

What does Our Experience of COVID-19 Teach Us?

Shivcharan Prasad and Ipsita Roy*

Department of Biotechnology, National Institute of Pharmaceutical Education and
Research Sector 67, S.A.S. Nagar, Punjab-160062, India

*Correspondence: ipsita@nipr.ac.in

1. INTRODUCTION

Viral diseases pose the greatest concern for human health. Some of the major epidemics have turned into pandemics, such as severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), HIV, influenza A (H1N1) pdm/09, and most recently, COVID-19. It soon became a major burden for all affected countries, which disturbed social and economic development. As of March 5, 2021, there have been over 116 million confirmed COVID-19 cases and over 2.5 million deaths reported worldwide (<https://www.worldometers.info/coronavirus/>, accessed on 05.03.2021). COVID-19 could cost the global economy about USD 4.1 trillion (<https://cepi.net/about/whyweexist/>; accessed on 05.03.2021). This is not the first time that humans have encountered coronavirus; several other zoonotic outbreaks of coronavirus have been reported earlier. Among these was the SARS-CoV (Severe Acute Respiratory Syndrome coronavirus) outbreak in 2003 in some parts of China which later spread to a few other countries. There were around 8000 confirmed cases and 774 reported deaths (Lundstrom, 2020). Another outbreak of coronavirus occurred in Saudi Arabia and other Middle Eastern countries in 2012 and was named as MERS-CoV (Middle East Respiratory Syndrome coronavirus) (Al-Osail & Al-Wazzah, 2017). Although the disease did not exhibit a widespread outbreak, it resulted in a very high fatality rate, with 855 cases and 333 deaths (Lundstrom, 2020).

COVID-19, on the other hand, has affected almost all the countries or territories around the globe. Statistics for some of the most affected countries is shown in Fig 1.

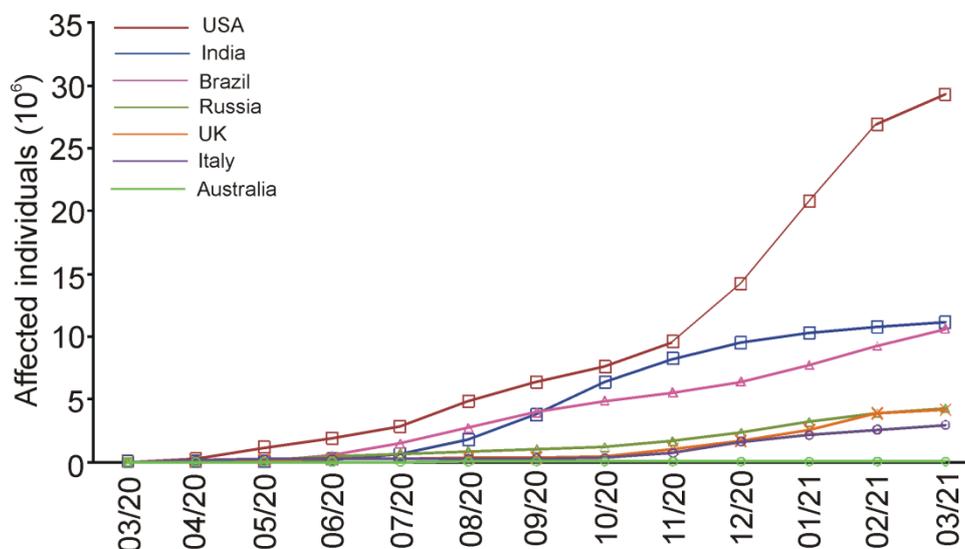


Figure 1: Some of the countries affected by COVID-19, data shown on the first of each month (<https://www.worldometers.info/coronavirus/>, accessed on 05.03.2021).

The focus of this mini review is on the experience gained by different sectors during this challenging time and how that experience can be utilized to ensure a better response to the next public health threat.

2. BIOLOGY OF CORONAVIRUS

Coronaviruses are a class of enveloped positive-sense single-stranded RNA viruses that cause respiratory symptoms and sometimes, enteric, hepatic or neuronal disorders (Masters, 2006). Coronaviruses are members of the family *Coronaviridae* and subfamily *Orthocoronavirinae*. The subfamily is further divided into alphacoronaviruses and betacoronaviruses which infect mammals, while gammacoronaviruses and deltacoronaviruses can infect birds too. The avian infectious bronchitis virus, which causes respiratory disease with low fatality in poultry but not other birds, is a gammacoronavirus. Like all other RNA viruses which infect eukaryotic cells, the genome of coronavirus shows capping at the 5' and 3' untranslated regions which allows it to utilize the machinery of the host cells for its replication. The genome of coronavirus is also unusually large as compared to other RNA viruses. It varies between 26 – 32 kb (Woo et al., 2010) and contains multiple ORFs. Compared to this, the genome size of the

poliovirus, another positive strand RNA virus is ~7500 nucleotides (Tavares et al., 2013) while the genome size of the segmented influenza A virus is 13,588 nucleotides (Ghedini et al., 2005). Larger genome sizes have been inversely correlated with mutation rates which may affect their adaptation to hosts (Lauber et al., 2013).

Infection by coronaviruses which use humans as hosts, e.g. HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1, can be acute or chronic, and usually cause mild symptoms associated with ‘common cold’. However, the recently emerged members, *viz.* SARS-CoV, MERS-CoV and SARS-CoV-2, have far deadlier consequences with some of them showing significant fatality rates. Therapeutic strategies targeting SARS-CoV-2 concentrate on both prophylactic (Table 1) and curative (Table 2) aspects, with variable results.

Table 1: List of vaccines against SARS-CoV-2 which are approved and are under development [<https://www.raps.org/news-and-articles/news-articles/2020/3/covid-19-vaccine-tracker>, <https://covid19.trackvaccines.org/vaccines/>]

Authorized/Approved vaccine				
Name	Vaccine type	Primary developer	Country of origin	Authorization/Approval
Comirnaty (BNT162b2)	mRNA-based vaccine	Pfizer, BioNTech; Fosun Pharma	Multinational	Approved in 63 countries, 9 trials in 9 countries
Moderna COVID-19 Vaccine (mRNA-1273)	mRNA-based vaccine	Moderna, BARDA, NIAID	USA	Approved in 40 countries, 5 trials in 1 country (Phase 3 clinical trials)
COVID-19 Vaccine AstraZeneca (AZD1222); also known as Covishield	Adenovirus vaccine	BARDA, OWS	UK	Approved in 53 countries, 18 trials in 13 countries (Phase 3 clinical trials)
Sputnik V	Non-replicating viral vector	Gamaleya Research Institute, Acellena Contract Drug Research and Development	Russia	Approved in 29 countries, 15 trials in 6 countries
CoronaVac	Inactivated vaccine (formalin with alum adjuvant)	Sinovac	China	Approved in 9 countries, 11 trials in 5 countries

Authorized/Approved vaccine				
Name	Vaccine type	Primary developer	Country of origin	Authorization/ Approval
BBIBP-CorV	Inactivated vaccine	Beijing Institute of Biological Products; China National Pharmaceutical Group (Sinopharm)	China	Approved in 15 countries, 6 trials in 7 countries
EpiVacCorona	Peptide vaccine	Federal Budgetary Research Institution State Research Center of Virology and Biotechnology	Russia	Approved in 1 country, 2 trials in 1 country
Convidicea (Ad5-nCoV)	Recombinant vaccine (adenovirus type 5 vector)	CanSino Biologics	China	Approved in 3 countries, 6 trials in 6 countries
Covaxin	Inactivated vaccine	Bharat Biotech, ICMR	India	Approved in 2 countries, 5 trials in 1 country
JNJ-78436735 (formerly Ad26.COV2.S)	Non-replicating viral vector	Janssen Vaccine (Johnson & Johnson)	The Netherlands, USA	Approved in 3 countries 6 trials in 17 countries, (Phase 3 clinical trials)
Vaccine candidates in development				
Candidate	Mechanism	Sponsor	Trial phase	Institution
NVX-CoV2373	Protein subunit	Novavax	Phase 3	Novavax
RBD-Dimer	Recombinant vaccine	Anhui Zhifei Longcom Biopharmaceutical, Institute of Microbiology of the Chinese Academy of Sciences	Phase 3	Various
ZyCoV-D	DNA vaccine (plasmid)	ZyduS Cadila	Phase 2	ZyduS Cadila
CVnCoV	mRNA-based vaccine	CureVac; GlaxoSmithKline	Phase 2b/3	CureVac
INO-4800	DNA vaccine (plasmid)	Inovio Pharmaceuticals	Phase 2/3	Center for Pharmaceutical Research, Kansas City, Mo.; University of Pennsylvania, Philadelphia
VIR-7831	Plant-based adjuvant vaccine	Medicago; GlaxoSmithKline; Dynavax	Phase 2/3	Medicago

Vaccine candidates in development				
Candidate	Mechanism	Sponsor	Trial phase	Institution
hAd5-Covid-19	Adenovirus-based vaccine	ImmunityBio; NantKwest	Phase 2/3	
UB-612	Multitope peptide-based vaccine	COVAXX	Phase 2/3	United Biomedical Inc. (UBI)
Abdala (CIGB 66)	Protein subunit vaccine	Finlay Institute of Vaccines	Phase 2	Finlay Institute of Vaccines
BNT162b1	mRNA-based vaccine	Pfizer, BioNTech	Phase 1/2/3	Multiple study sites in Europe, North America and China
AdCLD-CoV19	Adenovirus-based vaccine	Cellid; LG Chem	Phase 1/2a	Korea University Guro Hospital
Nanocovax	Recombinant vaccine (Spike protein)	Nanogen Biopharmaceutical	Phase 1/2	Military Medical Academy (Vietnam)
EuCorVac-19	nanoparticle vaccine	EuBiologics	Phase 1/2	Eunpyeong St. Mary's Hospital
IIBR-100	Recombinant vesicular stomatitis virus (rVSV) vaccine	Israel Institute for Biological Research	Phase 1/2	Hadassah Medical Center; Sheba Medical Center Hospital
Recombinant (SF9 cell)	Protein subunit	West China Hospital, Sichuan University	Phase 1/2	West China Hospital, Sichuan University
VLA2001	Inactivated vaccine	Valneva; National Institute for Health Research (NIHR)	Phase 1/2	Multiple NIHR testing sites
No name announced	Adjuvanted protein subunit vaccine	CEPI	Phase 1/2	
AG0301-COVID19	DNA vaccine	AnGes, Inc.	Phase 1/2	AnGes, Inc.; Japan Agency for Medical Research and Development
BECOV2B	Protein subunit	Biologicals E limited	Phase 1/2	Biologicals E limited, India
GX-19N	DNA vaccine	Genexine	Phase 1/2	
ARCT-021 (LUNAR-COV19)	Self-replicating RNA vaccine	Arcturus Therapeutics and Duke-NUS Medical School	Phase 1/2	Duke-NUS Medical School, Singapore

Vaccine candidates in development				
Candidate	Mechanism	Sponsor	Trial phase	Institution
No name announced	Protein subunit vaccine	Sanofi; GlaxoSmithKline	Phase 1/2	Various
AV-COVID-19	Dendritic cell vaccine	Aivita Biomedical, Inc.	Phase 1b/2	Rumah Sakit Umum Pusat Dr Kariadi
PTX-COVID19-B	mRNA-based vaccine	Providence Therapeutics; Canadian government	Phase 1	
COVI-VAC	Intranasal vaccine	Codagenix; Serum Institute of India	Phase 1	
AKS-452	Protein subunit	University Medical Center Groningen, Akston Biosciences Corporation	Phase 2	
CORVax12	DNA vaccine (plasmid)	OncoSec; Providence Cancer Institute	Phase 1	Providence Portland Medical Center
MVA-SARS-2-S	Modified vaccinia virus ankara (MVA) vector vaccine candidate	Universitätsklinikum Hamburg-Eppendorf; German Center for Infection Research; Philipps University Marburg Medical Center; Ludwig-Maximilians - University of Munich	Phase 1	University Medical Center Hamburg-Eppendorf
COH04S1	Modified vaccinia virus ankara (MVA) vector vaccine candidate	City of Hope Medical Center; National Cancer Institute	Phase 1	City of Hope Medical Center
CoVac-1	Multi-peptide vaccine candidate	University Hospital Tuebingen	Phase 1	University Hospital Tuebingen
AdimrSC-2f	Protein subunit vaccine	Adimmune	Phase 1	Adimmune
baCTRL-Spike	Monovalent oral vaccine (bifidobacteria)	Symvivo	Phase 1	Symvivo Corporation
COVAX-19	Monovalent recombinant protein vaccine	Vaxine Pty Ltd.	Phase 1	Royal Adelaide Hospital
DeINS1-2019-nCoV-RBD-OPT1	Replicating viral vector	Xiamen University, Beijing Wantai Biological Pharmacy	Phase 1	Jiangsu Provincial Centre For Disease Control and Prevention
GRAd-COV2	Adenovirus-based vaccine	ReiThera; Leukocare; Univercells	Phase 1	Lazzaro Spallanzani National Institute for Infectious Diseases

Vaccine candidates in development				
Candidate	Mechanism	Sponsor	Trial phase	Institution
Sclamp	Protein subunit vaccine	CSL; The University of Queensland	Phase 1	
SCB-2019	Protein subunit vaccine	GlaxoSmithKline, Sanofi, Clover Biopharmaceuticals, Dynavax and Xiamen Innovax; CEPI	Phase 1	Linear Clinical Research (Australia)
VXA-CoV2-1	Recombinant vaccine (adenovirus type 5 vector)	Vaxart	Phase 1	Vaxart
AdCOVID	Intranasal vaccine	Altimune	Phase 1	University of Alabama at Birmingham

BARDA: Biomedical Advanced Research and Development Authority, part of the HHS office of the assistant secretary for preparedness and response, was established to aid in securing our nation from chemical, biological, radiological, and nuclear (CBRN) threats, as well as from pandemic influenza (PI) and emerging infectious diseases (EID); **NIAD:** National Institute of Allergy and Infectious Diseases; **ICMR:** Indian Council of Medical Research; **CEPI:** The Coalition for Epidemic Preparedness Innovations (CEPI) is a foundation that takes donations from public, private, philanthropic, and civil society organizations, to finance independent research projects to develop vaccines against emerging infectious diseases (EID); **OVS:** Operation Warp Speed is a collaboration of several US government departments including Health and Human Services (HHS) and subagencies, Defense, Agriculture, Energy and Veterans Affairs and the private sector. OVS has funded JNJ-78436735 (Janssen), mRNA-1273 (Moderna), and NVX-CoV2373 (Novavax), V590 (Merck/IAVI), V591 (Merck/Themis), AZD1222 (AstraZeneca/University of Oxford), and the candidate developed by Sanofi and GlaxoSmithKline; **COVAX:** The COVAX initiative, part of the World Health Organization's (WHO) Access to COVID-19 Tools (ACT) Accelerator, is being spearheaded by the Coalition for Epidemic Preparedness Innovations (CEPI); Gavi, the Vaccine Alliance; and WHO. The goal is to work with vaccine manufacturers to offer low-cost COVID-19 vaccines to countries. CEPI's candidates from companies Inovio, Moderna, CureVac, Institut Pasteur/Merck/Themis, AstraZeneca/University of Oxford, Novavax, University of Hong Kong, Clover Biopharmaceuticals, and University of Queensland/CSL are part of the COVAX initiative.

Table 2: Current therapeutic trials to target SARS-CoV-2 infection

Study identifier	Drug	Sponsor	Stage	Status
NCT04452435	C21	Vicore Pharma AB	Phase 2	Results not reported
NCT04445272	Tocilizumab (anti-cytokine therapy)	Fundacion SEIMC-GESIDA/ Roche Pharma AG, Dynamic Science S.L	Phase 2	Results not reported
NCT04356937	Tocilizumab	Massachusetts General Hospital/ Genentech	Phase 3	Drug was not found efficacious in preventing death or intubation.

Study identifier	Drug	Sponsor	Stage	Status
NCT04646109	Ivermectin	Afyonkarahisar Health Sciences University/ NeuTec Pharma	Phase 3	
NCT04390022	Ivermectin	Clinica Universidad de Navarra, Universidad de Navarra/Barcelona Institute for Global Health	Phase 2	No efficacy observed upon early administration in low risk patients; significant lowering of viral and IgG load observed.
NCT04343092	Ivermectin (add-on therapy)	University of Baghdad	Phase 1	Better efficacy and safety profile of ivermectin along with hydroxychloroquine and azithromycin
NCT04523831	Ivermectin Plus Doxycycline	Dhaka Medical College	Phase 3	Effective in mild-to-moderate cases within 72 h along with standard supportive care, without the need for hospitalization.
NCT04422561	Ivermectin (prophylaxis)	Zagazig University	Phase 2, Phase 3	Significantly lower incidences of development of disease in healthcare workers when compared with the control arm.
PMID 33592050	Ivermectin (prophylaxis)	AIIMS Bhubaneswar	Epidemiological (case-control study)	Significantly lower incidences of development of disease in healthcare workers with two doses when compared with the control arm. No efficacy seen with a single dose.
NCT04542694	Favipiravir	Promomed, LLC	Phase 3	Negative PCR by day 10 [98 / 100 in the FV group, 79 / 100 in the SoC group] (P=0.00016). SoC: Std. of care
NCT04280705	Remdesivir	National Institute of Allergy and Infectious Diseases (NIAID)	Phase 3	Remdesivir showed lower recovery time (10 days) as compared to placebo (15 days).
NCT04292730	Remdesivir	Gilead Sciences	Phase 3	Moderately ill patients receiving longer treatment (10 days) reported no difference while those receiving treatment for a shorter period (5 days) showed better clinical status distribution.

Study identifier	Drug	Sponsor	Stage	Status
NCT04292899	Remdesivir	Gilead Sciences	Phase 3	Severely ill patients receiving treatment for 5 or 10 days did not show any significant difference.
NCT04329923	Hydroxychloroquine	Ravi Amaravadi, University of Pennsylvania	Phase 2	Study was terminated because no significant difference in disease incidence was observed between hydroxychloroquine and placebo.
NCT04435808	Hydroxychloroquine (prophylaxis)	University of New Mexico	Phase 1, Phase 2	Terminated for futility
NCT04491994	Hydroxychloroquine	UNICEF/ Pak Emirates Military Hospital	Phase 3	No effect on disease progression or virus clearance was observed when combined with standard-of-care.
NCT04491240	MSC-derived exosome	Samara Regional Medical Center Dynasty	Phase 1, Phase 2	
PMID 32380908	MSC-derived exosome	Authors/ Christ Hospital	Non-randomized open-label cohort study	Safety was established, with 83% survival rate and improvement in clinical parameters.
NCT04343261	Convalescent Plasma	Saint Francis Care	Phase 2	Safety was established in critical patients who were administered with convalescent plasma from recovered donors (1:320 anti-SARS-CoV2 IgG titre); likely to be efficacious if administered at an early stage.
NCT04446429	Proxalutamide (anti-androgen)	Applied Biology, Inc.	-	Safety was established, with no serious adverse event compared to 27% in control.
NCT04410159	Gargling	Universiti Sains Islam Malaysia	Phase 2	Gargling with 1% povidone-iodine (Betadine®) and essential oils (Listerine®) was found to be efficacious in management of the early stage of the disease.
NCT04331366	Bidirectional Oxygenation Valve	Emory University	-	

*Only completed studies have been included (Accession date: Feb. 19, 2021)

3. LESSONS LEARNT

3.1. Ebola Virus Disease (EVD) outbreak

Countries need to support their core infrastructure to detect and respond to public health outbreaks. Collaborative research must be carried out in partnership with affected communities and across sectors. By investing in robust health systems, it is possible to have a rational response strategy in place (Moon et al., 2017). The Ebola outbreak in West Africa in 2014-2016 is a case in point. It was observed that many frontline health workers lacked appropriate training in emergency preparedness and response, several of them worked in unsafe environment with subpar equipment. This frail system resulted in more than 800 healthcare workers being infected (Piot et al., 2019). Since then, several initiatives have been taken by WHO to advance national and global awareness. One approach was to implement the Joint External Evaluation (JEE) tool to independently assess national response mechanisms to public health threats, whether natural, accidental or intentional, as per their obligation under the International Health Regulations (2005) (Leigh et al., 2018). By mid-2019, 100 countries had already completed this voluntary external evaluation (<https://www.cdc.gov/globalhealth/healthprotection/ghs/ihr/index.html>; accessed on 24.02.2021). The 73rd World Health Assembly organized by WHO in November, 2020 adopted resolution EB146.R10 to strengthen preparedness for health emergencies and commitment to better prepare for health emergencies such as COVID-19, through “full” compliance with the International Health Regulations (2005) (<https://www.who.int/westernpacific/about/how-we-work/programmes/who-health-emergencies-programme>; accessed on 05.03.2021). Another initiative of WHO has been the Health Emergencies Programme to reinforce operational capabilities and to support countries in their preparedness against public health emergencies. The Coalition for Epidemic Preparedness Innovations (CEPI) was launched at Davos in 2017. This is a global venture with stakeholders from public, private, philanthropic and civil society organisations working together to develop vaccines against infectious diseases and to facilitate availability of such vaccines to the affected population as required. In partnership with Gavi, the Vaccine Alliance and WHO, CEPI is leading a global alliance (COVAX) with the aim of equitable distribution of 2 billion doses of vaccine by December, 2021. The Pandemic Emergency Financing Facility (PEF) set up by the World

Bank aims to fund research to develop preventive strategies for high-severity outbreaks becoming pandemics (<https://www.worldbank.org/en/topic/pandemics/brief/pandemic-emergency-financing-facility>; accessed on 05.03.2021).

Global initiatives need to be supplemented with local/national measures. One of the major hindrances in the development of infrastructure for health management has been sporadic and inadequate funding (Moon et al., 2017). The promises to nurture research and development in health sciences and health management die out as the public health threat passes till the next calamity strikes. The layout of developed countries is higher for both health as well as R&D activities while it is significantly lower in the developing countries. In 2018, Germany spent 11.43% and 3.09% of its GDP on health and R&D respectively while U.S.A. spent 16.89% and 2.84% respectively on the same activities. On the other hand, India spent a meagre 3.54% and 0.65% of its GDP on health and R&D respectively, during this period while China spent 5.35% and 2.19% and Brazil spent 9.51% and 1.26% respectively. Early investment to strengthen and incentivize R&D on infectious agents is a necessity. Despite early studies on EVD in the 1970s, no approved drugs, vaccines or rapid diagnostic tests were available when the outbreak occurred in West Africa (Piot & Spencer, 2018). Another factor is the political stability in the affected country. Although the EBV outbreak in Democratic Republic of the Congo in 2018-2020 saw a synchronized response both nationally and internationally, cases in the eastern part of the country could not be contained because of the uncertain political situation which has seen civilians and healthcare workers being targeted. In February of this year, cases of EVD were reported in Gouécké sub-prefecture of Guinea. The Ministry of Health, along with WHO and GOARN (Global Outbreak Alert and Response Network), has initiated a planned response scheme to contain the outbreak. The effort underlies the need for collaboration between different agencies, equitable access to sophisticated infrastructure and having a standard operating procedure in place for rapid and secure response.

Of concern has been the persistence of Ebola viral particles in patients long after the symptoms had disappeared in survivors. After the declaration of end of EBV transmission by WHO at the end of 2015 in Guinea, the country reported four deaths in

the following 8-16 weeks which were diagnosed as being due to EBV infection (Diallo et al., 2016). Sequencing showed that this virus was the same as the previous one, thus eliminating the possibility of a fresh round of animal-to-human transmission. Epidemiological tracing showed that a survivor of the previous outbreak had transferred it to the current cases via seminal fluid. RT-PCR analysis showed persistence of viral RNA in the semen for 531 days. The virus survived in immunologically protected testes, and its rate of replication and rate of mutation were low (Diallo et al., 2016). Following this, a cohort study was carried out in EBV survivors in Sierra Leone (Deen et al., 2017). Detection of viral RNA was 100% in semen of survivors immediately upon discharge and decreased slowly with time. Even after 13-15 months and 16-18 months after discharge, 11% and 4% survivors, respectively, tested positive for the presence of viral RNA (Deen et al., 2017). These results suggest that long-term monitoring of survivors of viral infections, including COVID-19, needs to be an essential component of their post-discharge care. This will eliminate the possibility of viral survival in immune-protected tissues and organs.

3.2. Genome library

As the COVID-19 pandemic has shown, information about the viral genome is the key to the development of any treatment strategy. Genome libraries need to be set up as online databases which are freely accessible and permit rapid international sharing of viral sequencing data. This will help the international research community to collaborate and understand the disease, and develop therapeutic approaches. At present, there are two major genome data sharing platforms for COVID-19. GISAID hosts more than 4,50,000 viral genomes and the International Nucleotide Sequence Database Collaboration (INSDC) (comprising of the EMBL's European Bioinformatics Institute (EMBL-EBI), the DNA Data Bank of Japan (DDBJ) and the National Library of Medicine's National Center for Biotechnology Information (NCBI)) currently hosts 2,70,000 raw SARS-CoV-2 sequences and 55,000 consensus or assembled genomes. GISAID platform was set up about a decade back to share sequence information about the influenza virus. The same tool was used by China to share initial sequence of SARS-CoV-2. Concerns have been raised by the scientific

community over access and availability of data in GISAID (Hendriksen et al., 2019; Van Noorden, 2021). These need to be addressed fast to accelerate research especially on coronavirus variants. Such genome databases need to be established and/or strengthened for other pathogens as well. For a newly encountered pathogenic virus, these libraries will provide a rational starting point for development of therapeutic strategy, diagnostic tools and vaccines.

3.3. Surveillance

WHO has recognized that lower spread of the most recent EBV outbreak in Guinea has been, in part, due to surveillance and earlier identification of patients and their contacts. Contact tracing has emerged as a useful tool in countries which have successfully controlled the spread of COVID-19. Algorithms have been developed which are capable of scanning and picking up even small outbreaks and potentially not allowing them to turn into epidemics. These networks, e.g. GPHIN (Global Public Health Information Network, a collaborative effort between Health Canada and WHO) and ProMED-mail (International Society of Infectious Diseases), scan all types of news sources for cases of disease outbreaks. ProMED is an open access tool and allows users to contribute data through the 'SUBMIT INFO' tab. Since many of the newly emerging potential pandemics exhibit symptoms common to other less severe diseases, as has been seen with COVID-19, concerns have been raised about the utility of such surveillance tools. Nevertheless, monitoring digital platforms in this age may act as 'word-of-mouth' for spread of information and may serve as a useful auxiliary tool to monitor spread of infection. The case of EBV infection via sexual transmission, described above, points to the need of continued surveillance, especially in affected areas.

3.4. Chain for transfer of information to policymakers: Role of healthcare workers

The need to strengthen battle preparedness of frontline healthcare workers has been evidenced during the current pandemic. This is particularly true for reaching populations in remote and rural areas. There is a need to develop and revise national guidelines, standard operating procedures and continuous training and refresher

modules in line with the latest information and national resources. Good health is the foundation for building a sustainable society. The starting point of this activity is the primary healthcare workforce as they are the primary implementation point for any health mission. In the context of India, millions of Anganwadi and ASHA (Accredited Social Health Activists) workers provide selfless service to uphold the community healthcare framework. They are the primary contact points for the vulnerable population, the women and children. Apart from promotion of healthy practices, they are also responsible for providing information about health and vaccination programmes, nutrition, hygiene and give preliminary support and first aid. Because of their knowledge about the healthcare system and their experience and familiarity with the local population, Anganwadi and ASHA workers can be used to provide much more support to the system than what they currently do. With the right training and adequate monetary compensation, they may emerge as skilled primary healthcare providers. Such workers are indispensable for improvement of healthcare infrastructure. This workforce will obviously be valuable much beyond the current COVID-19 pandemic and need to be recognized as an essential pillar of the public healthcare system in the country.

3.5. Drug repurposing

Any unprecedented pandemic requires rapid response by the research community to develop vaccines and therapeutics. While the development of vaccines may take years, drug repurposing can offer disease mitigation much quicker. Drug repurposing studies present a promising and accelerated strategy to develop therapy because these drugs have known safety profiles (Gupta & Roy, 2021). For example, in case of COVID-19, many research publications reported sets of experimentally validated drugs as potential COVID-19 therapies within a very short period of time. These have been used to develop the COVID-19 Drug and Gene Set Library (<https://amp.pharm.mssm.edu/covid19/>), a collection of drug and gene sets related to COVID-19 research from multiple sources (Kuleshov et al., 2020). Similar databases may be developed for other infectious diseases too. Libraries directed against conserved regions can be immediately tested against any newly emerging strain.

3.6. Traditional medicines

While research continues to develop therapeutic molecules against emerging health threats, traditional medicines, e.g. Ayurveda and Chinese traditional medicine, have also shown important benefits. Most traditional medicines operate under a holistic mode; the emphasis is on curing the patient rather than the disease alone. The Ministry of AYUSH has several schemes to promote Indian traditional medicines. In the context of COVID-19, several plant products have been listed as ‘immune boosters’ and have been of use in treatment. It needs to be emphasized that SARS-CoV-2, like any other pathogen, is more infectious to individuals with low immunity. Hence, immune boosters serve an essential purpose. In many cases, there is no single component which is responsible for efficacy but a fixed combination of components. The wider acceptability of traditional medicines can be ensured by subjecting these combinations to the same rigorous testing as other therapeutic molecules.

3.7. Response of local governments

The response of the southern state of Kerala to COVID-19 has been appreciated far and wide, including WHO. Kerala was able to utilize the lessons learnt during disasters in the past few years to build a robust emergency response protocol. It involved the community and frontline health workers optimally for contact tracing and isolation, gathering and dispersal of information, which allowed benefits to percolate to the ground level. Utilizing the advantages of low-cost telemedicine portals like e-sanjeevani and Arogyakeralam, encouraging campaigns like ‘break the chain’, etc. have been some other approaches. Probably due to its previous experience, Kerala has also seen the benefits of investment in setting up a robust healthcare infrastructure, which has certainly helped the state. Importantly, Kerala has also set up centres to address the psychological vulnerability of patients and survivors, an approach which has now been adopted in many other states. The experience and infrastructure of Kerala in utilizing neighbourhood groups, as in Kudumbashree, a community network to eradicate poverty and empower women, can easily be adapted by other states without high investment (<https://www.who.int/india/news/feature-stories/detail/responding-to-covid-19---learnings-from-kerala>; accessed on 05.03.2021). Investment in health services and R&D mission, however, is necessary.

Some East Asian countries have had an enviable track record in containing the spread of COVID-19. South Korea did not follow strict lockdown protocols. However, the lessons that it learnt during the previous MERS outbreak helped it to manage this epidemic without any visible stringent measures. The citizens cooperated by following social distancing norms and wearing masks as they remembered the consequences of the MERS outbreak in 2015 which infected ~17,000 citizens. Contact tracing was also started early, again a fallout of the MERS lesson. There was cooperation between the government, citizens and the scientific community, with each carrying out its designated function in a professional manner. South Korea has an efficient public health insurance system; the government invested in building a robust health ecosystem so that the adversities of MERS infection were not repeated. In January 2020, when the world was slowly waking up to the reality of COVID-19, South Korea had already started preparation toward large-scale testing for SARS-CoV-2.

Taiwan is another country that showed remarkable foresight in tackling COVID-19. The commonality with South Korea was the investment in a strong healthcare system which was already in place when COVID-19 struck. It was apprehended that proximity of Taiwan to mainland China would result in Taiwan becoming a ‘hotspot’ of COVID-19. Taiwan reported the absence of any positive case in the community by April, 2020 and this was achieved without a lockdown (Summers et al., 2020). There were well-defined nodal points, with Taiwan CDC and Central Epidemic Command Centre in leadership roles. Travel restrictions were imposed on passengers from all high risk countries/regions as early as January, 2020 which was later extended to other travelers. Officials had legal access to travel history of their citizens on national insurance which made identification of potential cases easier. Taiwan utilized big data and informatics not only for tracing and containing the pandemic, it also kept an open communication channel to fight misinformation (Wang et al., 2020). Wearing of masks was made compulsory; contact tracing used manual and digital modes. A comparison between spread of COVID-19 in Taiwan and New Zealand, which followed almost similar measures but with vastly different results, showed that the Taiwanese success is linked to the presence of dedicated national institutions to tackle infectious diseases (Summers et al., 2020). Taiwan also set up a National Health Command Centre (NHCC) after the SARS-CoV-2 outbreak whose primary responsibility is to respond to emerging health threats. The protocols devised after

previous outbreaks by these agencies were such that they could be adapted to any emerging infection. On the other hand, New Zealand had no centralized coordinated response and the containment protocols relied on influenza virus as a model which follows a different course than SARS-CoV-2 (Summers et al., 2020).

The upside of this preplanning was that since citizens were able to carry out their normal daily routine, their livelihood was not affected and the economy of the country remained strong and productive.

Singapore too imposed strict border control measures very early during the outbreak which allowed it to contain imported cases (Chen et al., 2020). Strict legal measures were adopted to ensure compliance with social distancing norms. Cooperation with academia, increase in bed capacity in hospitals, granting tax rebates and extension of insurance coverage to all COVID-19 patients were some other measures followed by Singapore. Almost complete lockdown measures were implemented on April 7, 2020, which has given rise to the term ‘circuit breaker’ (Chen et al., 2020).

4. CONCLUSION

Coordination and preparedness are two key words which emerge from the review above. Regions which were ready with a coordinated plan and had the infrastructure to follow it up were able to avoid the most adverse consequences of the pandemic. Strengthening of the grassroot healthcare workers and bringing them within the domain of the national healthcare system is another key take-home lesson. Clear and transparent statements and risk communication will ensure wider trust of the general public in the system. Investment in R&D and health ecosystem has to take place before the next calamity strikes. Research is a continuous process and makes incremental changes in our knowledgebase in any area. This has been made clear during the current pandemic. Prior and planned investment would have eliminated the need to divert all funds to development of therapeutic strategies, investing it in uplifting the economy. This would also have allowed the economy to remain viable and productive. Stockpiling of broad spectrum antiviral drugs and facilities for mass production of vaccines needs to be in place. This is not an individual but a collective responsibility and requires synergy between science and society. Science and society go hand in hand and one cannot move ahead without the other.

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