

COVID-19 Resurgence in 2025: India's Continuing Public Health Challenge

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Abstract

The year 2025 has witnessed the resurgence of COVID-19, reigniting concerns at both global and national levels regarding the persistent threat posed by SARS-CoV-2. In early 2025, India witnessed a moderate resurgence of COVID-19, characterized by the emergence of Omicron sub-variants and a rise in mild-to-moderate infections. As of mid-June, active COVID-19 cases in India totalled approximately 6,000–7,400, with hotspots in Kerala (~2,100 cases), Delhi (~600), Maharashtra (~500), and several other states. The Indian SARS-CoV-2 Genomics Consortium (INSACOG) has identified key sub-lineages including JN.1, LF.7, NB.1.8.1, and recently XFG. These variants are associated with immune evasion and increased transmissibility, though current data indicate cases remain predominantly mild, with low hospitalization and death rates. India's diagnostic efforts include scaling next-generation RT-PCR, antigen testing, and expanded genomic sequencing. Therapeutic protocols adhere to WHO recommendations, incorporating antivirals, immunomodulators, and oxygen therapy. Most cases are managed on an outpatient basis due to limited severity. India's vaccination campaign, totalling over 2.4 billion doses, has encountered booster gaps. Variants under monitoring have prompted targeted booster drives, especially for high-risk groups. Fresh public health measures, mask advisories, reinforced surveillance, and state-led containment efforts aim to curb further spread. This review provides a detailed assessment of the evolving COVID-19 situation in India, outlining current challenges, national response efforts, and future directions to mitigate the ongoing health crisis.

Keywords: COVID-19 resurgence, COVID-19 India 2025, Omicron sub-lineages 2025, pandemic preparedness India, India's vaccine development, pandemic resilience India

INTRODUCTION

The global COVID-19 pandemic, caused by SARS-CoV-2, has profoundly impacted public health systems, economies, and societies worldwide since its detection in late 2019 [1]. India, being the second most populous country, faced multiple waves of the pandemic, with significant loss of life and strain on its healthcare infrastructure, especially during the Delta and initial Omicron surges [2]. By late 2022 and throughout 2023, India achieved relative stability, aided by extensive vaccination efforts, the development of hybrid immunity through previous infections, and widespread adoption of preventive health measures.

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The decline in cases and severity led to a gradual lifting of restrictions, resumption of economic activities, and a sense of normalcy. However, as seen historically with respiratory viruses, SARS-CoV-2 continues to evolve. In 2025, new sub-lineages of the Omicron variant, including JN.1, LF.7, NB.1.8.1, and XFG, have been detected, triggering localized surges in infections across several Indian states [3]. These variants exhibit increased transmissibility and partial immune evasion but, as of now, largely cause mild disease in most cases. India's socio-demographic characteristics, high population

density, urban crowding, socio-economic disparities, and inconsistent healthcare access create vulnerabilities for recurrent waves of infection. Factors, such as waning immunity, delays in booster dose administration, increased mobility, reopening of schools and public places, and mass religious and cultural gatherings, have collectively contributed to the current resurgence [4].

INSACOG and public health authorities have intensified genomic surveillance to monitor viral evolution. Although severe disease and mortality remain low compared to earlier waves, the persistence of community transmission and the potential for further viral mutations necessitate heightened vigilance [3]. The need to strengthen booster vaccination campaigns, particularly among vulnerable populations, alongside robust testing, early detection, and sustained public health messaging is critical to prevent escalation. This review provides an in-depth, updated overview of India's COVID-19 scenario in 2025, focusing on emerging variants, epidemiology, diagnostic advancements, therapeutic protocols, vaccination challenges, and evolving public health strategies essential to mitigate the ongoing threat (Figure 1).



Figure 1. COVID 19 Re-emergence in 2025.

DRIVERS OF COVID-19 RESURGENCE IN 2025 [5–7]

The resurgence is shaped by a distinct set of scientific, socio-economic, and policy-level factors, beyond simple viral evolution. One of the primary concerns is the underestimation of long-term immunity. While the initial vaccine rollout and widespread infections provided substantial immunity, the durability of this protection against evolving variants remains variable, especially among the elderly, immunocompromised individuals, and those who missed booster doses. Moreover, immunity gaps persist due to vaccine hesitancy, misinformation, and logistical hurdles in reaching remote or marginalized populations.

Another underappreciated driver is pandemic fatigue within both the public and healthcare systems. After years of restrictions, many individuals have relaxed adherence to preventive behaviors, including mask-wearing, hand hygiene, and avoidance of crowded spaces. This behavioral complacency, particularly during major events, such as festivals, and religious congregations, has accelerated transmission in densely populated urban settings. Climate and seasonal trends, such as the winter months, when respiratory infections typically rise, have coincided with the resurgence, further compounding transmission rates.

Economic considerations have also played a subtle yet significant role. The emphasis on reviving livelihoods and restoring pre-pandemic activities has led to increased domestic mobility, crowded marketplaces, and a surge in international travel, often without robust screening or quarantine protocols. Additionally, gaps in India's healthcare infrastructure, particularly in rural areas, have impeded early detection and containment of outbreaks. While major cities benefit from genomic surveillance and rapid diagnostics, smaller towns and villages continue to face shortages of medical resources, healthcare personnel, and reliable testing facilities.

Thus, the drivers of COVID-19's resurgence in 2025 extend beyond viral mutations. They reflect a complex web of immunological realities, socio-behavioral patterns, public health fatigue, and systemic inequities. Tackling these multifaceted contributors requires more than medical interventions; it necessitates sustained public engagement, targeted healthcare investments, adaptive policy measures, and equitable access to prevention and care.

EPIDEMIOLOGY OF THE 2025 COVID-19 RESURGENCE IN INDIA

The epidemiological landscape has been characterized by localized outbreaks, predominantly driven by the spread of new Omicron sub-variants with enhanced transmissibility and partial immune escape. Data from INSACOG and state health departments indicate that as of mid-2025, sporadic surges have occurred in Kerala, Delhi, Maharashtra, West Bengal, and a few northeastern states [6]. Unlike the large national waves seen during the Delta and early Omicron periods, the current resurgence has been geographically heterogeneous, with urban centers and high-density populations experiencing more pronounced spikes. Kerala has reported the highest number of active cases, accounting for nearly one-third of the national total, followed by Delhi and Maharashtra.

A significant proportion of the new cases are classified as mild, with symptoms resembling those of seasonal flu, including fever, sore throat, fatigue, and mild respiratory discomfort. Hospitalization rates have remained low, with fewer severe cases requiring intensive care or ventilatory support compared to earlier waves. Mortality rates have not shown a substantial increase, largely due to existing immunity levels and ongoing vaccination efforts. Nevertheless, seroprevalence studies suggest waning antibody levels among the general population, particularly in individuals who received their last vaccine dose over a year ago or have not been infected recently. This has resulted in increased susceptibility to symptomatic reinfections, particularly among healthcare workers, the elderly, and individuals with comorbidities [3–8]. From a temporal perspective, the resurgence has demonstrated seasonal fluctuations, with cases peaking during colder months when indoor gatherings increase, consistent with trends observed for other respiratory viruses.

DIAGNOSIS AND SURVEILLANCE EFFORTS IN INDIA

Robust diagnostic and surveillance infrastructure has been pivotal to India's pandemic response, particularly during the 2025 resurgence of COVID-19. Building on lessons from previous waves, the Indian government has strengthened multi-layered detection strategies to rapidly identify infections, track viral evolution, and monitor community transmission.

The cornerstone of diagnostic testing remains reverse transcription-polymerase chain reaction (RT-PCR), considered the gold standard for detecting SARS-CoV-2. Over 3,000 government and private laboratories across India, accredited by the Indian Council of Medical Research (ICMR), continue to

offer RT-PCR testing. To improve accessibility and turnaround time, next-generation, high-throughput RT-PCR platforms have been deployed in metropolitan areas and COVID-19 hotspots [5–9]. In parallel, rapid antigen tests (RATs) are widely utilized for symptomatic individuals and travellers. RATs provide results within minutes, allowing swift isolation and contact tracing, although their lower sensitivity compared to RT-PCR makes them more suitable for preliminary screening.

Recognizing the importance of early warning systems, India has significantly expanded wastewater surveillance networks. Sewage-based epidemiology, coordinated by institutions, like INSACOG and CSIR-affiliated laboratories, enables detection of SARS-CoV-2 RNA in community wastewater, providing early signals of rising transmission, even before symptomatic cases emerge. Genomic surveillance remains a key pillar of India's COVID-19 strategy. The Indian SARS-CoV-2 Genomics Consortium (INSACOG), comprising over 50 laboratories, systematically sequences viral genomes from positive cases to identify new variants, track their spread, and assess their public health implications. INSACOG data have been instrumental in detecting emerging sub-lineages [3].

Moreover, digital platforms, like the Aarogya Setu app and CoWIN portal, have been repurposed to support contact tracing, vaccine status monitoring, and dissemination of public health advisories. Recent updates have integrated alerts for high-transmission zones and potential exposure notifications, enhancing community awareness and individual risk mitigation [6]. At the community level, Integrated Disease Surveillance Programme (IDSP) teams collaborate with local health workers to conduct syndromic surveillance, especially in underserved rural and semi-urban areas where formal diagnostic infrastructure may be limited.

India's diagnostic and surveillance efforts in 2025 represent a coordinated, multi-tiered approach combining molecular testing, rapid screening, wastewater monitoring, genomic tracking, and digital tools.

TREATMENT AND THERAPEUTIC STRATEGIES IN THE INDIAN CONTEXT

The treatment framework for COVID-19 in India during the 2025 resurgence is characterized by a shift towards precision healthcare, community-level interventions, and preparedness for future variants. While most cases triggered by the Omicron sub-lineages remain mild, India's evolving therapeutic strategies are designed to address potential escalations and ensure equity in access.

A key focus has been on decentralizing COVID-19 management. Community health centers and primary care units, particularly in semi-urban and rural regions, have been equipped with standardized COVID-19 treatment kits containing essential medicines, pulse oximeters, and rapid antigen test kits. This grassroots approach reduces the burden on tertiary hospitals and ensures early intervention. In addition to symptomatic care, India has expanded its use of evidence-based, adjunct therapies aimed at minimizing disease progression. Vitamin D supplementation, zinc, and immune-boosting nutraceuticals are being encouraged, especially among vulnerable groups, to enhance general respiratory health [6–10].

India's pharmaceutical sector has prioritized the domestic manufacture of essential COVID-19 therapeutics to ensure affordability and accessibility. Generic production of antiviral agents has scaled up, with special emphasis on rural distribution channels and government stockpiles to avoid shortages during case surges. Innovative drug repurposing research is underway within India, exploring the potential of existing medications, like inhaled budesonide, novel anti-inflammatory agents, and combination therapies, to mitigate severe outcomes. Furthermore, India has launched clinical studies investigating traditional medicine systems, such as Ayurveda and Siddha formulations, for their adjunctive role in COVID-19 recovery a culturally significant component of the nation's healthcare landscape. Mental health support and rehabilitation services have been integrated into COVID-19 treatment frameworks, recognizing the psychological toll of prolonged illness, isolation, and post-COVID conditions. Mobile health units and helpline services provide counseling, particularly in regions with limited mental health infrastructure [11, 12].

India's preparedness also includes the strategic stockpiling of medical oxygen, portable concentrators, and critical care equipment. The "Oxygen for All" initiative continues to enhance oxygen generation capacity in district hospitals to ensure readiness for severe case spikes. Importantly, public awareness campaigns addressing the dangers of self-medication, antibiotic misuse, and misinformation about unproven therapies are ongoing. These efforts are vital to counteract the spread of myths and promote adherence to scientifically validated treatment protocols.

PIPELINE MEDICATIONS AND FUTURE THERAPEUTICS RELEVANT TO INDIA [13]

India has emerged as both a significant contributor to global COVID-19 research and a beneficiary of international drug development efforts. In response to the ongoing threat of new SARS-CoV-2 variants, several promising medications and future therapeutics are in various stages of research, clinical trials, or regulatory evaluation, with a focus on scalability, affordability, and relevance to India's healthcare landscape.

One of the most anticipated candidates is Ensitrelvir (marketed as Xocova in Japan), an oral 3CL protease inhibitor developed by Shionogi. This antiviral has shown promise in reducing viral load and symptom duration in mild-to-moderate COVID-19 cases, with ongoing Phase 3 trials assessing its efficacy against Omicron sub-lineages [14]. Indian pharmaceutical companies are in discussions for technology transfer and potential domestic manufacturing, which could enhance treatment accessibility. Another notable advancement is the development of broadly neutralizing monoclonal antibodies, designed to target conserved regions of the spike protein less susceptible to mutation. International candidates, such as SAB-185, a polyclonal antibody therapy, and variant-adapted monoclonals are being explored, with Indian research institutes, like ICMR and DBT, that are collaborating on indigenous biologics with similar mechanisms.

Repurposed drugs continue to be investigated, including host-directed therapies, like Baricitinib and newer anti-inflammatory agents, aimed at preventing cytokine storms and severe respiratory complications. Several Indian trials are assessing the role of combination therapies involving antivirals, immunomodulators, and supportive care to improve outcomes, particularly in high-risk groups. India's scientific community is also contributing to the next generation of COVID-19 vaccines, many of which have therapeutic potential. Bharat Biotech and Serum Institute are developing variant-specific booster formulations, while mRNA and intranasal vaccine platforms are being optimized for both prophylactic and post-exposure settings [15, 16].

In addition, AI-driven drug discovery platforms are being leveraged by Indian biotech startups to identify new small molecules and peptide-based therapeutics targeting viral replication mechanisms beyond the spike protein, addressing concerns of ongoing viral evolution. Traditional medicine research remains active, with controlled studies investigating specific Ayurvedic formulations, polyherbal extracts, and immunomodulatory compounds for their potential to complement conventional treatments, though rigorous scientific validation is ongoing.

VACCINATION AND IMMUNIZATION CHALLENGES IN INDIA

India's vaccination drive against COVID-19, which began in January 2021, is among the largest immunization efforts globally, with over 2.4 billion doses administered by 2024 [6]. However, as of 2025, the nation faces significant challenges in sustaining immunity levels, closing booster dose gaps, and addressing emerging variant concerns.

The initial phase of India's COVID-19 vaccination campaign, primarily utilizing Covishield (AstraZeneca's ChAdOx1), Covaxin (Bharat Biotech's inactivated vaccine), and later, Corbevax and intranasal iNCOVACC, contributed to broad immunization coverage. By late 2023, most of the adult population had received at least two doses, and many high-risk individuals had been administered precautionary booster doses. Despite these achievements, the resurgence in 2025 highlights concerning

gaps. First, waning immunity, particularly among those vaccinated over a year ago without boosters, has led to increased susceptibility to symptomatic infections. Current variant-specific boosters, especially for Omicron sub-lineages, have been slow to roll out at scale.

One key hurdle is vaccine hesitancy, notably in rural regions, socio-economically disadvantaged communities, and among specific demographics, such as pregnant women and younger adults. Misinformation regarding vaccine side effects, distrust in government health programs, and logistical barriers continue to undermine efforts [15]. India's complex geography and population density further strain equitable vaccine distribution. While urban centers, like Delhi, Mumbai, and Bengaluru, maintain relatively high vaccination rates, several remote and underserved districts in the northeastern states, tribal regions, and parts of Uttar Pradesh, Jharkhand, and Chhattisgarh lag significantly.

A major scientific challenge is the evolving nature of SARS-CoV-2. The current Omicron sub-lineages, though less severe, partially evade immune protection conferred by earlier vaccines. India's vaccine manufacturers, including Serum Institute of India and Bharat Biotech, are actively developing updated booster formulations targeting these variants, but regulatory approvals and production scale-up take time [16, 17]. India has also explored intranasal vaccine platforms, intended to provide mucosal immunity, reduce transmission, and complement injectable vaccines. However, uptake has been limited, and large-scale efficacy data specific to newer variants remains under evaluation. Cold chain infrastructure, though improved, faces strain during mass vaccination campaigns, particularly in rural and high-temperature zones. Additionally, real-time monitoring of vaccine coverage and breakthrough infections requires better integration of digital health platforms, like CoWIN, with on-ground health worker reports.

While India's COVID-19 vaccination program has made commendable progress, persistent challenges, waning immunity, booster rollout delays, regional disparities, hesitancy, and variant-driven uncertainties pose ongoing obstacles. Strengthening public health communication, expanding targeted booster coverage, enhancing last-mile delivery, and accelerating variant-adapted vaccine availability are imperative to mitigate future outbreaks and bolster national health security.

PUBLIC HEALTH INTERVENTIONS AND NATIONAL RESPONSE

India's approach to the 2025 COVID-19 resurgence has been marked by rapid, state-led responses coordinated at the national level. In early May–June, the Union Health Ministry convened high-level review meetings, involving the DGHS, ICMR, NCDC, IDSP, and INSACOG, to assess preparedness and reinforce hospital readiness focusing on oxygen supply, isolation capacity, ventilators, ICU beds, and essential medicines. Through the Integrated Disease Surveillance Programme (IDSP) and ICMR's sentinel network, states are implementing weekly monitoring of ILI and SARI presentations [4, 6]. Any rise in SARI cases prompts immediate RT-PCR testing and genomic sequencing to detect new variants. Several states have reinstated mask mandates, particularly for vulnerable cohorts. Kerala, for example, mandated mask-wearing in hospitals, high-risk zones, and among elderly and comorbid individuals. Karnataka similarly required masks for older adults after detecting JN.1 sub-lineage circulation. Local authorities have reintroduced preventive restrictions, including limiting large indoor gatherings to 50% capacity, implementing hybrid schooling systems, and enhancing domestic travel screening at airports and railway stations.

States are also renewing hospital readiness: Kerala mandated mock drills and revised facility safety protocols in all public and private healthcare facilities [18]. Rajasthan directed district-level hospital preparedness reviews including oxygen and ICU readiness. Punjab's Health Minister emphasized zero tolerance for negligence, inspecting hospital wards, reassuring the public, and urging continued masking even with low case numbers.

The national advisory urges citizens to:

- Avoid crowded spaces when symptomatic.
- Adhere to hygiene protocols (mask-wearing, handwashing).
- Stay updated on vaccinations.
- Seek testing if suffering ILI/SARI symptoms.

India has mobilized multi-tiered public health interventions from enhanced surveillance and diagnostic capacity to mask mandates, hospital preparedness, and public advisories demonstrating a coordinated and effective resurgence response grounded in recent government directives and data.

STRENGTHENING INDIA'S HEALTH SECURITY AND PANDEMIC PREPAREDNESS

The resurgence of COVID-19 in 2025 has reinforced the urgency of bolstering India's health security framework and pandemic preparedness. While India has made significant strides in healthcare infrastructure, vaccination programs, and genomic surveillance, emerging infectious diseases continue to pose complex challenges that demand systemic reforms, investment, and coordinated action. A cornerstone of strengthening India's pandemic resilience is the sustained enhancement of the Integrated Disease Surveillance Programme (IDSP). Expansion of real-time disease tracking, digitized health reporting systems, and integration with national and state-level health databases are essential to detect outbreaks early and facilitate rapid response [19]. Laboratory and diagnostic capacity remain critical. The Indian Council of Medical Research (ICMR) has emphasized scaling up genomic sequencing capabilities under INSACOG, ensuring decentralized access to advanced testing, and building laboratory networks in underserved regions. This approach enables the timely identification of new variants, monitoring of antimicrobial resistance trends, and improved understanding of disease dynamics.

India's public health response requires strengthening healthcare workforce preparedness. Continuous training, recruitment, and retention of frontline health workers, including epidemiologists, lab technicians and community health volunteers, are pivotal. Pandemic-specific simulation exercises and capacity-building programs can ensure readiness during future health emergencies. The pandemic underscored vulnerabilities in critical care infrastructure, particularly oxygen supply chains, ICU capacity, and rural healthcare accessibility. The government has initiated investments in oxygen generation plants, mobile health units, and telemedicine platforms to address gaps, but further scale-up and equitable distribution remains priorities.

Vaccine security and innovation are central to preparedness. India's robust domestic vaccine manufacturing ecosystem offers a strategic advantage, but ongoing support for research, public-private partnerships, and accelerated regulatory pathways for variant-specific vaccines are vital to maintaining immunization momentum [20]. Strengthening India's pandemic preparedness also requires adopting a One Health approach, recognizing the interconnectedness of human, animal, and environmental health. Surveillance of zoonotic diseases, antimicrobial resistance monitoring, and cross-sector collaboration between health, agriculture, and environmental agencies are crucial to mitigating future spillover events. Moreover, public health education, combating misinformation, and fostering community engagement are essential to build trust, promote vaccine acceptance, and ensure adherence to preventive behaviors.

India's global leadership in health diplomacy, including contributions to the COVAX initiative and collaborations with the WHO and other international bodies, positions the country to play a key role in shaping equitable, resilient, and coordinated global pandemic response frameworks.

CONCLUSION AND FUTURE PROSPECTS FOR INDIA

The COVID-19 resurgence in 2025 has reaffirmed that infectious disease threats are dynamic, evolving, and require continuous adaptation in both policy and practice. India's response to the current wave has demonstrated significant progress in healthcare delivery, diagnostics, and research; yet the resurgence has also revealed persisting vulnerabilities that must be proactively addressed. Looking

ahead, India's capacity to mitigate future waves of COVID-19 and other emerging infections will depend on its ability to sustain long-term public health vigilance while avoiding complacency. Finally, India's leadership in vaccine development, generic medicine manufacturing, and global health diplomacy positions the country to safeguard not only its population but also contribute meaningfully to global pandemic control efforts. By embracing innovation, fostering trust, and strengthening systems, India can transform the challenges of 2025 into opportunities for building a robust, equitable, and health-secure future.

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