Saving a Billion: How India Confronted the COVID-19

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Summary

Protecting a population of 1.35 billion people from a global pandemic is no mean task. Yet, through rigorous contagion mitigation initiatives and proactive disease control measures, India managed to keep the COVID-19 contagion under check with just around .0077 percent of its population being infected at its current spiral. Here's a cursory assessment of how this was done.

The outbreak of the Coronavirus (COVID-19) in the final months of 2019 in China had led to a global pandemic with the disease-causing pathogen, the SARS-CoV-2 (Severe Acute Respiratory Syndrome-Coronavirus-2), spreading virulently to almost all habitable land on Earth within a matter of 2-3 months. Even over six months after its first imprint in Wuhan, the pathogen remains unconquerable with over 4 million being infected and more than three lakh people dead. Most nations have largely responded uniformly by locking down economies and halting all ways of outdoor lives to break the chain of contagion. Yet, most of the heavily-affected countries, particularly the populous ones, have had their own distinct operational experiences and institutional challenges in the dual effort of halting the spread of the virus and effectively curing the infected populace.

Unlike the high-casualty rates in the Western world, known for superlative health-care systems and practices, the developing world, particularly China and India, which together accounts for close to one-third of world population, has had comparatively much lesser infection and mortality rates from the pandemic. While the Chinese experience has been mired in secrecy despite being the source of the outbreak, India's COVID-19 campaign, with its extensive population imprint and transparent disease control measures, provides significant insights for global public health systems and pandemic management strategies.

Protecting 1.35 billion people from an epidemic involves a colossal political and policy challenge. There are some key attributes to the strategies that India adopted in dealing with the spread of CoV-

2, which has ensured that the country's infection rate remains below .0077 percent of its total population, and deaths even a further minuscule percent of that.[1] Even at the current peaking rate of the first wave,[2] the infection spiral is expected to be around one to one and a half lakh, though it could be premature to predict how the subsequent waves, if at all they occur, will turn out to be. How should the Indian Novel Coronavirus experience be evaluated?

First, despite being of third-world standards, India's public health systems responded and functioned robustly to tackle the COVID-19 challenge in contrast to what was seen as world-class health-systems collapsing under the weight of the rapid contagion in western nations. India's public health infrastructure was instantly prepared to provide free and dedicated trauma care and treatment to the affected communities, whereas it was widely reported that the health care system in western nations was not easily accessible and costly.[3] Public health care institutions in many of the western countries had reportedly turned into critical care systems that resulted in large segments of infected patients having to confine to home-isolation and over-the-counter drugs thus aggravating the risk of those with co-morbidities. This was in sharp contrast to the scenario in India where COVID-positive patients were subjected to instant clinical exposure in highly-sanitized public health premises and provided with dedicated treatment and highest possible recovery opportunities.

Second, India managed to inhibit rapid initial virus contagion by early restriction of flights from affected countries (especially in the first wave of global CoV-2 imprint), enforcing access control at border points, initially, and thereafter (by early March) closing borders and terminating all international traffic from and to the country. This was in sharp contrast to the situation in many Western capitals where international air traffic and free movement of people, particularly in transit hubs like London, were happening uninhibited despite virulent spread in the region. By implementing early access control and opportunity denial, India was highly effective in delaying the swift surge of virus transmission in the country though many early infected carriers had already entered the country by the time these measures were initiated.

Third, unlike the rampant community spread that was witnessed in many of the Western hotspots, India was effective in mitigating rapid community spread as a national phenomenon though mild trends of community spread were subsequently evident in various localized hotspots in some parts of India. The Indian epidemic map of the CoV-2 spread is largely about primary to secondary spread in the initial phase and tertiary spread in the later phases which amounted to the expansion of infected clusters but rarely moving towards a community spread that could have entailed a spill-over beyond the clusters.[4] Nonetheless, there were certain pockets in the country – for example, Dharavi in Mumbai, Jehangirpuri in Delhi and Koyembedu Market in Chennai – that were instances of localized community spreads but sealed off through rigorous containment measures, which ensured that the spike seen during the second and third phases of contagion mitigation could be controlled and streamlined towards disease termination or herd immunity.

Having identified these significant divergences from how the rest of the world dealt with the CoV-2, India's response strategies could be described through two key elements:

(a) Contagion Mitigation

Since 30 January 2020, when the first COVID-19 case in the country was identified in Kerala, the country's contagion course has been akin to a roller-coaster ride. With its experience of containing an outbreak of Nipah virus in 2018,[5] Kerala managed to control the spread of the initial CoV-2 cases through immaculate mitigation measures including patient isolation, contact tracing and clinical improvisation, an exercise it pursued on a sustained basis to come up with the most efficient response methods in India.[6] The significant gap between patient zero in January and the sudden spiral through fresh cases in Delhi and Telangana in the first week of March could be attributed to the decision to enforce surveillance at airports with an initial focus only on East Asian hotspots like China and South Korea and later expanded to other affected regions like the Middle East and Europe. While the first case was a direct Wuhan import, the slow but certain surge in the rest of India since early March can be attributed to the cases from the Middle East and Europe who either evaded entry-point monitoring or were asymptomatic.

The decision to follow the Chinese model of lockdown for contagion mitigation was intended to contain infection within the then-existing clusters and deny the scope for a community spread through an extended mutation period of around 21 days, assuming the extent of spread could have been evident and mapped by then. These calculations went awry as spontaneous new clusters formed by undetected external inducers - cases like the Tablighi Jamaat spreading across the country, arrivals from the Middle East causing clusters in Maharashtra, pilgrim- and traveller-driven spirals in Punjab, among others causing primary-to-secondary spiral in the 21-day mutation period. This was followed by swift secondary and tertiary spread leading to the expansion of clusters and creation of new ones (as in West Bengal), and the migrant exodus from cities to states like Bihar and Uttar Pradesh (UP) being later cases.

While the initially infected states like Kerala, Rajasthan, Karnataka and UP had used effective tools of mitigation including rigorous containment of hotspots, contact tracing and clinical exposure to stem the spread, there are later cases like Gujarat, Tamil Nadu, West Bengal and Punjab (besides Maharashtra) where the dynamics of community spread and cluster bulges are beyond easy explanations. Notwithstanding these conditions, the fact that India's infection rate remains around .0077 percent and may not spiral beyond a population imprint of 1-1.50 lakh can be attributed to the success of contagion mitigation strategies covering 1.3 billion people.

(b) Disease Control

COVID-19 being a disease caused by a new pathogen, notwithstanding its other Coronavirus familial links,[7] is yet to be confronted with a potent treatment remedy even as various anti-viral drug-combinations are being tried out as placebo formula and data collated from patient trials. Of the over 25 drugs that were proposed for repurposing for COVID-19 treatment, the ones that found greater acceptance include: Lopinavir/ritonavir, which is a combination medicine for HIV and used earlier also for SARS and MERS, the earlier two coronaviruses;[8] Hydroxychloroquine, a widely used anti-malarial drug, after initial preference as a placebo pivot is now preferred as a precautionary dose for health workers;[9] Mycobacterium W, an anti-leprosy drug; Tocilizumab, an immunomodulator used to treat Arthritis; Favipiravir which was anti-viral treatment for Influenza;[10] and Remdesivir that was developed as a

treatment for respiratory viruses and tested earlier on Ebola, SARS and MERS, but is now being positioned as the most promising prospect for COVID-19 treatment.

Though there were initial unconfirmed reports that Kerala had tried out the lopinavir/ritonavir on its first three COVID-19 patients, both Kerala and Rajasthan were later allowed to try out this combination dose on patients.[11] Following these experiences, the Indian Council of Medical Research (ICMR) had approved extensive usage of this combination even as other anti-virals were subjected to clinical trials.[12] In fact, a governmental task force had found Favipiravir and Tocilizumab as among the most promising drugs for potential use against Covid-19 though results from further clinical trials were awaited.[13] Notwithstanding these findings, it is Remdesivir that has found greater acceptance in many countries and the favourite in the World Health Organisation's (WHO) Solidarity Trials.[14] Originally a drug developed for the treatment of Ebola by US-based Gilead Sciences in 2014, it was used to treat SARS and MERS patients, though without much success.

While authoritative medical journals like *Lancet* has dismissed any significant clinical benefits from Remdesivir to speed up recovery time,[15] the US Food and Drug Administration (FDA) had approved emergency-use authorization based on Gilead's claim of improved recovery time seen during patient trials. India had started clinical trials of four drugs at nine designated hospitals and had received over a thousand doses of Remdesivir from WHO as part of the Solidarity Trials.[16] Accordingly, the Indian Institute of Chemical Technology (IICT) has initiated the key starting materials (KSM) to develop the pharmaceutical ingredient of the drug and conducted technology demonstrations for drug manufacturers to begin commercial production of Remdesivir in India, even if under compulsory patent in the event Gilead refuses to license Indian manufacturers.[17] Health advocacy groups have asked the government to rescind the Gilead patent to ensure the Remdesivir's greater availability, thus indicating its increasing acceptance as the frontline drug against COVID-19.

The other key aspect of India's disease control strategy has been the efforts to set up a dependable testing and surveillance infrastructure. Identifying a COVID-19 infected person or a CoV-2 carrier is a complex and uncertain endeavour if one considers the fact that over 60-65 percent of India's COVID-19 patients have turned out to be asymptomatic.[18] The initial efforts at preemption in the February-March period was centred on heightened monitoring of international arrivals at airports which hinged on one simple benchmark – whether an in-bound traveller showed COVID-19 symptoms. That a thermal scanning of body temperature or assessment of visible conditions was not good enough was amply proven by how CoV-2 managed to enter the country and caused the subsequent contagion.

Accordingly, the actual detection of COVID-19 cases in the country effectively happened only when people who were subjected to compulsory isolation tested positive, which led to a whole series of tracking and hospitalization protocols including contact tracing (states like Kerala used to publish route maps of the positive cases to prompt social reporting from impact zones), quarantine measures and clinical exposure. For a considerable part of the initial contagion period (March-April), testing was confined to quarantine zones and of symptomatic or suspected cases. The grave shortage of RT-PCR (Real-time reverse transcription-polymerase chain reaction) kits and absence

of production facilities in the country seriously curtailed the ability to measure community spread and intensity of anti-bodies presence, besides limiting detection of infections in asymptomatic and immune communities. While the rejection of China-origin RT-PCR kits came as a further setback, the swift breakthrough attained by the National Institute of Virology, which developed an indigenous anti-body test kit, enabled the government to announce a population serosurvey in all 733 districts of the country and scale up to over 1 lakh daily tests nationwide.[19] The enhanced testing ability, in fact, allowed the government to ramp up diagnostic and clinical infrastructure with a realistic picture of the CoV-2 spread.

The way forward

Over three and a half months after the first infection was reported in the country and over 50 days after the country implemented complete lockdown, India's COVID-19 cases are surging towards the one-lakh mark. As in the case of other populous countries, two variables will determine the future course of this campaign: (a) the progress towards vaccine development and availability, and (b) the creation of herd immunity in communities and regions across the country.

While some reports indicate that at least three dozen initiatives are ongoing to develop a sustainable vaccine to subdue the CoV-2, the troubling question is about the actual time needed to develop a credible vaccine and ensure its global reach, and whether commercial and political interests will make the availability of the vaccine(s) a costly affair. Even as the WHO considers 5-7 of the ongoing initiatives as promising,[20] declarations by institutions in Italy and Israel of vaccine and anti-body breakthroughs have not, surprisingly, found much endorsement. This could be because a credible vaccine process could take between 2-5 years to be proven as effective after many rounds of trials on animals and humans.[21]

While the efforts of the global initiatives are to develop a credible vaccine in 12-18 months, it is noteworthy that over 14 projects have been commissioned by various bio-research institutes across India to develop a vaccine in the shortest possible time.[22] Notwithstanding such substantial push by the Indian government to gain an indigenous vaccine breakthrough, India has also partnered with some of the global projects with the Serum Institute joining hands with the Oxford University Vaccine Group.[23]

Even if the vaccine projects may not come in time to resolve the current waves of contagion, there is now greater acceptance of the need for communities to develop herd immunity to halt the further spread of CoV-2. Herd immunity, which presupposes that the healthier members of a community with their strong immune systems will break the contagion chain of the pathogen, is not a phenomenon on which faith can be irrefutably placed.[24] Besides the fact that countries like the United Kingdom and Sweden which attempted herd immunity initially saw massive death spirals, especially among vulnerable age groups, the assumption that immune people could stymie its further spread seems too costly a gamble considering the prevailing belief that healthy carriers of the virus can transmit it on to vulnerable sections while they remain unaffected.[25] Consequently, not many countries were willing to subject their populace to herd immunity experimentations though in cases like Italy and Spain there are indications that communities that have survived the virus onslaught might have developed natural herd-immunity. The clamour to lift

lockdowns, open economies and restore normal life in the US, UK and even India seems to be driven by the belief that beyond a threshold of contagion spike, herd immunity will naturally set in.

Albeit it might be difficult to surmise whether herd immunity is beginning to form in India with its young and healthy population anchoring the shield for the community, a realistic picture could only emerge only when the country returns to normal life, which, in turn, could also aggravate the risk of a second wave when full-fledged transportation movement and economic activity is revived. The challenge will be to augment the public health infrastructure and precautionary protocols in a manner that will enable India to effectively tackle future waves.

Endnotes:

[1] As of May 15, 2020, which happens to be 105 days after the first COVID—19 case was reported in Kerala, and 52 days after a nationwide lockdown was enforced on March 24, 2020, the total cases of infection in the country were 85,761 with 2752 deaths and 53, 219 cases of patients under treatment.

[2] The question of contagion wave had different connotations as governments are yet to conclusively determine between phases of spikes, surges and spreads. In India, for example, it is widely assumed that the first wave that started from early March is peaking at the moment. Public health groups have warned that the second wave might be in coming months, probably followed by subsequent waves. On the other hand, some states that had successfully contained the first bout of infections have seen recurrences that raise the question whether they amounted to new contagion waves. In fact, Wuhan, the original epicenter, is reportedly witnessing a new wave.

[3] For some reports on this aspect, see Dylan Scott, "Coronavirus is exposing all of the weaknesses in the US health system," *Vox*, March 16, 2020, https://www.vox.com/policy-and-politics/2020/3/16/21173766/coronavirus-covid-19-us-cases-health-care-system; Prabhjot Singh, "Why the US Health Care System Failed the Coronavirus Test?" *Foreign Policy*, May 12, 2020, https://foreignpolicy.com/2020/05/12/why-us-health-care-system-fail-coronavirus-test-cant-handle-covid19/; MelissaGodin, "Why is Italy's Coronavirus Outbreak So Bad?" *Time*, March 10, 2020, https://time.com/5799586/italy-coronavirus-outbreak/; Denise Chow and Emmanuelle Saliba," Italy has a world-class health system. The coronavirus has pushed it to the breaking point," NBC News, 19 March 2020, https://www.nbcnews.com/health/health-news/italy-has-world-class-health-system-coronavirus-has-pushed-it-n1162786; Selim Gonen, "Europe's healthcare system fails in the face of coronavirus emergency," *Daily Sabah*, 26 March 2020, https://www.dailysabah.com/world/europe/europes-health-care-system-fails-in-the-face-of-coronavirus-emergency;

[4] Community spread is in itself an ambiguous concept. As per the widely espoused meaning, community spread of the CoV-2 is supposed to have happened when people, who are mostly asymptomatic, and have no history of contact with a COVID-19 patient or have travelled to an affected region, has been infected with the virus. On the other hand, community spread can logically be seen as happened when an existing cluster expands rapidly to swarm a neighbourhood or contiguous areas through secondary and tertiary transmission. At the initial stages of the virus spread in India, there were attempts made to understand extent of community spread by testing existing patients with benchmark conditions similar to COVID symptoms but without a history of contact or foreign travel.

[5] Kairvy Grewal, "How Kerala's experience in tackling Nipah in 2018 will help it contain coronavirus," *The Print*, February 3, 2020, https://theprint.in/theprint-essential/how-keralas-experience-in-tackling-nipah-in-2018-will-help-it-contain-coronavirus/359037/.

[6] Kerala had two subsequent waves of district-wide outbreaks in Kottayam (Italy-origin traveler as source) and Kasargod (Middle-East returnee as source) and numerous, but minor localized spreads including the latest instance of a resurgence caused by infected in-bound travellers. For a recent analysis, see Julia Hollingsworth and Manveena Suri, "The way these Indian states handled coronavirus shows where you live matters," *CNN*, May 13, 2020, https://edition.cnn.com/2020/05/12/asia/india-coronavirus-kerala-flatten-curve-intl-hnk/index.html.

[7] Among the seven versions, the SARS-CoV, MERS-CoV and SARS-CoV-2 are supposed to

cause severe illnesses while the other versions, namely, HKU1, NL63, OC43 and 229E, display milder symptoms. See Kristian G. Andersen, et.al, "The proximal origin of SARS-CoV-2," *Nature Medicine*, No. 26, 17 March 2020, https://www.nature.com/articles/s41591-020-0820-9.

[8] For an analysis, see Jienchi Dorward and Kome Gbinigie, *Lopinavir/ritonavir: A rapid review of effectiveness in COVID-19*, The Centre for Evidence-Based Medicine, University of Oxford, 14 April 2020, https://www.cebm.net/covid-19/lopinavir-ritonavir-a-rapid-review-of-the-evidence-for-effectiveness-in-treating-covid/.

[9] Many sections in the global health community, however, cast aspersions on it as a proven remedy. Nonetheless, the drug is extensively being administered as precautionary dose for health workers in many affected sectors. See Joshua Geleris, et.al, "Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19," *The New England Journal of Medicine*, 7 May 2020, https://www.nejm.org/doi/full/10.1056/NEJMoa2012410.

[10] Favipiravir is a generic version of Fujifilm Toyama Chemical's Avigan and has been approved in Japan for the treatment of novel influenza virus infections. Glenmark Pharmaceuticals was permitted by Indian government to clinical trials on Favipiravir for COVID-19 patients in India, "Glenmark initiates Phase 3 clinical trials on Favipiravir to check efficacy on COVID-19 patients," *Economic Times*, May 12, 2020.

[11] While both attempts had shown encouraging results, the Italian citizen on whom it was tested in Rajasthan had later died, reportedly due to co-morbidities. See "COVID-19: Anti-HIV drugs administered on Italian couple at Jaipur hospital," *Economic Times,* March 11, 2020, https://health.economictimes.indiatimes.com/news/industry/covid-19-anti-hiv-drugs-administered-on-italian-couple-at-jaipur-hospital/74568247; "For the first time in Kerala, doctors try anti-HIV drug on COVID-19 patient," *Manorama Online,* March 19, 2020, https://english.manoramaonline.com/news/kerala/2020/03/19/first-time-in-kerala-doctors-try-anti-hiv-drug-on-covid-19-patient.html

[12] Mohana Basu, "HIV drug combo approved by ICMR for coronavirus treatment fails clinical trials in China," *The Print*, March 24, 2020, https://theprint.in/health/hiv-drug-combo-approved-by-icmr-for-coronavirus-treatment-fails-clinical-trials-in-china/386865/.

[13] Nikhil Ghanekar, "Govt Task Force Ranks Favipiravir, Tocilizumab as Most Promising Drugs Against Covid-19," *News18*, April 27, 2020, https://www.news18.com/news/india/coronavirus-treatment-update-covid-19-cure-medicines-favipiravir-tocilizumab-hydroxchloroquine-2595057.html.

[14] "Solidarity" clinical trial for COVID-19 treatments," WHO, https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments (accessed on May 15, 2020).

[15] The claim about Remdesivir is that it inhibits the enzyme (RdRp) and stops replication of the CoV-2 inside a human cell. The patient trials reportedly demonstrated ability of the drug to cure patients in 11 days compared to 15 days of placebo remedies. See Yeming Wang, et.al, "Redmesivir in adults with severe COVID:19: a randomized, double-blind, placebo-controlled, multicentre trial," *The Lancet*, 29 April 2020.

[16] Divya Rajagopal, "India to test four drugs for Covid-19 as part of the WHO solidarity trial," *The Economic Times*, May 15, 2020, https://economictimes.indiatimes.com/industry/healthcare/biotech/healthcare/india-to-test-four-drugs-for-covid-19-as-part-of-the-who-solidarity-trial/articleshow/75721525.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst.

[17] Joe C. Mathew, "Coronavirus cure: Cipla, Dr Reddy's in race to manufacture Gilead's Remdesivir in India," *Business Today*, May 7, 2020, https://www.businesstoday.in/latest/trends/coronavirus-gilead-to-partner-with-local-firms-for-remdesivir-production-in-india/story/401387.html.

[18] Chetan Chauhan, "Coronavirus outbreak: 50 to 82% Covid cases in India are asymptomatic," *Hindustan Times*, April 19, 2020.

[19] The anti-SARS-CoV-2 human IgG ELISA antibody test kit, also called the COVID Kavach Elisa, is approved for mass production. Sumi Sukanya Dutta, "Zydus to produce India's first antibody testing kit," *Morning Standard*, May 11, 2020. "India increases testing capability to 1 lakh a day," *The Hindu*, May 14, 2020.

[20] Among the top vaccine quests are the ones by Moderna, an initiative supported by the US National Institute of Health; the joint project of the Oxford Vaccine Group and Jenner Institute, which is developing a recombinant adenovirus, christened as ChAdOx1 nCoV-19; the project funded by Bill and Melinda Gates foundation called the COVID-19 Therapeutics Accelerator; and venture of Hong Kong based firm CanSino Biologics, all of which have started initial trials.

[21] While Italian firm Takis announced successful test of a COVID vaccine on mice, the Israeli Institute of Biological Research claimed to have isolated a "monoclonal neutralizing antibody" that attacks the novel coronavirus and neutralizes it in the body of the carrier. "Italian firm claims to have developed vaccine that neutralises coronavirus in human cells," *Indian Express*, May 6, 2020; Shubham Sharma, "Has Israel developed a COVID-19 vaccine? Here's what we know," *Newsbytes*, May 7, 2020, https://www.newsbytesapp.com/timeline/Science/60745/284137/israel-develops-antibody-capable-of-neutralizing-novel-coronavirus.

[22] Chethan Kumar, "Coronavirus: 14 projects in 8 cities lead India's vaccine hunt," *Times of India*, May 16, 2020.

[23] The Oxford Group's vaccine has directly moved to human trails as the safety of ChAdOx1 nCoV-19 was already proven in animal trials when it was earlier tested for MERS. Sudhir Suryawanshi, "COVID-19 vaccine will be kept affordable: Serum Institute of India CEO," *New Indian Express*, May 1, 2020.

[24] Gypsyamber D'Souza and David Dowdy, *What is Herd Immunity and How Can We Achieve It With COVID-19?* Bloomberg School of Public Health (John Hopkins University), April 10, 2020, https://www.jhsph.edu/covid-19/articles/achieving-herd-immunity-with-covid19.html.

[25] R. Prasad, "Aiming to achieve herd immunity naturally is 'dangerous'," warns WHO," *The Hindu*, May 16, 2020.