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Review Article: Covid Series

Current Understanding, Knowledge Gaps and a Perspective on the Future of COVID-19 Infections: A Systematic Review

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Abstract

A novel coronavirus infection, which began as an outbreak of unusual viral pneumonia in Wuhan, a central city in China, has evolved into a global health crisis. The outbreak is an unembellished reminder of the hazard coronaviruses pose to public health. Government and researchers around the world have been taking swift measures to control the outbreak and conduct aetiological studies to understand the various facets of the outbreak. This review is an attempt at providing an insight about the current understanding, knowledge gaps and a perspective on the future of coronavirus disease 2019 (COVID-19) infections. All the authentic data published so far on COVID-19 has been systematically analysed. PubMed, NCBI, World Health Organisation, Ministry of Health and Family Welfare (India), and Centers for Disease Control and Prevention databases and bibliographies of relevant studies up to 22nd June 2020 have been included. The Wuhan outbreak is a stark reminder of the continuing threat posed by zoonotic diseases to global health. Despite an armamentarium of Government officials, researchers and medical fraternity working towards the containment of this novel coronavirus viral pneumonia continues to spread at an alarming rate infecting multitudes and claiming hundreds of lives.

Keywords: COVID-19, human coronavirus, nCoV-2019, severe acute respiratory syndrome coronavirus 2, Wuhan coronavirus

Introduction

As the December sun rose on the Chinese horizon, the world woke up with a start and witnessed the emergence of coronavirus disease 2019 (COVID-19). Future historians will remember the year 2020 as the year of Wuhan coronavirus. The cases clinically resembled viral pneumonia while showing an epidemiological link to the Huanan Seafood Wholesale Market, where the sale of live animals was taking place.[1] Based on the lessons learned during the previous coronavirus epidemics, China was able to recognise the outbreak within a few weeks, sequence the viral genome and share the data internationally. This paved the way for the development of rapid assays, as well as vaccine development initiatives throughout the world.

The causative agent of the mystery pneumonia has been identified as a novel coronavirus through deep sequencing and aetiological investigations carried out by at least 5 independent laboratories of China.[2] The World Health Organisation (WHO) announced an official name for the disease caused by the novel coronavirus as COVID-19 on 11th February 2020. On the same date, the International Committee on Taxonomy of Viruses announced 'severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)' as the name of the new virus because the virus is genetically related to the coronavirus responsible for the SARS outbreak of 2003.[3] The majority of initial cases gave a history of direct or indirect contact with the Wuhan Huanan Seafood Wholesale Market, which is believed to be the place of origin of the outbreak of the COVID-19. On 31st January 2020, the WHO declared the outbreak a 'Public Health Emergency of International Concern'.[4] On 11th March 2020, the WHO declared COVID-19 as a pandemic.[5] The sporadic renaissance of new coronaviruses (CoVs) is a stark reminder of the incessant threat of zoonotic diseases and their devastating health and economic impact.[1,4]

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Data Sources and Resource Selection

We systematically reviewed the published work using the terms novel coronavirus 2019, COVID-19, SARS-CoV-2, Wuhan outbreak, viral pneumonia, human coronavirus, etc. PubMed, NCBI, WHO, Ministry of Health and Family Welfare (MoHFW, India), Indian Council of Medical Research (ICMR, India) and Centers for Disease Control and Prevention databases were searched up to 22nd June 2020 and bibliographies of relevant studies were included. A total of 47 studies were referred to for this review. We extracted COVID-19 outbreak and genomic data as reported in various studies discovered through this methodology, and presented in tables, figures or graphs in the most relevant of these studies.

Coronavirus Outbreaks: The Story Thus Far

Coronavirus was first identified in the mid-1960s. Human coronaviruses (HCoVs) represent a major group of CoVs associated with multiple respiratory diseases of varying severity.[6,7] The first two HCoV, HCoV-229E and HCoV-OC43, were studied extensively from 1965 to the mid-1980s. They were responsible for causing mild infections resulting in common cold.[8] SARS-CoV emerged in 2002–2003 in Guangdong, China causing atypical pneumonia, respiratory failure and acute respiratory distress syndrome.[9] The virus affected 8096 people causing severe pulmonary infections and resulted in 774 deaths.[10] Subsequent phylogenetic studies pointed to the origin of SARS-CoV to civet cats and bats.[11] The renewed interest in this virus family resulted in the identification of two more HCoVs, i.e., HCoV-NL63, discovered in a child with bronchiolitis in the Netherlands[12] and HCoV-HKU1 from an adult with chronic pulmonary disease in Hong Kong in 2005.[13] The Middle East respiratory syndrome (MERS)-CoV epidemic surfaced in Saudi Arabia in 2012 with similar clinical symptoms as SARS-CoV but with a much higher mortality rate (35%).[8] When compared to SARS-CoV, which exhibits super-spreader events, the transmission of MERS-CoV was geographically defined.[14] The timeline of the emergence of various HCoVs is shown in Figure 1.

Why is Severe Acute Respiratory Syndrome Coronavirus 2 A Novel Coronavirus?

The WHO has classified the SARS-CoV-2 virus as a β coronavirus of Group 2B.[15] Initial analysis has suggested that SARS-CoV-2 has a close evolutionary association with the SARS-like bat CoVs.[16] The genome of CoVs ranges between approximately 26,000 and 32,000 bases and includes a variable number of open reading frames (ORFs).[14,17] The first ORF encodes 16 non-structural proteins and other ORFs encode accessory proteins and structural proteins.[18] The four major structural proteins include the spike surface glycoprotein (S), small envelope protein (E), matrix protein (M) and nucleocapsid protein (N) [Figure 2]. The spike surface glycoprotein plays an essential role in binding to receptors on the host cell and determines host tropism.[19,20] The spike proteins of SARS-CoV and MERS-CoV bind to different host receptors via different receptor-binding domains (RBDs). SARS-CoV uses angiotensin-converting enzyme 2 (ACE2) as one of the main receptors[21] with CD209 L as an alternative receptor,[22] whereas MERS-CoV uses dipeptidyl peptidase 4 (DPP4, also known as CD26) as the primary receptor. The SARS-CoV-2 virus is found to have 79% and 50% identity at the nucleotide level to SARS-CoV and MERS-CoV, respectively.[23] Some of the notable differences at the amino acid level are, 8a protein is present in SARS-CoV and absent in SARS-CoV-2 the 8b protein is 84 amino acids in SARS-CoV, but longer in COVID-19 causing virus, with 121 amino acids; the 3b protein is 154 amino acids in SARS-CoV, but shorter in SARS-CoV-2. In total, there are 380 amino acid substitutions between the amino acid sequences of SARS-CoV-2 and the corresponding consensus sequences of SARS and SARS-like viruses.[14] The phylogenetic trees of their orf1a/b, spike, envelope, membrane and nucleoprotein are also clustered closely with those of the bat, civet and human SARS CoVs.[24] Due to very limited knowledge of this novel virus, a reasonable explanation for the significant number of amino acid substitutions between the SARS-CoV-2 and SARS or SARS-like CoVs is not yet deciphered. For example, no amino acid substitutions were present in the receptor-binding motifs that directly interact with human receptor ACE2 protein in SARS-CoV,[21] but six mutations occurred in the other region of the RBD. Whether these differences could affect the host tropism and transmission property of the SARS-CoV-2 virus compared to SARS-CoV is worthy of future investigation. The comparison of the three major HCoVs (SARS, MERS, SARS-CoV-2) is tabulated in Table 1.[25]

In a study published by Zhang *et al*., a total of 169 genomes of the SARS-CoV-2 virus were examined and two major genotypes, Type I and Type II were identified. Type I is further divided into Type IA and IB. Type II strains have been found to be more contagious and thus predominant in infections throughout the world. The authors also found that there are

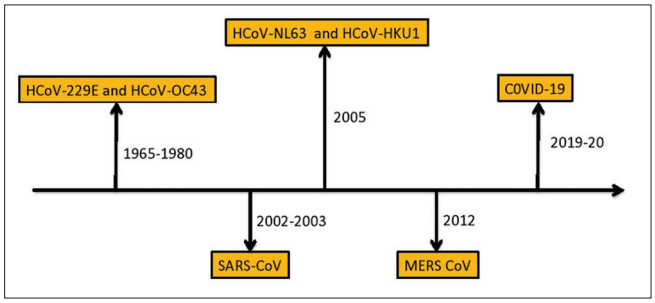

Figure 1: The timeline of emergence of various human coronaviruses[8]

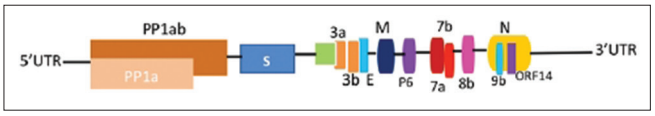

Figure 2: The genome of severe acute respiratory syndrome coronavirus 2[14]

Table 1: Comparative analysis of severe acute respiratory syndrome, middle east respiratory syndrome and coronavirus disease 2019[25]

	SARS	MERS	COVID-19
Place of origin	China (Guangdong, November 2002)	Saudi Arabia (September 2012)	China (Hubei December 2019)
Global spread	26 countries	27 countries	>200 countries/regions
Total cases	8096	2494	8,242,999 confirmed (still continuing)[5]
Age (years), mean (range)	39.9 (1-91)	56 (14-94)	49 (21-76)
Male:Female ratio	1.1:25	3.3:1	2.7:1
Mortality rate	10%	37%	≈3%
Possible source	Bats		
Intermediate host	Civet cats	Dromedary camels	Pangolins (??)[26]
Transmission	Respiratory droplet		
Incubation period	2-7 days	2-14 days	2-14 days[4]
Primary receptor	ACE2	Dipeptidyl peptidase 4	ACE2[22]
Symptoms	Upper respiratory, lower respiratory and gastrointestinal symptoms	Upper respiratory and lower respiratory symptoms	Mainly lower respiratory and gastrointestinal symptoms[27,28]

SARS: Severe acute respiratory syndrome, MERS: Middle East respiratory syndrome, COVID-19: Coronavirus disease 2019, ACE2: Angiotensin-converting enzyme 2

several clades in Type II (Group 1–3). Group-1 of Type II are identical, suggesting they were likely originated from the same transmission source. Group-2 and Group-3 share at least one mutation, indicating that they shared the same transmission source.[29] Distinct viral clades have a likely impact on COVID-19 pathogenesis and spread. Indian strains mainly belong to two clades, i.e., clade I and G.[30]

Sardar *et al*. conducted an integrated sequence-based analysis of SARS-CoV2 genomes from India, Italy, USA, Nepal and compared with the Wuhan SARS-CoV-2 genome. It was observed that all the genomes shared 99% similarity with the Wuhan (SARS-CoV-2) genome. Each genome was observed to be carrying unique mutations except the genome from Nepal, which shares 100% similarity with the Wuhan genome. Indian SARS-CoV-2 genome was observed to carry mutations in orf1ab, nsp2, nsp3, helicase, ORF8 protein and spike surface glycoprotein. The spike surface glycoprotein mutation (A930V (24351C>T) is unique to the Indian SARS-CoV-2, strains.[26]

Although the natural host of SARS-CoV-2 is yet to be identified, the possibility of the animal to human transmission cannot be ruled out. Researchers from China, have put forward a hypothesis that pangolins (long-snouted, ant-eating mammals), used in traditional Chinese medicine, maybe the animal source of the COVID-19 outbreak. The genetic constitution of the virus isolated from this scaly animal has been found to be around 99% similar to that of the currently circulating virus.[31]

Contaminated surfaces are known to be significant vectors in the transmission of infections in the hospital as well as community. The duration of the persistence of viable virus on various inanimate surfaces is affected markedly by temperature and humidity conditions. In a study published in the New England Journal of Medicine (March 2020), SARS-CoV-2 was found to be more stable on plastic and stainless steel than on copper. Although the virus titer was greatly reduced, the virus was found to survive for 72, 8–24 and 4–8 h on plastic/stainless steel, cardboard and copper surfaces, respectively.[32]

COVID-19 Pathogenesis

The initial attachment of the virion to the host cell is initiated by interactions between the S protein and ACE2 receptor. COVID-19 virus primarily infects intra-epithelial cells within the lung. The virus is capable of entering macrophages and dendritic cells but only leads to an abortive infection. Despite this, infection of these cell types may be important in inducing pro-inflammatory cytokines that may contribute to disease.[33] Significantly high levels of cytokines and chemokines were noted in COVID-19 patients, which included Interleukin (IL) 1-β, IL-1RA, IL-7, IL-8, IL-9, IL-10, basic fibroblast growth factor-2, granulocyte colony-stimulating factor (GCSF), granulocyte macrophage-CSF, interferon (IFN)-γ, IP-10, monocyte chemoattractant protein-1 (MCP-1), macrophage inflammatory protein 1 (MIP-1)α, MIP-1 β, PDGFB, tumor necrosis factor alpha (TNFα) and vascular endothelial growth factor-A. The severe cases admitted to the intensive care unit showed high levels of pro-inflammatory cytokines, including IL-2, IL-7, IL-10, GCSF, IP-10, MCP-1, MIP-1α and TNFα, which are thought to promote the severity of the disease.[4] Infection has been found to cause ciliostasis of epithelial cells in the lower respiratory tract. The exact mechanism of lung injury and the cause of severe disease in humans remains undetermined.[34]

The symptoms of COVID-19 appear after approximately 5.2 days.[27] The period from the onset of symptoms to death ranged from 6 to 41 days, with a median of 14 days. This duration is dependent on the age of the patient and the status of his/her immune system. The period is shorter among patients of age >70 years compared with those under the age of 70.[35] The most common symptoms associated with COVID-19 at the onset of illness are fever, cough and fatigue.[1,4] Further

symptoms include sputum production, headache, haemoptysis, diarrhoea, dyspnoea and lymphopenia.[4] Chest computed tomography scan may show pneumonia and signs of acute respiratory distress syndrome and acute cardiac injury. In severe cases, multiple peripheral ground-glass opacities have been observed in subpleural regions of the lungs.[28]

Knowledge of viral dynamics and host response is necessary to design vaccines and antiviral treatment. In a study conducted in Hongkong in 23 patients, median viral load in posterior oropharyngeal saliva or other respiratory specimens at presentation was 5·2 log10 copies per mL (interquartile range 4·1–7·0). Salivary viral load was highest during the 1st week after symptom onset and subsequently declined with time. In one patient, viral RNA was detected 25 days after symptom onset. In 16 patients where sera were available 14 or longer after onset, it was shown that both IgG and IgM antibodies started to increase on around day 10 after symptom onset, and most patients had seroconversion within the first 3 weeks. IgG and IgM antibody level against the SARS-CoV-2 internal nucleoprotein and the surface spike RBD correlated with neutralising activity.[36]

Epidemiology - The Oriental Origin

In December 2019, Wuhan, Hubei province, China, became the centre of an outbreak of pneumonia of unknown cause. All the cases shared history of exposure to the Huanan seafood market.[4] On 31st December 2019, the local health authorities issued an epidemiological alert and the market was shut down on 1st January 2020 [Figure 3]. Meanwhile, 59 suspected cases were transferred to a designated hospital starting from 31 December 2019. An expert team of physicians, epidemiologists, virologists and government officials was soon formed to tackle the situation. Suspected patients were isolated in Jin Yin-tan Hospital (Wuhan, China). By 2nd January 2020, 41 admitted patients were identified as laboratory-confirmed cases for a novel coronavirus using real-time reverse transcriptase-Polymerase Chain Reaction (targeting envelope gene) and next-generation sequencing.[14,27,35]

The Malignant Spread

Soon after, cases were reported from all over the world. As

Figure 3: The timeline of sequence of events for coronavirus disease 2019[25]

per data reported by national authorities by 10:00 CEST 22nd June 2020, globally, there are 8,860,331 cases and 465,740 deaths. The feeling that China has contained the outbreak had not completely sunk in and investigations into the origin of the pandemic were to resume when a cluster of cases have been detected in Beijing associated with a wholesale market. Chinese authorities have reported a total of 172 cases since 11th June, including 158 in Beijing, 10 linked cases in Hebei Province, 2 in Liaoning Province, 1 in Sichuan Province and 1 in Zhejiang Province by 18th June 2020. Outside China, >200 countries/regions have been affected, with >150 countries having local transmission of the disease. The WHO risk assessment shows a very high risk for COVID-19 at a global level.[5] The rate of secondary and tertiary transmission is of grave concern and misinformation and fear are rampant. Thousands of 'COVID warriors' all around the world are infected with COVID-19, and as countries implement scaled-up diagnosis and surveillance, the risks posed by inadequate protective gear and shortages in testing kits are getting heightened.[28]

Indian Scenario

Currently, India has 425,282 confirmed cases, 237,196 cured/discharged cases and 13,699 deaths, as on 22nd June 2020, 08:00 IST.[37] India has taken preemptive and pro-active response to COVID-19 pandemic, motivated with high-level political commitment. The Indian Government is working to enhance preparedness and has declared COVID-19 a 'notified disaster'. Prime Minister of India, exercising his powers under section 6 (2) (i) of the Disaster Management Act, 2005, issued orders of complete lockdown with effect from 25th March 2020. All travellers, returning from or having visited any COVID-19 affected region during their travel after 15th February 2020 are being quarantined for a minimum of 14 days. Screening of passengers is being done across all airports, seaports and border crossings. Community surveillance, isolation wards, quarantine facilities, infection prevention, trained workforce and risk communications and community engagement for COVID-19 are being further strengthened for day-to-day operations.[37,38] Since the lockdown, there has been mass production as well as the import of personal protective equipment, disinfectants, hand sanitisers, ventilators and other respiratory support systems. The number of cases has now become insignificant, with focus shifting to testing with optimum capacity, preventing mortality and localising the infection as the country has entered into the phase of unlocking step by step. A significant leap has been seen in the testing capacity throughout the country. Whereas, viral diagnostics was earlier confined to a handful of government-approved Viral Research and Diagnostic Laboratories, now there are over 992 laboratories across India testing for SARS-CoV-2 (until 22nd June 2020, there were 726 Government and 266 private laboratories for testing of COVID-19, through real-time reverse transcription polymerase chain reaction (RT-PCR), TrueNat and CBNAAT).[39]

National Institute of Virology, Pune of the ICMR remains the apex laboratory for quality assurance for the testing for COVID-19.

Laboratory Diagnosis

Sample collection and testing strategies

Diagnostic testing for COVID-19 is critical to tracking the virus, understanding epidemiology, informing case management and to suppressing transmission. The surveillance definitions provided by the WHO has been depicted in Table 2.[40] The WHO recommends the collection of both nasopharyngeal and oropharyngeal swabs for the diagnosis of COVID-19 (As per the WHO guidelines 19th March 2020). Other respiratory specimens that can be collected include sputum, endotracheal aspirate, bronchoalveolar lavage or tissue from biopsy or autopsy. Paired serum for serological testing of antibodies against pan-coronavirus can also be collected (acute-1st week of illness and convalescent-2–3 weeks later).[41] ICMR has approved a few rapid antibody detection kits for COVID-19, where a positive test indicates exposure to SARS-CoV-2; a negative test does not rule out COVID-19 infection.[42] To contain the spread of COVID-19 infection in India, ICMR has given its revised strategy for testing. ICMR recommends testing of all symptomatic (ILI symptoms) individuals: with a history of international travel in the past 14 days, with contacts of laboratory-confirmed cases, health-care workers/frontline workers involved in containment and mitigation of COVID19, within hotspots/containment zones, among returnees and migrants within 7 days of illness; all patients of Severe Acute Respiratory Infection; asymptomatic direct and high-risk contacts of a confirmed case to be tested once between day 5 and day 10 of coming into contact and all hospitalised patients who develop ILI symptoms. The emergency procedure should not be delayed for the lack of test.[39]

Table 2: Case definitions[40] (as per World Health Organization, Interim guidance 20th March, 2020)

Suspect case
A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), and a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset; or
A patient with any acute respiratory illness and having been in contact with a confirmed or probable COVID-19 case (see definition of contact) in the last 14 days prior to symptom onset; or
A patient with severe acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; and requiring hospitalization) and in the absence of an alternative diagnosis that fully explains the clinical presentation
Probable case
A suspect case for whom testing for the COVID-19 virus is inconclusive*
OR
A suspect case for whom testing could not be performed for any reason
Confirmed case: A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms
Contact: A contact is a person who experienced any one of the following exposures during the 2 days before and the 14 days after the onset of symptoms of a probable or confirmed case
Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 min
Direct physical contact with a probable or confirmed case
Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment; OR
Other situations as indicated by local risk assessments

For confirmed asymptomatic cases, the period of contact is measured as the 2 days before through the 14 days after the date on which the sample was taken, which led to confirmation. *Inconclusive being the result of the test reported by the laboratory

Sample packaging and transport

For the transport of samples for viral detection, viral transport medium should be used. All samples should be transported to the laboratory at 2°C–8°C, if ≤5 days and –70°C (dry ice), if >5 days. All specimens to be transported (UN 3373 or UN 2814) in triple packaging consisting of a leak-proof primary receptacle covered with absorbent material, a secondary package of the sealed plastic bag and a rigid outer box with cushioning material. The package should be properly labelled and be accompanied by a duly filled requisition form and bills. Biosafety level 2 facilities are recommended for diagnostic testing.[41]

Methods for the detection of severe acute respiratory syndrome coronavirus 2

Several in-house and commercial assays are under development or have been developed to detect SARS-CoV-2 by real-time RT-PCR. Table 3 shows the various assays in use and the target genes.[43] Several rapid assays that detect IgG and IgM antibodies have also been marketed and can be useful for surveillance and the detection of asymptomatic infections.

Other assays for the detection of COVID-19 include viral culture, electron microscopy, and serological tests, COVID-19 virus can be isolated in human airway epithelial (HAE) cells, VERO E6 and Huh-7 cell lines. The cytopathic effects have been observed 96 h after inoculation on surface layers of HAE cells. A lack of ciliary beating has been observed under the electron microscope. The pathological features of COVID-19 greatly resemble those seen in SARS and MERS coronavirus infection.[44]

Treatment and Prevention

The treatment strategies being tried currently include nucleoside analog (favipiravir and ribavirin), RNA polymerase inhibitors (remdesivir and galidesivir), protease inhibitors (lopinavir and ritonavir), immune modulators such as chloroquine and monoclonal antibodies (IFN alfacon-1).[45] The initial clinical trial has shown that dexamethasone, a corticosteroid can be lifesaving for patients who are critically ill with COVID-19. According to preliminary findings, the treatment was shown to reduce mortality by about one third and one fifth among patients on ventilators and patients requiring only oxygen, respectively. Further research and large

Table 3: Summary of Indian Council of Medical Research approved kits for molecular assays[43]

Country	Name of Company	Name of Kit	Gene targets
United states	ABI (Applied Bio-Systems)	TaqMan 2019-nCov control kit v1	Orf1ab, S, N
Germany	Altona Diagnostic	RealStar SARS-CoV-2 RT-PCR kit 1.0	E, S
India	ADT India LTD, New Delhi	LyteStar 2019-nCoV RT PCR Kit 1.0	E, RdRp
India	Angstrom Biotech Pvt. Ltd, Rajasthan	ANGPCR 2019-nCoV	Orf1ab, N
China	BGI Genomics	Real Time Fluorescent RT-PCR Kit for detecting 2019-nCoV	Orf1ab, N
United States	Cepheid	Xpert Xpress SARS-CoV-2	N2, E
China	Daan Gene Co. Ltd., China	Daan Gene Co. Ltd	Orf1ab, N
India	GCC Biotech Pvt. Ltd, 24 Parganas, West Bengal	DiagSure nCOV-19 detection assay (Taqman based)	Orf1ab, N
South Korea	GeneMatrix	NeoPlex COVID-19 detection kit	RdRp, N
India	Gene Path Diagnostics	GenePath CoViDx One RT-qPCR v2.1.1	N1, N2
India	Genome Diagnostics Pvt. Ltd., New Delhi	Genosens nCOV 2019 real time PCR kit	Orf1ab, E, N
India	Helini Biomolecules, Chennai	Helini coronavirus real-time PCR kit	RdRp, Orf
Singapore	JN Medsys PTD. Ltd.	Protect COVID-19 RT-qPCR Kit	N1, N2
India	KILPEST (3B BlackBio Biotech India Ltd., Bhopal	TRUPCR SARS-CoV-2RT-qPCR kit version 2	RdRp, N
South Korea	Kogene Biotech, Seoul	Power check 2019 nCoV real time PCR kit	RdRp, E
South Korea	LabGenomics	LabGun Real Time PCR Kit	RdRp, E
India	Medsource Ozone Biomedicals, Faridabad	COVID-19 RT-PCR kit	Orf1ab, N
India	Meril Diagnostics, Vapi, Gujarat	Meril COVID-19 One-step RT-PCR Kit	RdRp, N
South Korea	OSANG Health Care	Gene finder COVID-19	RdRp, N
Switzerland	Roche Diagnostics	Light mix modular SARS-CoV-2	RdRp
China	Sansure Biotech Inc., Changsha	2019-nCoV nucleic Acid diagnostic kit (PCR-fluorescence probing)	Orf1ab, N
South Korea	Seegene	Allplex 2019-nCoV assay	RdRp, N, E
South Korea	SD Biosensor	nCoV real-time detection kit	Orf1ab, E
India	3B Black Bio Biotech India Ltd.	TRUPCR SARS-CoV-2 RT-qPCR Kit (V-3.2)	RdRp, N, E

*The above kits are validated with the batch number provided by ICMR. Manufacturer is responsible for batch to batch consistency. US-FDA real-time PCR kits can be used directly after approval from DCGI. The list of US-FDA SARS-CoV-2 real time PCR kit can be found at: https://www.finddx.org/covid-19/pipeline/. E: Envelope protein, RdRp: RNA-dependent RNA polymerase, N: Nucleocapsid protein, ORF1ab: Open reading frame 1a and b, RdRp: RNA-dependent RNA polymerase, RT-PCR: Reverse-transcription polymerase chain reaction, S: Spike protein, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, ICMR: Indian Council of Medical Research

randomised control trials are needed to produce actionable evidence into these treatment strategies.[46]

As of 18th June 2020, there are 13 vaccine candidates in the clinical trial with nonreplicating viral vector platform-based vaccines ChAdOx1-S (University of Oxford/AstraZeneca), Adenovirus Type 5 Vector (CanSino Biological Inc./Beijing Institute of Biotechnology) and LNP encapsulated mRNA (Moderna/National Institute of Allergy and Infectious Diseases) being the front runners having entered phase two of trial. The Indian candidates include codon deoptimised live attenuated vaccines by Codagenix/Serum Institute of India; Indian Immunologicals Ltd/Griffith University and non-replicating viral vector platform with recombinant deactivated rabies virus-containing S1 by Bharat Biotech/Thomas Jefferson University are in pre-clinical trial.[47] However, in the absence of a licensed vaccine/antiviral drug, non-pharmaceutical interventions, such as hand hygiene, social distancing and respiratory etiquettes, are the most powerful weapon against COVID-19.

Contributions of microbiology fraternity

Microbiologists had a vital role to play as the pandemic struck the world. Beginning from the identification of the causative agent and sequencing of the viral genome to deciphering the phylogenetic aspect. Furthermore, developing protocols for specimen collection and handling; strategies for testing; setting up the laboratory with BSL requirements; working towards novel and cost-effective diagnostic tests; establishing and supervising the infection prevention and control measures.

Conclusion

Global economic growth in 2020 has been significantly abridged. COVID-19 is not just an epidemic but also an infodemic, with the bombardment of information in both scientific journals as well as social media. Rapid dissemination of trustworthy information and peer-reviewed research is needed the most during this period of uncertainty. Deciphering the immunologic response to infection, the antibody kinetics, range of genetic diversity and its effect on test performance might hold a clue to the burning question in every person's mind irrespective of the region, race, caste and colour, 'When and how is this pandemic going to stop???'.

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Conflicts of interest

There are no conflicts of interest.

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