India's COVID-19 Catastrophe: Cause, Effect & Future Trends

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Abstract

The COVID crisis in India shows no sign of abating. The country of 1.4 billion has passed 30.5 million COVID-19 infections and over 402,000 deaths. Even government figures are likely underestimated due to problems with testing and reporting in the country. Reasonable estimates due to under reporting and lack of testing put these figures at three times higher. The new cases and deaths are predicted to rise by September 2021. The situation is bad in the main cities, but also that it is worse in the poorer and rural areas where lack of healthcare resources has made those populations most vulnerable to the disease. There is an urgent need for rapid tests for quantification of infectiousness to triage patients. In traumatised India, saving lives has become the highest priority to be achieved by vaccinating 70 per cent of the adult population. Over 200 million population have been vaccinated. India's monthly COVID vaccine manufacturing capacity is about 60 - 65 million doses against the final requirement of 1.45 billion doses to cover 70 per cent adults. Even though the second surge is on a decline in most of the states, mucormycosis continues to be a public health concern. There are 41,000 mucormycosis cases reported during the second wave. Daily increase in Delta plus variant cases should alert the Policy-makers. It has a very high transmissibility. Genomic testing & surveillance of mutations to limit fresh twist of pandemic is a necessity. Only a few drugs have emerged as approved COVID-19 treatments. Where are we with drug treatment? Over 30 billion USD have been spent on vaccine development because it has a market. Very little is spent on research on drug discovery. There has not been any significant antibiotic molecule for the last two decades. Politics has played and continues to play a big part in the spread of the virus but it is a situation that needs a global approach. Tiding over a pandemic requires detailed preparation at multiple levels on the part of the State. New ways to prevent, detect, track and treat SARS-CoV-2 infections are crucial keeping in view the rise of more-transmissible viral mutants like Delta plus.

1. Introduction

The coronavirus (COVID-19) is affecting 222 countries and territories. India is suffering the world's worst COVID-19 crisis. The daily infection rate is over 400,000 and the daily death toll, in excess of 4000, is very likely an undercount. The health system has broken down, with scarcities in everything from hospital beds to oxygen.

Some seropositive surveys have been done, indicating that perhaps 20% to 30% of the overall population had been exposed. In large cities such as Mumbai and Delhi, in the areas that were surveyed, it appeared that 50% to 60% had been exposed. Decades of underinvestment in public health, with inadequate diagnostic capacity and programmatic agility, have created challenges in the implementation of test, trace, and treatment strategies at scale [1].

One of the critical errors India made was in vaccine procurement. In January 2021, the government ordered only 11 million doses from Serum Institute of India. Together, Serum Institute and Bharat Biotech can currently produce roughly 90 - 100 million doses in a month. But those firms also have export commitments, especially to the WHO's COVAX program.

How long it will take for the virus to become endemic depends on how much vaccine coverage we can get and how quickly, as well as how long protection lasts, what proportion of the population gets infected, and what kind of mutant viruses develop.

2. A Human Catastrophe

The first red flag ought to have gone up when cases started rising in March 2021. On March 10, nearly 20,000 new cases were reported; on March 24, the number had spiked to 50,000. New daily cases on April 4: 100,000; April 14: 200,000; April 21: 300,000 and May 7: 414,000.

On April 21, India recorded a total of 314,835 new daily cases—the highest single-day tally for any country since the beginning of the pandemic. It overtook the US's single-day January record of 297,430. The rate of progression from 200,000 to 300,000 was far swifter than in the US. There were 2102 deaths on 21 April. Since then, the numbers have continued to swell.

On April 15, India crossed 200,000 new cases daily, doubling to 400,000 cases on April 30, with a total of 32 million active cases.

What Went Wrong?

After a drop in cases last year, there was a sense that India had weathered the worst the virus could give her—that the country had come through and it was

time to open up. That complacency hurt India's people. People let their guard down too soon. India should have gathered better-quality scientific data, which it did not. India's relative success against the first wave of infections also likely led to it not swiftly preparing enough vaccines for its own population.

The government did not anticipate such a harsh second wave and has mishandled the vaccine roll-out, which was sluggish and did not encompass the demographic breadth it should have. The government kept private players out of the vaccination drive, massively curtailing its reach. Only 8% of India's population has received one dose of the vaccine so far, and only 1.3% has been fully vaccinated. In comparison, the US has fully vaccinated 26% of its population, and the UK has inoculated 16% [2]. The government underestimated the number of doses that would be needed if the numbers turned grim and is now scrambling to find the necessary shots. It also failed to strengthen its health infrastructure during the months when the virus appeared to have been tamed.

India needed to administer ten million shots daily, instead of being complacent with three million doses a day. In view of the stocks available and manufacturing capacity, that target seems months away—if it is even possible to achieve at all. Vaccinating a critical mass of the population is the only real solution to this devastating crisis. But in a country as large, diverse and populous as India, that is a challenge of mammoth proportions.

3. A More Deadly Second Wave

On May 6, India saw the highest daily tally of new SARS-CoV-2 infections ever recorded in the world—414,000—taking its pandemic total to 16 million cases, second only to the US, and recording more than 200,000 deaths. "Official statistics in India are often doctored and there was tremendous pressure to report less," Kutty told *The BMJ*, [*BMJ* 2021; 373:n1124] adding that there is a lack of transparency in the figures for infections and mortality too.

With a reported 0.25 million deaths, the official figures in India are likely to be much lower than the actual numbers. "Testing was limited, and so many who weren't tested were admitted to hospitals. When these patients die, their deaths are not recorded as COVID-19 deaths and that death can also occur much later after discharge." [3] A study in *Lancet Global Health* in February indicated that the first wave infected up to 50% of people in urban areas [4].

The second wave seems to be spreading more to rural areas, where people travel far to get to the nearest health centers. In the state of Punjab, health records show that over 80% of patients have severe symptoms once they arrive, due to the delays caused by travel [5].

The spike is thought to be due to the rise of variants (UK, India double-mutant), relaxation of public health standards as though the pandemic were over, large rallies, super-spreader events, and seasonality (the virus is more effective when humidity levels are low). By early or, at the latest, mid-March, it was clear from the data that India was heading towards trouble. The Kumbh Mela Shahi Snans in March and April, when over six million people gathered without masks or so-

cial distancing, may be counted as the largest super-spreader event in the history of this pandemic.

The analysis, based on data collected from Parliament documents and official press releases, reveals as of September 22, last year, India had 247,972 oxygen-supported beds. By January 28 of this year, the number had fallen to 157,344—a decrease of 36.54%. In the same period, the number of ICU beds for COVID-19 patients saw a decrease of 46%, falling from 66,638 on September 22 to just 36,008 on January 28. If we combine the number of oxygen-supported beds and ICU beds, there was a 38% decline in these four months. Furthermore, India had 33,024 ventilators as of September 22. By January 28, the number had fallen to 23,618—a decline of 28% [6].

This was a substantial augmentation of resources under the constraints of a pandemic. However, despite these advances, there were reports about COVID-19 patients struggling to get hospital beds, indicating that India still needed to enhance its infrastructure in case a second wave hit the country. September was also when India reached the peak of the first wave of coronavirus infections. On September 17, the country reported 97,894 cases, the highest point in the first wave. Thereafter, India's COVID-19 cases started decreasing for nearly four and a half months, until mid-February. As of December 29, 2020, India had 270,710 oxygen-supported beds, 40,486 ICU beds and 40,627 ventilators [7].

Despite ample warnings of an impending second wave of COVID-19 from health experts and a parliamentary committee, this strengthened health infrastructure in India was very short-lived. In just one month, the number of beds plummeted as the central and state governments became relaxed and lowered their guards, possibly because daily cases were reducing. After the first wave, the sense of urgency to ramp up health infrastructure in the country declined [8].

The scale of decline in India's health infrastructure after the first wave can be gauged from the fact that although there were 270,710 oxygen-supported beds on December 29, 2020, by January 28 the figure fell to just 157,344—a fall of 42%. The decline in ICU beds and ventilators was 11% and 42%, respectively. On April 9, 2021, the Union Health Ministry in a press statement said the country had substantially ramped up hospital infrastructure for management of COVID-19. It said there were 75,867 ICU beds and 255,168 oxygen-supported beds in the country. Although the figure for ICU beds was higher compared to December 29, 2020, oxygen-supported beds were still lower. The number of ventilators wasn't mentioned.

4. Variants vs Vaccines

More than 142 million people in the US and 33 million people aged 18 and over in the UK have received at least one dose of a COVID-19 vaccine—around 43% and 64% of the eligible population, respectively [9]. In contrast, around 16.94 million people in India had received at least one dose of the vaccine, as of May 9, the Indian health ministry reported. That's just over 8% of India's total popula-

tion. Experts have blamed a slow vaccine rollout and shortage of supply for this poor showing. India would need to administer 10 million doses a day to vaccinate all adults within the next five to six months—and that is assuming enough doses are available [10]. Funds should not be a constraint. At an assumed average price of INR 250 per dose, the cost of administering two doses to every one of the 70 crore adults will require INR 35,000 crore.

The causes of COVID-19 Virus Mutation include uninterrupted transmission due to lack of COVID Appropriate Behaviour, as the Virus transmits, it acquires added fitness, random error during replication, and immune pressure after treatment (convalescent plasma, vaccination, monoclonals).

A mutant is seen in spike protein of Delta Variant K417N in UK, labelled as Delta+ (Delta.AY.1.). It is yet to determine its Ro/mortality factors. It may be resistant to monoclonal antibody cocktail introduced in India Delta variant (B.1617.2) has been in circulation in India

Daily increase in Delta plus variant cases should alert the policy-makers. It has a very high transmissibility. Genomic testing and surveillance of mutations to limit fresh twist of pandemic is crucial.

The "Indian variant" of SARS-CoV-2 (more accurately called B.1.617) is one of the factors responsible for increase in new cases during the second wave in India and has spread to many other countries including the UK. There is growing evidence that it spreads faster than the B.1.1.7 variant from the UK. There are three notable sub-variants of B.1.617. The one of most concern is called B.1.617.2, which was first detected in India in December 220. It remained rare until early March, when it became the dominant variant reported. One more subvariant "B.1.617.1" was also first detected in India in December 2020. By late March half of all reported sequences there were B.1.617.1, but the proportion fell in April. B.1.617.2 has become the most common variant reported in India. Some B.1.617.1 viruses have an additional mutation called V382L in the spike protein. This is what is meant by the term "triple mutant". Most of the coronavirus variants can be detected only by sequencing the genome of the virus. World Health Organization reclassified the highly contagious triple-mutant COVID variant spreading in India as a "variant of concern," indicating that it's become a global health threat. The variant known as B.1.617, has been found in preliminary studies to spread more easily than the original virus and there is some evidence it may be able to evade some of the protections provided by vaccines. Even though there is increased transmissibility demonstrated by some preliminary studies, there is a need for further research about this virus variant in this lineage in all of the sub lineages. More sequencing targeted sequencing to be done. A variant can be labelled as "of concern" if it has been shown to be more contagious, more deadly or more resistant to current vaccines and treatments.

New names have been given to Variants of Concern: B.1.1.7 is now "Alpha", B.1.351 is "Beta", P1 is "Gama" and B.1.617.2 "Delta".

Heterologous vaccination regimens against COVID-19 provide an opportunity to speed up vaccination campaign worldwide, maximising their impact on the control of the pandemic. Measures to control COVID-19 variants include evaluating existing vaccines for efficacy against variants. If current vaccines are inadequate, assess the effectiveness of new vaccines or modified vaccines against variants. Reduce the risk that additional Variant of Concern will emerge. Coordinate worldwide response.

Genomic Analysis and Surveillance is of paramount importance as every 11th day COVID-19 is making change in its Genome. An Indian Variant is expected to be cause of next wave in Europe/USA. Brazil and its variant will be a cause of concern for next few months. Brazilian or South African Variant may cause rise of cases in India. The rise of more-transmissible viral mutants demands new ways to prevent, detect, track and treat SARS-CoV-2 infections.

5. Cause and Effect

Despite this surge, as of now, India's COVID mortality rate is 140 dead per 1 million people. This compares to 401 for the world average, 1762 for the US, and 1869 for the UK. It puts India 119th in the world in this measurement, which is the most important statistic for comparison purposes.

Although India is a vaccine powerhouse that produces vaccines to protect the world, it didn't purchase enough doses to protect itself. Instead, while vaccination rates remained low at home, India exported over 60 million shots to bolster its standing on the world stage. Any Indian leader would have faced challenges. In India, hundreds of millions of poor people live cheek by jowl—easy targets for a highly contagious virus. India has long neglected public health, spending less than USD 100 per capita per year, according to the World Bank—less than many other developing nations [11].

India started its immunization program on January 16, with healthcare workers at the front of the line and a target of reaching 300 million people by July-August. It is using a vaccine developed at home by Bharat Biotech and the Indian Council of Medical Research, as well as another licensed from AstraZeneca. Antibody tests done on more than 700,000 people by diagnostics company Thyrocare Technologies showed that 55% of India's population may have already been infected. The World Health Organization says at least 60% to 70% of the population needs to have immunity to break the chain of transmission. The government has cherry-picked results that suggested a move toward herd immunity. Though several factors are at play and new, more dangerous virus variants may also be involved, many people blame the elections [12].

The B.1.617 variant of COVID-19 was first detected in India in October 2020. The strain involves two variants of the virus. The E484Q mutation has characteristics of a previously detected variant—E484K—which was seen in the fast-spreading Brazilian and South African variants, making it highly transmissible. The L452R mutation, on the other hand, helps the virus evade the body's

immune response. The double-mutation strain was subsequently named B.1.617. The variant spreading in India is more contagious and has some mutations that potentially could make it resistant to antibodies that are generated by vaccines. B.1.617 is now being seen as three variants of interest, B.1.617.1, B.1.617.2 and B.1.617.3, the middle one of which officially became a variant of concern (VOC). This variant seems more transmissible than "wild-type" SARS-CoV-2. There is an urgent need for rapid tests for quantification of infectiousness to triage patients. In traumatised India, saving lives has become the highest priority to be achieved by vaccinating 70 per cent of the adult population. These factors contributed to the massive outbreak of the infection in the second wave. Tweaking of existing vaccines should be done at the earliest opportunity; otherwise, the Pfizer or Moderna vaccines must be allowed in India [13].

6. Health Infrastructure

Health services across states are on the verge of a breakdown. Some streets outside medical facilities have become crowded with the seriously ill, their loved ones trying to arrange stretchers and oxygen supplies for them as they plead with hospital authorities for a place inside. The government announced that military medical infrastructure would be made available to civilians and that retired medical military personnel would be helping out in COVID treatment facilities. But the COVID-19 pandemic is only going to get worse. India will need an extra 500,000 ICU beds, 200,000 nurses and 150,000 doctors in the next few months to respond to the challenge. At present, India has only 75,000 to 90,000 ICU beds and almost all are already occupied, when the second wave of the pandemic has not even reached its peak yet.

For every patient who tests positive, there are 5 to 10 people who are positive but not tested. That means over 2 million people are getting infected every day in India, even now. Statistically, 5% of the positive patients need an ICU bed, irrespective of their age. On average, a patient in ICU spends at least 10 days there. India needs to create at least 0.5 million additional ICU beds now.

Hospitals need doctors, nurses and paramedics in that order. India needs to produce at least 0.2 million nurses and at least 0.15 million doctors in the next few months who are dedicated to managing COVID for the next year. India has about 0.22 million nursing students who have finished their three-year nursing training course who are preparing for their exams. The government can consider these students as graduates and deploy them to work in COVID wards/ICU wards for one year.

There are also 0.13 million young doctors today preparing for NEET examinations to get into post-graduate courses against 35,000 positions. Nearly 100,000 young doctors can be offered jobs to meet the immediate need. India must be prepared for the third wave.

Court Interventions

Courts have been proactive with their timely intervention, advising the gov-

ernment to safeguard the lives of India's people. On May 9, 2021, the Supreme Court of India convened an independent task force of experts on the COVID crisis to study and recommend, on a scientific and rational basis, the allocation of oxygen, medicines, medical resources and vaccines across the country. The government had failed us. During the course of hearing, it was suggested by the Court that an "expert body" involving national experts with experience in health institutions be set up as a National Task Force that will be responsible for providing public health responses based upon a scientific approach to the issues concerning the pandemic situation. It is necessary that an effective and transparent mechanism be set up within the Union Government for the purpose of allocating medical oxygen to all states and UTs for use during the COVID-19 pandemic. The Union Government has agreed to set up a National Task Force to streamline the process. This Task Force would be tasked inter alia with formulating a methodology for the scientific allocation of oxygen to the states and UTs [14].

7. Critical Analysis of the COVID Catastrophe

The spike in cases is partially due to variants of the coronavirus circulating in India at the moment. At least two important dominant variants have emerged: one is a UK variant, and the other is an Indian variant. Last month, the Indian government reported that 80% of cases in Punjab were due to the highly contagious UK variant, which is known as B.1.1.7 [15]. Meanwhile, the Indian variant (known as B.1.617) has multiple sub-lineages with slightly different characteristic mutations. The WHO classified it as a variant of interest in its epidemiological update on the pandemic last week [16].

Since launching its mass inoculation drive in January, India has administered over 160 million vaccine doses as of April 30, according to government data. These include 9,412,140 Health Care Workers (HCWs) who have taken the first dose and 6,241,915 HCWs who have taken the second dose [17]. This implies that a little over 10% of the population has received at least one of the two shots required. But the percentage of people who have completed their vaccination is only about 2% of the total population—around 27.9 million as of April 2021. Starting in May, India is opening vaccinations to anyone age 18 and older. The kind of herd immunity India needs to reduce transmission can only be achieved through vaccination. It will take many months before a critical mass is vaccinated against COVID.

India is presently facing vaccine shortages, and several states have reportedly run out of supply, exacerbating a dire second wave of infections that has left hospitals and morgues overflowing while families scramble for increasingly scarce medicines and oxygen [18]. The supply crunch is expected to last through July, according to Adar Poonawalla, CEO of India's top vaccine maker, Serum Institute, which is producing AstraZeneca's shot [19]. He recently told the *Financial Times* that his firm is set to increase vaccine production capacity from

about 60 - 70 million doses a month to 100 million [20]. Furthermore, New Delhi has recently approved the Russia-developed Sputnik V and authorized foreign-made vaccines that have been granted emergency approval by the US, UK, European Union, Japan and World Health Organization-listed agencies [21].

8. Preparedness for a Third Wave

Given the high levels at which this virus is circulating, India may see a third wave of the coronavirus pandemic. Vaccines will need to be updated to deal with new strains that have accelerated contagion in India, overwhelming hospitals and killing thousands. India must prepare for Phase3, and surveillance is the priority of the hour.

The public health measures that work best are those that the people voluntarily adopt because they see them to be in their own best interests, drastically reducing transmission. A study found that countries where masks were widely used (either because of government orders or cultural norms) had lower per-capita mortality from COVID than countries where there was no universal masking. A smaller study of transmission among family members in Beijing households found that face masks were 79% effective in preventing transmission when they were used by all household members [22].

8.1. A COVID-Adaptive Future

Genomic sequencing must be integrated with routine epidemiologic surveillance. India needs to vaccinate approximately 800 million adults with two doses. At a rate of ten million doses a day, it will take India five to six months to vaccinate the adults. Rapid vaccination is crucial. There is also need for assessing the effectiveness of vaccines against variants. Containment measures and messaging must be intensified, interstate mobility must be restricted, ban large gatherings must be banned. A national mask mandate in public places and transportation must be issued, and the capacity for testing and COVID-care capacity must be scaled up. Public-private partnership is the key. India needs strong data to understand the interplay of vaccines and variants. Post-marketing surveillance studies for safety and real-world effectiveness of multiple vaccines need to be carefully set up for a decentralized health system.

India needs a richer health data infrastructure moving forward. Additionally, a social safety net must be provided to the poor, to the vulnerable, to the daily wage earners; they need incentives to comply with public health guidelines. The virus and variants will remain a part of our lives for the foreseeable future. The value of every human life should be equal across the world. No one in the world will be safe until everyone in the world is safe. Our health is interconnected.

Health infrastructure has collapsed in several cities. State governments are scrambling to build up new infrastructure, making announcements this month about suddenly commencing the construction of new healthcare facilities or oxygen plants. However, this frenetic activity comes in the middle of an ongoing

and exponential rise in cases, whereas it should have come before [23].

8.2. Act Faster, Act Now

Containing biological and social contagions requires credible reassurance to quell panic, and for people to wear masks and obey rules of physical distancing. Government should engage with experts to determine how to uphold restrictions and manage the harsh second and third waves scientifically.

India must make COVID vaccination free and compulsory for all Indians. Start a mass vaccination program and achieve this target at the earliest. Import vaccines to the extent necessary. Next-generation COVID-19 vaccines are supposed to be better. Furthermore, Variant of Interest Genomic analysis is needed (presently at less than 1% in India). Triple mutations of COVID have been detected in some samples. Previously, double mutations were seen. As the virus replicates faster, transmission rates increase and the chances of mutations become high. It should be possible to tweak existing COVID-19 vaccines, should new variants emerge that escape the immunity such vaccines confer.

The "neighborhood concept" can be useful. Create small setups in local areas with home oxygen concentrators under the supervision of a qualified physician through help lines for treating COVID patients. It is nearly 30% of patients presently admitted in hospitals to make beds available for patients with high oxygen demand. India has limited time, as COVID moves faster than its ability. Policy adjustments and innovations (efforts to address social protection gaps and expand support in the immediate instance) are crucial. India's best shot at tackling the outbreak is by stepping up its vaccination efforts. Furthermore, social protection must be strengthened in the long term.

9. The Way Forward

In India, the number of daily infections has risen to a new high of 0.41 million. India is contributing over 40% to the number of daily new infections worldwide. Currently, the most palpable and visceral crisis in the country is a shortage of oxygen, ICU beds, and admission to hospitals. The more the virus spreads, the more chances it has to mutate and create variants that may eventually resist current vaccines, threatening to undermine other countries' progress in containing the pandemic. Although the immediate priority is saving the lives of those already sick, vaccinating all is considered crucial to stop the virus from spreading. An equitable distribution of the vaccine around the world is essential. If the Indian outbreak can't be contained and spreads to neighboring countries with low vaccine supplies and weak health systems, the world risks replicating scenes witnessed in India, especially if newer, potentially more contagious variants are allowed to take hold. Because India has a leading role in making vaccines for other nations, failing to stop the spread of the virus there could endanger the vaccine rollout worldwide. There is a need to make COVID vaccination free and compulsory for all Indians. Start a mass vaccination program and achieve this

target at the earliest. Import vaccines to the extent necessary. The vaccination drive must be sustained over months, and the number of doses administered daily must far exceed the number of daily cases. Only then can India reverse the surge. New ways to prevent, detect, track and treat SARS-CoV-2 infections are crucial keeping in view the rise of more-transmissible viral mutants.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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