REVIEW ARTICLE





Infection and mortality trend of COVID-19 over the years in India and measures taken to curb the epidemic: a comprehensive review

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ABSTRACT

Background and Aims: The trend of COVID-19 infections in India has been dynamic as well as complex, with several peaks and troughs since the pandemic began, including the rise of advanced and more contagious variants of the virus, increased public complacency towards health guidelines, and the challenges posed by vaccine hesitancy and misinformation. The current article comprehends the patterns of COVID-19 infection in India, with highlights of infection patterns and mortality in several states.

Methods: With the use of keywords, we looked through the National Library of Medicine, Google Scholar, and PubMed electronic databases. We have all the specific information from the case reports and clinical series of the patients from the various COVID-19 pandemic waves in India. In order to assess the national impact of these epidemic waves, we then carefully review the case reports.

KEYWORDS

COVID-19, India, pandemic, comorbidities, virus, variants

Introduction

The SARS-CoV-2 virus is the causative agent for the highly contagious respiratory sickness known as coronavirus disease (COVID-19). From its first discovery in Wuhan, China in December 2019, it has spread globally, impacting millions of individuals in several nations, and causing significant disruptions to daily life (MacIntyre,

2020). The illness spreads mostly by respiratory droplets released when an infected person talks, coughs, or sneezes. It can also spread when a person touches a surface that has been contaminated with the virus and then touches their face. Several patients of COVID-19 tested positive for Covid but were not displaying any specific symptoms or were asymptomatic many others have shown minor symptoms in the early stages of infection like fever, exhaustion, dry cough, and loss of taste or smell (MacIntyre, 2020). Severe infections of could cause



pneumonia, acute respiratory distress syndrome (ARDS), and even mortality, especially in elderly people and people with underlying comorbidities.

The COVID-19 pandemic made its way to India in late January 2020, with the state of Kerala reporting the first verified cases (Andrews et al., 2020). The government quickly established steps to stop the pandemic's spread as it expanded throughout the nation, including lockdowns, travel restrictions, and the widespread usage of masks. Despite these measures, India has experienced a large and sustained increase in COVID-19 cases, leading to significant strain on the country's healthcare system and widespread disruptions of daily life. India has been one of the countries hardest hit by the pandemic, with high numbers of reported cases and deaths. The country has also faced significant challenges in its response to the pandemic, including a shortage of medical supplies, a strained healthcare system, and widespread misinformation about the virus and vaccines (Assefa et al., 2022).

However, India has also been at the forefront of the global response to COVID-19, with the country playing a major role in the production and distribution of COVID-19 vaccines, including the world's massive vaccine producer, the Serum Institute of India. In addition, India has implemented a large-scale vaccination campaign and has provided vaccines to many countries around the world to restrict the spread of infection (Purohit et al., 2022).

The initial epidemic wave of the pandemic in India began in early 2020 and continued into early 2021, with daily case numbers reaching their highest levels in September and October of that year reporting 90,000 cases per day(World Health Organization (WHO), n.d.). After a period of decline, a second epidemic wave of infections began in 2021 and was even more severe than the first, with daily case numbers reaching all-time highs in May 2021 and a third wave of infections was observed from January to March of the year 2022 showing a returning surge in the number of cases

around 37,000 each day (World Health Organization (WHO), n.d.). Since then, the number of daily cases has declined, but the situation remains fluid. The trends in COVID-19 cases in India are influenced by a variety of factors, including the spread of new and more contagious variants of the virus, the availability and effectiveness of vaccines, and the effectiveness of government measures to contain the pandemic. The mortality rate in India however remained subpar with the highest of 12% in Jharkhand ("COVID19 STATEWISE STATUS," 2023).

Patients infected by COVID-19 developed severe symptoms with pre-existing conditions. Diabetes mellitus and hypertension prevalence were observed to be the highest in COVID-19 patients during the initial and following epidemic wave followed by ischemic heart disease and respiratory disorders. Along with these chronic heart diseases, malignancy, hypothyroidism, asthma, tuberculosis, and mucormycosis were also observed in a significant total of patients (Siddiqi et al., 2022).

Epidemic Waves of COVID-19 infection in India

The epidemic wave of the COVID-19 pandemic in India started in late January 2020 and continued through the early months of the year, with the first confirmed cases reported in the state of Kerala. In the early stages of the pandemic, reported cases in India were relatively low however, as the virus spread more widely, the number of cases increased rapidly, and by September 2020, India had reported over 90,000 cases per day(World Health Organization (WHO), n.d.). During the first epidemic wave, the government implemented multiple measures to try to slow the spread of the virus, including lockdowns, travel restrictions, widespread use of masks, and increased testing. Despite these efforts, the number of cases continued to rise, reaching a peak of nearly 100,000 cases per day in October 2020 (World Health Organization (WHO), n.d.). The infection pattern of COVID-19 in India's key states is shown in Figure 1. Except for



Jharkhand, which reports 12% mortality, all states exhibit rates of between 1% and 2%.

This large and sustained increase in COVID-19 cases lead to significant strain on the country's healthcare system. The first wave was characterized by a shortage of medical supplies, such as oxygen and hospital beds, and a lack of preparedness for a large-scale pandemic. The Indian government and private sector made efforts to increase the production and distribution of medical supplies and to expand hospital capacity, but the scale of the outbreak overwhelmed the country's healthcare system. In addition, India faced challenges in controlling the spread of the virus, including widespread misinformation about the virus and vaccines, and a lack of public trust in the government's response to the pandemic. Despite these challenges, the Indian government and private sector continued to work to slow the spread of the virus and provide care to those affected.

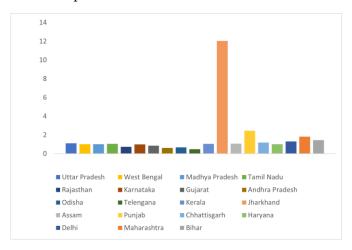


Figure 1. Graph depicting the percentage mortality by COVID-19 in major states of India until 15 Feb. 2023 ("COVID-19 STATEWISE STATUS," 2023).

After the first wave, there was a period of decline in the number of cases, with daily case numbers falling to below 20,000 in early 2021. However, a second epidemic wave of infections began on March 13, 2021, peaked on April 23, and was even more severe than the first, with daily case numbers reaching all-time highs of over 400,000 in May 2021 (World Health Organization (WHO), n.d.). This wave was driven by several factors, including the spread of new and more contagious variants of the virus,

increased social mixing as restrictions were lifted, and a low level of public compliance with health guidelines. In addition, the country experienced several large gatherings, such as religious festivals and political rallies, which likely contributed to the spread of the virus.

In response to the second wave of the pandemic, the Indian government once again implemented measures such as lockdowns and travel restrictions and has ramped up its COVID-19 vaccination campaign. The most severely affected states included Maharashtra, Kerala, Karnataka, Andhra Pradesh, Tamil Nadu, Andhra Pradesh. Delhi, Uttar Pradesh, and West Bengal. By the end of June 2021, the increase in instances during the second wave had begun to stabilize. Figure 2 represents the total cases detected versus deaths in the first and second waves of COVID-19 in India. During the first wave, beginning in March 2020 and peak observed in September 2020, the country reported a total of 10, 654,533 confirmed cases and 153,339 deaths, according to data from the Ministry of Health and Family Welfare (Government of India, 2020). Nonetheless, it is important to keep in mind that the official statistics could not accurately depict the actual scope of the outbreak because certain incidents and fatalities might go unreported or be missed. Also, during the first wave, there were considerable doubts about the veracity of the data, particularly in regard to the infrastructure for testing and reporting in various regions of the nation. During the second wave of COVID-19 in India, which began in February 2021, the country witnessed a sharp increase in the number of cases and deaths. As of September 2021, the total number of confirmed cases during the second wave in India was over 33 million, with a total of over 440,000 deaths (World Health Organization (WHO), n.d.)

India reported 7,000–9,000 new COVID-19 cases every day in November 2021 (World Health Organization (WHO), n.d.). Later, in the final week of November 2021, Omicron (B.1.1.529)—the fifth variant of concern (VOC) of SARS-CoV2—began to emerge. The third wave of COVID-19 infection began in January 2022. As the number of cases



increased dramatically, India reported over 317,000 new COVID-19 cases on January 19, 2022 (World Health Organization (WHO), n.d.). The Test Positive Rate (TPR), described as the percentage of all the coronavirus tests performed in a day that turned out to be positive was found to be increasing across almost all of India's states. The third wave of infection came to an end in late July 2022, with more than 80% of the adult population vaccinated people developing immunity to COVID-19 and the transmission of the variant and mortality was decreased ("Active COVID-19 Cases in India Decline," 2022).

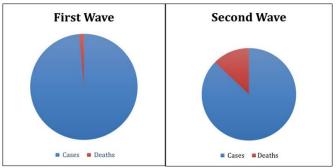


Figure 2. Comparison of the impact of different epidemic waves (World Health Organization (WHO), n.d.) ("COVID-19 STATEWISE STATUS," 2023) (Government of India, 2020).

During the COVID-19 pandemic, several variants of the virus were prevalent in India infecting large amounts of the population and leading to an epidemic wave. Some of the most significant variants declared as variants of concern by the World Health Organisation (WHO) that have been active in India include:

Alpha variant (B.1.1.7): This variant was unearthed in the United Kingdom in late 2020 and quickly became the globally dominant variant until the Delta variant emerged. Alpha was 50-75% more transmissible than previously circulating strains. According to some studies, the Alpha variant is related to more severe illnesses (Duong, 2021).

Delta variant (B.1.617.2): This lineage was discovered in India in December 2020 and was the most common variant worldwide until the Omicron variant emerged. The Delta variant was more transmissible than the Alpha variant and was linked to a higher risk of severe disease and hospitalization

(Duong, 2021). Several studies suggest that the vaccine's effectiveness against symptomatic Delta infection is slightly reduced but remains high against severe illness and hospitalization.

Beta (B.1.351 lineage): In late 2020, this variant, also known as 20H/501Y.V2, was discovered and predominated in South Africa. Despite being discovered in other countries, including the United States, it never became a globally dominant variant (Duong, 2021). The primary concern with the Beta variant was immune evasion: convalescent and post-vaccination plasma did not neutralize viral constructs containing the Beta spike protein as well as those containing the wild-type spike protein.

Gamma (P.1 lineage): In December 2020, this variant, also known as 20J/501Y.V3, was first discovered in Japan and was prevalent in Brazil. It was later discovered in other nations, including the United States, but it did not become the most common variant worldwide. The variant's multiple mutations raised concerns regarding increased transmissibility and immune effect(Duong, 2021) ("Gamma (P.1)," 2021).

Omicron (B.1.1.529) and its sub-lineages: The Omicron variant was originally described in November 2021 from Botswana and very soon after from South Africa. It was swiftly discovered in many other nations where it was also linked to substantial rises in reported illnesses. It was linked to an upsurge in local infections in South Africa. The previous dominant sub-lineage was overtaken by Omicron sub-lineages with increasingly superior replication advantages. The first Omicron variant, sub-lineage BA.1, was followed by sub-lineage BA.2, which was later replaced by BA.4 and BA.5. Further Omicron sub-lineages, such as BQ.1, BQ.11, BF.7, BA.2.75, XBB, XBB.1, and XBB.1.5, which descended from several formerly circulating sub-lineages, have been becoming more prevalent globally (Zaman et al., 2022). Table 1 summarizes various variants isolated from Indian populations and their severity of symptoms.



Table 1. Summary of various variants isolated from Indian populations and their severity of symptoms.

SARS-CoV- 2 Variant	First reported		S	C
	Country	Time	Symptoms	Severity
Alpha variant (B.1.1.7)	United Kingdom	November 2020	ChillsLoss of appetiteHeadachesMuscle aches	Studies have suggested the B.1.1.7 lineage had infected people in the hospital and was deadlier than the original virus.
Delta variant (B.1.617.2)	India	December 2020	HeadachesSore throatRunning noseFever	Delta caused more severe disease than other variants in people who were not vaccinated. Early studies from Scotland and Canada, both cited by the CDC, suggested Delta was more likely to result in hospitalization in the unvaccinated.
Beta (B.1.351 lineage)	South Africa	July 2020 or August 2020	 Fever Chills Fatigue Cough Body aches Shortness of breath 	There was evidence to suggest that Beta may have been more likely than other variants to lead to hospitalization and death.
Gamma (P.1 lineage)	Japan	December 2020	Body achesFeverRunny noseOther aches	There is so far no strong evidence for an enhanced lethality due to this variant but more studies are required to verify this. The P1 variant is as much as 2.5 times more contagious than the original coronavirus.
Omicron (B.1.1.529)	South Africa	24 November 2021	 Body aches Asymptomatic infection Cough Fatigue Fever, Headache, Loss of smell or taste, — less common Nasal congestion or running nose Night sweats, — unique Omicron symptom, Skin rash 	Scientists are still working to learn more about whether the current Omicron strains cause more severe diseases than their predecessors. Data has suggested that the original Omicron strain was less severe, in general, than previous variants, according to the CDC

COVID-19 and comorbidities

During the period of the pandemic, several other diseases and complications affected people who were reported to be COVID-19 positive. By going through several statistical studies conducted in association with national hospitals in different cities and states we have collected data on different types of comorbidities that were prevalent during

different epidemic waves of COVID-19. Along with single comorbidity, there have been diseases which are caused by comorbidities along with COVID-19 leading to severe complications in those patients

(Siddiqi et al., 2022), (Lin et al., 2021). Several comorbidities were noted in COVID-19 patients during the first pandemic wave in India, with hypertension emerging as one of the most prevalent comorbidities among COVID-19 patients in India



followed by diabetes mellitus (Kumar et al., 2021). Furthermore, there were several case reports of rhino-orbital mucormycosis in patients with coronavirus disease 2019 (COVID-19), mostly from India (A. K. Singh et al., 2021). Research conducted in 2021 found that a total of 101 instances of mucormycosis in patients with COVID-19 had been documented worldwide, with 82 cases coming from India alone and 19 from the rest of the world (A. K. Singh et al., 2021). People with active COVID-19 infection and those who had recovered from it tended to have mucormycosis. Around 80% of patients had pre-existing diabetes mellitus, and 14.9% had concurrent diabetic ketoacidosis (DKA). In most cases, the main cause of COVID-19 was discovered to be corticosteroid use for therapy. The most common kind of mucormycosis infected the nose and sinuses (88.9%) followed by rhino-orbital cerebral mucormycosis (56.7%)(Kumar et al., 2021).

Individuals who already had chronic lung, renal, or cardiovascular disease were shown to be at risk for serious illness and mortality. Cancer patients who were infected by COVID-19 were also extremely at risk since their immune systems were frequently damaged by chemotherapy and other cancer therapies (Siddiqi et al., 2022).

The second epidemic wave of COVID-19 in India, which occurred in 2021 also presented itself with several comorbidities among COVID-19 patients. A study that was published in the Journal of the Association of Physicians of India found that approximately 30% of COVID-19 patients in India had diabetes and approximately 24% of patients had hypertension. Additionally, approximately 11% of patients had cardiovascular diseases, and 4% of patients had chronic kidney disease (Siddiqi et al., 2022), (Kute et al., 2022). Depression, anxiety as well as stress-related complications were very high during the pandemic, which mostly goes unnoticed but they are as serious comorbidities as any other physical condition (Sundarakumar et al., 2022).

It is crucial to remember that these comorbidities were recorded in COVID-19 patients

all over the world, not just in the second wave of cases in India. Yet, it is possible that the severity of the second wave in India was influenced by the high incidence of these comorbidities in the Indian population along with these severe comorbidities, there were other common presenting complications in symptomatic patients like joint pain, fatigue, shortness of breath, dry cough, chills, etc.

Major vaccines circulated in India

India has authorized several COVID-19 vaccines for use, the most prominently used vaccinations include Covishield, Covaxin, and Sputnik V.(Indian Council of Medical Research (ICMR), 2022)

- 1. Covishield is the Indian name for the Oxford-AstraZeneca vaccine, which is being manufactured by the Serum Institute of India, Pune It is a viral vector vaccine, which means it uses a weakened version of a different virus to deliver instructions to the body's cells to create an immune response against COVID-19. Covishield has been authorized for emergency use by the Indian government and has been widely used in the country's vaccination drive.
- 2. Covaxin is an inactivated virus vaccine developed by the Indian biotech company Bharat Biotech, Hyderabad in collaboration with the Indian Council of Medical Research, Delhi. It involves inactivating the SARS-CoV-2 virus so that it cannot cause disease, but can still stimulate an immune response in the body. Covaxin has also been authorized for emergency use in India.
- 3. **Sputnik V** is a vector vaccine developed by Russia's Gamaleya National Research Institute of Epidemiology and Microbiology. It uses two different adenoviruses as vectors to deliver the instructions for creating an immune response against COVID-19. Sputnik V has been authorized for emergency use in India.

Although the precise effectiveness rates of these vaccinations may vary, it has been demonstrated that



all of them are beneficial in avoiding COVID-19-related severe illness and hospitalization. In order to distribute these vaccinations to as many people as possible, the Indian government has launched a significant immunization drive, giving priority to high-risk populations including the elderly, frontline workers, and healthcare professionals.

Conclusion

The worldwide coronavirus disease 2019 (COVID-19) pandemic, which includes the COVID-19 pandemic in India, is caused by the severe acute respiratory syndrome coronavirus 2. (SARS-CoV-2). India has the second-highest number of confirmed COVID-19 infections in the world, behind only the United States, with 44,685,499 registered cases as of February 15, 2023, and the third-highest number of COVID-19-related fatalities, behind only Brazil and the United States ("COVID-19 Pandemic Death Rates by Country," n.d.).

On March 11, 2020, COVID-19 was declared a pandemic by WHO after it expanded to more than 114 countries, had 118,326 active cases, and resulted in 4292 fatalities (World Health Organization (WHO), n.d.)(Mander, 2022). The patterns of COVID-19 transmission in India are concluded by the present review study. India's experience with the first wave of the COVID-19 pandemic was major and difficult, but it also produced valuable lessons and enhanced the nation's readiness for subsequent pandemics. As time went by the virus evolved and mutated into different variants which caused new epidemics waves that were more serious than the previous (Duong, 2021). With the surge in daily reported cases and death numbers, the grim state of the COVID-19 pandemic made people take health-related issues and government-ordered policies for prevention and precaution more seriously. During the third COVID-19 epidemic wave, a surge in SARS-CoV-2 cases was caused by the VOC Omicron (B.1.1.529). Omicron BA.2 and BA.2.38 have mostly been found in India, according to the Indian SARS-CoV-2 Genomics Consortium (INSACOG's)

announcement on July 11, 2022, and the BA.2.75 subvariant has more mutations in SARS-CoV2's spike protein and other genes (Department of Biotechnology, 2022). COVID-19 also presented severe complications as the patients started to develop comorbidities and life-threatening illnesses. Every new epidemic wave has shown a high number of comorbidities and which were asymptomatic at early diagnosis (Siddiqi et al., 2022). COVID-19 has also impacted the developing countries' economies with a huge hit in several ways and one of the most prominent was due to serious comorbidities present among patients (A. K. Singh & Misra, 2020).

To slow down the spread of COVID-19, the Indian government declared a nationwide lockdown in March 2020. The government started a vigorous contact tracing program to find people who might have come into exposure to COVID-19-positive patients. The Indian government developed several COVID-19 treatment facilities around the nation, including hospitals and quarantine specifically for the disease and started administering vaccines free of cost to make them accessible to everyone (Purohit et al., 2022). India was one of the key players world's largest vaccination campaigns. Over 1.5 billion vaccine dosages have been operated in India following October 2022 (K. Singh et al., 2022).

According to the most recent update of March 2023, a total of 349 samples of COVID-19's XBB.1.16 variant, which might have been behind the recent rise of coronavirus cases in India, have been detected, according to INSACOG data (Department of Biotechnology, 2023). Although the strain has a higher reproductive number, the death rates are found to be minuscule. It is expected that with the countries better and improved healthcare facilities and readily available medical supplies, there won't be a dramatic instance of Covid emergency as witnessed in the past. This review highlights the key facts about COVID-19 disease in India to date and points out the major steps carried out by the Indian government to keep the pandemic under control.



Author Contributions

Prerona Boruah conceptualized the review work, and Priyadarshini Gupta and Riya Singh searched the literature and wrote the draft. Mala Parab and Pramodkumar P. Gupta helped with graphs and reviewed the overall article. Pranita Thakur and Mary David helped with revision of the draft. All authors admit mutually to submit for publication.

Data Availability Statement

All authors take responsibility for the integrity of the work. They confirm that this paper will not be published elsewhere in the same form, in English, or any other language, including electronically.

Conflict of Interest

We hereby declare that we have no conflict of interest.

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