involved in regulating Renin Angiotensin system, and its dysfunction is linked with aging, due to which more severe infections are observed in elderly and mild in children [3]. Recent data also indicates that rapid viral replication may cause epithelial and endothelial cell apoptosis and vascular leakage, triggering the release of pro-inflammatory cytokines and chemokines leading to 'cytokine storm' and extensive tissue damage [27]. Thus, the pulmonary inflammation can lead to systemic inflammatory response which could culminate in systemic shock and multiple organ failure [3,32].

Diagnosis

Diagnosis plays a crucial role in the containment of COVID-19 as its symptoms are non specific and cannot aid in diagnosis. Further, diagnosis would also enable rapid case identification, isolation, and contact tracing thereby implementing control measures to limit the spread [33]. A suspected case of COVID-19 refers to a patient having symptoms of acute respiratory disease along with a travel history or inhabitant of area with persistent local transmission or contact with COVID-19 patient or with person of similar travel history while a confirmed case refers to a person with confirmed laboratory test of COVID-19 infection, irrespective of clinical signs and symptoms [13,34]. Rapid sample collection and testing of suspected cases should be the priority to manage the further spread of the disease [35].

Sample collection

Adequate standard operating procedures must be followed and trained staff should collect, pack and transport the specimen and must consider every sample as potentially infectious. Specimen handling for molecular testing requires BSL-2 or equivalent facilities but for culturing the virus, BSL-3 facility is require at minimum [35].

Real-time RT-PCR assay

Confirmatory laboratory diagnosis for COVID -19 is based on real-time RT-PCR assay, a gold standard method to detect unique viral RNA sequences in throat and nasal swabs [2]. The N, E, S and RdRP genes are the commonly targeted viral genes [35]. The reverse transcriptase polymerase chain reaction (RT-PCR) is a sophisticated, multi step and time consuming test which needs to be done by a highly competent, well trained person who is well trained to run the test otherwise there will be always a chance of having high number of false positive and/or false negative results [3].

Serological tests

Serological analysis, mainly by Enzyme Linked Immunosorbent Assay (ELISA) that detects the presence of antibodies to coronavirus in blood sample is a useful method for rapid case-identification, contact tracing, detecting suspected clustering cases and for estimating case-fatality rate [36]. In cases where RT-PCR assays are negative but there is a strong possibility of epidemiological link to COVID-19 infection, serological testing could support diagnosis [35]. According to WHO, research on development of new serological tests is required to speed up the surveillance and for detection of virus at point of care [37].

Viral sequencing

To confirm the accuracy of molecular assays, a percentage of samples from clinical cases should be sequenced to check for viral mutations. Virus whole genome sequencing can also be used for molecular epidemiology studies and data could be submitted to public-access databases like GISAID, which intend to guard the rights of the submitting body [35].

Imaging

Imaging tests such as chest X-ray, CT scan are also helpful in understanding the patient's condition and thus managing the disease better by monitoring the alterations occurring in respective organs [38,39]. However some confirmed patients show normal CT images thereby highlighting the need to confirm the infection by viral RNA detection.

Emerging diagnostic strategies

Novel point-of-care tests are coming up which would enable diagnosis without sending samples to centralized facilities, thereby transforming the rate and quantity of tests that could be performed [40]. Lateral flow antigen detection for SARS-CoV-2 is one such approach under development for COVID-19 detection [33,41]. Smartphone surveillance of the disease is another strategy that provides communication between patients and health care workers and also helps in sharing epidemiological data onto public health databases to further coordinate outbreak response [33]. Government of India has launched a COVID-19 tracking mobile application, Aarogya setu to spread the awareness, track the cases and connect essential health services to Indians [42].

Preventive measures

Given the high transmission rate of SARS-CoV-2 and lack of vaccine and effective treatment strategies till date, community health and infection control measures are urgently required to limit the further spread of the virus [5].

For common people

WHO has listed some precautionary measures and advice for the public such as avoiding contact with sick people, particularly those with cough and acute respiratory infections, frequently washing hands with soap and water or use of alcohol based disinfectant solution especially after coming from outside, avoiding touching of mouth, nose and eyes, regular cleaning of gadgets, door knobs as well as frequently used objects. Further, people with mild symptoms of acute respiratory infection should self isolate and also practice cough etiquette i.e. maintaining distance, use tissues or clothing while coughing or sneezing. However, if condition worsens i.e. high grade fever, cough and breathing difficulty, prompt medical advice should be taken. Besides these, contact with animals or their excretions, visiting markets and public places should be avoided [43].

For community

Social distancing i.e. maintaining at least 1 metre (3 feet) distance between self and anyone coughing or sneezing has also been listed by WHO as an important protective measure against the new coronavirus. At the community level, crowded areas and large-scale gatherings should be avoided. The use of mask by healthy people in public places is currently not recommended by WHO however, in some countries it has been made

mandatory in accordance with local customs or in accordance with advice by national authorities in the context of COVID-19 [44,45]. Initially, to combat the viral spread, most of the countries have imposed complete lockdown along with sealing of their borders and strict travel restrictions at both national and international level. Installing disinfectant tunnels at public places is coming up as an innovative strategy to combat coronavirus besides regular sanitization of public places.

For healthcare workers

The greatest risk of disease transmission is to the healthcare workers and is important to protect them to ensure continuity of care and prevent transmission of infection to other patients by continuous monitoring of these individuals [44]. Patients should be placed in isolated rooms or cohorted together. The rooms, surfaces and equipment should be decontaminated with disinfectants like sodium hypochlorite. Healthcare workers should be provided with N95 respirators and appropriate personal protective equipment (PPE). Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. Patients should be discharge from hospitals after clinical recovery and two negative RT-PCR tests conducted at 24 hour interval [18].

Public health approach of ayurveda and yoga

The Ministry of AYUSH, Government of India recommends ayurveda and yoga as the prophylactic strategies for COVID-19. Drinking hot water and herbal decoctions (ginger, black pepper, turmeric, cinnamon, giloy), gargling and steam inhalation are some of the ayurvedic measures that should be practiced regularly. Various herbs like *Withania somnifera* (Ashwagandha), *Asparagus racemosus* (Shatavari), *Tinospora cordifolia* (Guduchi), *Phylanthus embelica* (Amalaki), and *Glyceriza glabra* (Yashtimadhu) are potential immunomodulators and are being considered for COVID-19 prophylaxis and adjuvant effect. As rising cases of COVID-19 has created stress and anxiety in public, pranayama and meditation are simple yet useful home based practices to cope with it [46].

Current treatment strategies

Due to the lack of confirmed treatment for COVID-19, various treatment strategies are mainly symptomatic and supportive so as to maintain the vital signs, proper hydration, nutrition and regulating fever and cough. Some of the ongoing treatment strategies are as follows.

Chloroquine and hydroxychloroquine

Chloroquine is a 9-aminoquinoline known since 1934, and is a generic drug mainly for malaria and immune mediated diseases [47]. Chloroquine has been reported to alter the pH thereby preventing the binding of virus to the ACE-2 receptor [3,12,48]. Besides preventing the internalization of virus, chloroquine can also function at post-entry stages of 2019-nCoV infection [49]. Hydroxycholoroquine in combination with azithromycin has been found to have better efficacy for COVID-19 patients than hydroxycholoroquine alone but detailed clinical trials are still needed to confirm its efficacy [50].

Remdesivir

National Institute of Allergy and Infectious Disease, USA has initiated a clinical trial with remdesivir, a nucleoside analog, based on its effectiveness with SARS-2002 and MERS-2012 [3]. Wang et al. revealed that remdesivir and chloroquine were highly effective in controlling SARS CoV-2 in vitro and has also been found to be successful in treating the first case of COVID-19 in USA but its effectiveness and efficacy still needs to be validated [5,12,49].

Favipiravir

It is an anti-viral drug being currently tested in various clinical trials for COVID-19 and has shown positive outcome in two trials while results from other trials are awaited [51].

Protease-inhibitors

Certain protease-inhibitors have also been targeted as potential drugs for COVID-19 treatment [52]. Ritonavir, a potent protease inhibitor, has also been found to reduce significantly the load of β-coronavirus in COVID-19 patient in Korea when treated with lopinavir/ritonavir (Kaletra®, AbbVie, North Chicago, IL, USA) [53].

Dexamethasone

This is a steroid that has been used in various inflammatory disorders and certain cancers. Results of a clinical trial from the United Kingdom (UK) has shown the efficacy of dexamethasone for critically ill COVID-19 patients as mortality was found to reduce by about one third for patients on ventilators and by about one fifth for patients requiring oxygen [54].

Arbidol

It is an indole-derivative molecule that has been approved as prophylactic and therapeutic agent for respiratory viral infections and has been found to be effective against COVID-19 in vitro [47]. A randomized clinical trial of arbidol in coronavirus patients is underway in China [55].

Convalescent plasma therapy

Passive immunization with combination of convalescent plasma, lopinavir and interferon-beta/ribavirin was used during MERS [2,56]. Duan et al (2020) have documented that convalescent plasma therapy given to 10 patients of COVID-19 with severe illness, has been found to be well tolerated and improved the clinical condition by neutralizing viremia [57]. However, the optimal dose, time point, as well as the clinical benefit of this therapy, needs further investigation in larger well-controlled trials and needs approval.

SARS-CoV-2 vaccine development

Attempts are being made to find out the most effective mode to combat or overcome both the morbidity and mortality as early as possible either by medication or by prophylactic measures. In this regard, scientists across the globe are trying to develop SARS-CoV-2 vaccine by using different targets including inactivated virus vaccine, live attenuated vaccine, antibody vaccine, DNA vaccine, recombinant protein subunit vaccine, and mRNA vaccine. Till date, as such no approved vaccine has come up for SARS-CoV-2, however, some vaccine candidates have reached stage 1 or 2 clinical trials (**Table 1**). A major challenge in vaccine development against SARS-CoV-2 RNA virus is its high mutation rate and lack of proofreading by its RNA dependent RNA polymerase (RdRp). The high mutation rates lead to viral evolution and genome variability, posing hindrance in vaccine development and contributing to drug resistance [58]. Above all, great challenge lies ahead of scientific community, as till today except rabies RNA virus, no effective vaccine has come up for viruses like influenza, HIV and people have to learn to live

with it as it may be continue to exist in endemic state. However, as the expertise of scientists in future cannot be ruled out, thus we should not leave our hope to get a vaccine for SARS-CoV-2 at the earliest.

Table 1: Candidate vaccines under clinical trials to combat SARS-CoV-2 [70].

S. No.	Platform	Type	Developer	Current stage
1	RNA	Lipid nanoparticle-encapsulated mRNA 1273	Moderna/National Institute of Allergy and Infectious Diseases	Phase 2
2	Non Replicating Viral Vector	Adenovirus Type 5 Vector	CanSino Biological Inc./Beijing Institute of Biotechnology	Phase-2
3	Non Replicating Viral ector	ChAdOx1	University of Oxford	Phase 1/2
4	RNA	3 Lipid nanoparticulate-mRNAs	BioNTech/Fosun Pharma/Pfizer	Phase 1/2
5	Inactivated	Inactivated	Beijing Institute of Biological Products/ Sinopharm	Phase 1/2
6	Inactivated	Inactivated	Wuhan Institute of Biological Products/ Sinopharm	Phase 1/2
7	Inactivated	Inactivated + alum	Sinovac	Phase 1/2
8	DNA	DNA plasmid vaccine with electroporation	Inovio Pharmaceuticals	Phase 1

Impact of COVID-19

Impact on life

- **Educational impact:** The COVID-19 pandemic has led to the closure of schools, colleges and universities which would have a drastic impact on children's social life and learning in various countries and has moved towards online teaching methods. However, school closures alone would prevent only 2–4% of deaths, much less than other social distancing measures [59, 60].
- **Emotional impact**: The outbreak of coronavirus has emerged as a tragedy and the rapidly evolving situation has caused a substantial psychological impact on the public. Escalating number of cases, increased media reporting and mass quarantine, concerns regarding food shortage amidst lockdown and uncertainty of the duration of the pandemic are some of the factors that have led to anxiety, stress and fear among people [61]. COVID-19 pandemic could also lead to psychiatric symptoms in people without mental illness or aggravate the condition of those with pre-existing mental illness and could drive an increase in suicide rates in 2020 [62].
- **Cultural impact:** The impact of COVID-19 on the cultural sector is being faced around the world with cultural events being cancelled, cultural institutions closed, community cultural practices suspended, artists unable to make ends meet and the cultural tourism sector greatly affected. According to UNESCO, 89% of the countries have closed their world heritage sites to the public [63].
- **Impact on health care system**: This pandemic has severely impacted human health and has led to crisis in the medical management worldwide [61]. The rapidly increasing demand on health facilities has caused physical as well as psychological stress to health care workers due to high workload and lack of protective devices [62]. Further, most health professionals working in isolation units are staying separately due to fear of infecting their loved ones and as they lack any training for mental health care, the outbreak has left the staff vulnerable to the emotional impact of coronavirus. Suicidal cases of health professionals have also been reported in India and Italy [62, 64]. Further, due to constant exposure while treating the COVID-19 patients, many doctors and health care workers have got infected and many of them died due to infection. Interestingly, it has been observed that death occurring due to heart attacks have decreased that may be due to reduced work pressure and improved life style during lockdown.

Impact on environment

On paying a closer look to all that is happening around human beings, the rapid spread of the disease is leading to morbidity and mortality, while on the other hand the flora and fauna are rejoicing the lockdown that has reduced human mobility and activity vis a vis transportation, shut down of industries resulting into purification of environment indicated by significant reduction in Pollutant Standards Index levels. NASA has also reported reduction in nitrogen dioxide and carbon dioxide emissions, the common tracers of air pollution worldwide since the outbreak of coronavirus [65]. More specifically, India's Central Pollution Control Board too has recently reported an improvement in air quality in the country with nearly 71% fall in nitrogen dioxide levels along with fall in the Air Quality Index (AQI) in several major cities like New Delhi, Kolkata, Mumbai, Bengaluru and Chennai. For instance, in New Delhi's, the capital city of India, AQI was recorded 112 on 2nd May, 2020 while last year, the index had crossed the 400 mark on several occasions and mostly stayed high [66].

Impact on economy

Health is fundamental for the prosperity of society, as fear and illness can stifle manufacturing, consumption, financial market, trade, travel and tourism thereby affecting the economy [67]. Besides the global health impact, COVID-19 continues to impose considerable uncertainty about its impact on the economy. Implementation of lockdown in various nations has brought the global economic activity to a standstill with daily wagers and small and medium business owners being most af-

fected due to loss of jobs and livelihood. The current estimated impact on global GDP growth for 2020 is around – 4%, with considerable downside risks if containment policies are extended [68]. It is feared that COVID-19 may turn out to be one of the most economically costly pandemics in recent history as it is imposing conspicuous impact on manufacturing, stock market, tourism and transportation, IT and telecom, entertainment industry, construction and real estate. Thus, prolonged economic shut down due to COVID-19 could have long-term consequences that are harder to quantify. The governments should implement skill building training programs, public-private partnerships; provide industrial upgrading incentives, expanded digital access for improving the economy. These measures would help to stabilize the domestic markets and build public confidence.

Future perspective

The situation with COVID-19 pandemic is ever evolving as the cases are increasing rapidly around the world. Strategic and Technical Advisory Group for Infectious Hazards (STAG-IH)-WHO has listed some recommendations to prevent the further transmission of infection and fighting against COVID-19. According to STAG-IH all countries need to rapidly and vigorously increase their preparedness and response actions based on WHO's four transmission scenarios i.e. countries with no cases, sporadic cases, clusters of cases, and community transmission (4Cs). Further, all countries should follow a set of response measures which include case and contact tracing; containment measures; public awareness about personal hygiene and preventive measures, making health care systems well equipped for surging cases, stronger infection prevention and control in health facilities and delay or cancellation of large scale public gatherings; active surveillance strategies and implement social distancing. Moreover, research gaps about COVID-19 should be attended which include understanding the natural history of infection to better describe its transmissibility; understanding the role of asymptomatic infection, comparative evaluation of different quarantine strategies for their effectiveness and social acceptability, encourage the development of point-of-care diagnostic tests, validation of existing serological tests and expedite the research on animal models for vaccine and therapeutic development [69].

Further, continued rapid sharing of data of public health importance as well as technical collaboration among clinicians, epidemiologists, and virologists will be crucial to fight against COVID-19. To entirely curb the coronavirus pandemic, it is important for international agencies and national governments to come together for developing and implementing policy solutions which requires concerted efforts and cooperation of people.

Conclusion

The outbreak of COVID-19 has become a clinical threat to the general population and healthcare workers worldwide and has brought human life to standstill. However, only effective antiviral therapy or vaccination may curb the disease and will be the best measure to contain it. At this moment of time, aggressive implementation of infection control measures i.e. prevention of human to human transmission, strict personal hygiene, self quarantine and coordinated international disease surveillance to prevent the spread of SARSCoV-2, is the need of hour. Both research and disease management efforts must be channelized towards proactive management strategies. WHO Director-General Dr. Tedros, has cautioned that we have a long way to go as this virus will be with us for a long time and the world cannot go back to the way things were. There has to be a "new normal" – a world that is healthier, safer and better prepared [13].

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