



COVID-19 in Republic of India: A Report on Situation and Precautionary Strategies to Global Pandemic

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ABSTRACT

The novel coronavirus (also known by SARS-CoV2, 2019-nCoV) is a new virus responsible for an outbreak of respiratory illness known as COVID-19, which has spread very quickly to more than 206 countries around the world. The CoVs belongs to subfamily Coronavirinae of Coronaviridae family comprising genera: α , β , γ , and δ . The study is based on recently available published research, review articles world-wide along and notification of national and International agencies about the global pandemic COVID-19. The mining of data and its statistical analysis was based on the modern reliable tools to work out the global and domestic scenario. In India, the first three cases identified were in Kerala on 30th January, 2020. Since then the India has more than 3537 COVID-19 positive cases with 83 deaths, and 274 completely recovered cases by April 05, 2020. Currently, the novel coronavirus disease has spread to alarming situation in various countries and Indian government also announced official lockdown for 21 days till 14th April, 2020). Based on WHO report, a total of 1,245,207 confirmed cases of coronavirus have been identified including a total of 67,910 deaths to COVID-19 outbreak and recovered 256,503 cases by 5th April, 2020. The potential of worldwide or cross boundary international spread of COVID-19 via commercial air travel had been assessed. In a nationwide address Hon'ble Prime Minister people to practice social distancing and self quarantine along with cleanliness and hygiene. This review be able to offer meaningful information for future and may facilitate agencies decision making on strategies to handle this global pandemic public health emergency at the community, national, and international level.

Key words: Novel coronavirus 2019-nCoV, COVID-19, Global Pandemic, Social distancing, Self Quarantine, Epidemic, Epicenter.

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INTRODUCTION

In history, mankind has witnessed plentiful pandemics where some were more catastrophic to humans than the others. We are once again experiencing a very difficult time battling an unseen enemy, the novel COVID-19 Coronavirus that was observed firstly in China's Wuhan city. The novel COVID-19 Coronavirus (also known by SARS-CoV-2, 2019-nCoV) is a new virus responsible for an outbreak of respiratory illness known as COVID-19, which has spread very quickly to several countries around the world. The outbreak of SARS-CoV-2 infection emerged in December 2019 in Wuhan, Hubei Province, China. So, the Chinese city of Wuhan is found to be the origin of the life threatening viral outbreak of novel Coronavirus (2019-nCoV) i.e. COVID-19 [1]. Coronaviruses (CoV) are non-segmented positive sense RNA viruses of the Coronaviridae family and the Nidovirales order that are widely distributed among humans and other mammals [1]. The family Coronaviridae is comprised of four genera: α , β , γ , and δ [2]. These viruses are common in animals worldwide, but very few cases have been known to affect humans. There are seven types of human coronaviruses: 229E (α -CoV), NL63 (α -CoV), OC43 (β -CoV), HKU1 (β -CoV), MERS-CoV (β -CoV), SARS-CoV (β -CoV), and SARS-CoV-2 (β -CoV). MERS-CoV, SARS-CoV, and SARS-CoV-2 can infect humans and cause severe pneumonia in many fatal cases [3]. All CoVs are pleomorphic RNA viruses which contain crown-shape peplomers (glycoprotein spike on a viral capsid or viral envelope) with size of 80-160nm [4]. While most human coronavirus infections are mild, the epidemics of the two betacoronaviruses, severe acute respiratory syndrome coronavirus (SARS-CoV) [5,6] and Middle East

respiratory syndrome coronavirus (MERS-CoV) have caused more than 10,000 combined cases over the past two decades, with mortality rates of 10% for SARS-CoV and 37% for MERS-CoV [1,7]. The SARS-CoV reservoir is uncertain, but bats and subsequent spread to Himalayan palm civets are hypothesized [8]. MERS-CoV is also of zoonotic origin in the Middle East, and is transmitted by camels [9]. SARS-CoV-2, with potential origin of bat, has appeared on the Huanan Seafood Market, where livestock are also traded, in China's Wuhan State of Hubei Province, and has been the subject of global attention because of an unexplained cause of pneumonia epidemic [4]. The World Health Organization (WHO) used the term 2019 novel coronavirus to refer to a coronavirus that affected the lower respiratory tract of patients with pneumonia in Wuhan, China [10,11,12]. Although several proteins lead to the virus development cycle and the invasion of the host, the spike protein is the most important factor in deciding the host range. The spike protein present on the virus surface plays important roles in cell receptor binding and membrane fusion [3,13,14]. Research is underway to better understand the transmissibility, severity and other characteristics associated with COVID-19. It seems that most early cases have some kind of history of interaction with the original seafood market [15]. But, Vietnam registered first case of 2019-nCoV on 24 January 2020 with no travel history from China, although its family member was the traveler from China. So it is considered as the first incidence of human to human transmission of corona virus. It also proves that this virus spread quickly human to human by transmission through close direct contact, aerosol and droplets generated by coughing and sneezing. Corona virus infected person has many common symptoms such as fever, cough, myalgia, tiredness, pneumonia and complicated dyspnea, whereas less common reported symptoms include headache, diarrhea, hemoptysis, runny nose, and phlegm-producing cough (Fig.1) [1]. Patients with minor symptoms have been reported to recover after one week while serious and severe cases have experienced progressive respiratory failure due to alveolar damage from the virus, which can lead to death [15]. To control this pandemic, prevention measures that may prevent or slow down the transmission of the COVID-19 have been implemented. These include case isolation, identification and follow-up of contacts, environmental disinfection, and use of personal protective equipments [16].

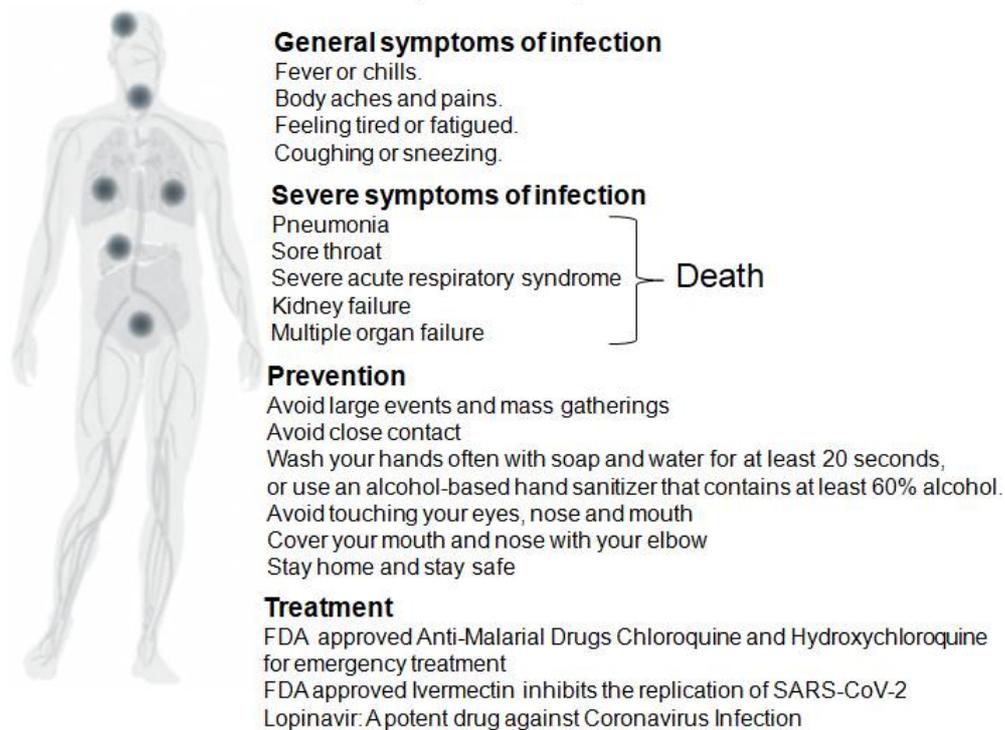


Fig. 1: COVID-19: General symptoms, prevention and treatment measure.

At present, it is not clear to what extent the COVID-19 epidemic would establish itself in India. According to a stochastic, dynamic model of the global air transport network, India ranks 17th among the countries at the highest risk of COVID-19 importation by air travel [17]. In India, the first three cases identified were in Kerala from 30th January to 3rd February, 2K20. These three patients had come back from Wuhan, China. Nearly a month later, on March 03, the country's next two cases were reported; one patient in

Delhi who had a history of traveling to Italy and the second in Hyderabad who had traveled from Dubai. Later on the same day, another case was identified from Jaipur as positive for COVID-19. To combat this situation, Ministry of Health and Family Welfare (MoHFW) of India had initially advised to refrain from travelling to China and quarantine of those coming from China. Although India imposed travel restrictions fairly early on the spread of COVID-19, and many states quickly moved to shut down public places, the country's high population density, overburdened public health infrastructure and high prevalence of non-communicable diseases (NCDs) all stack the odds against successful containment. Nevertheless, at this point in time, the absence of effective drugs to prevent/treat an attack is a significant concern. Currently, there is no specific antiviral drug for the treatment of CoV-associated pathologies. So, the 2019-novel coronavirus (nCoV) has been a big cause of 21st century catastrophe. As per WHO, 634,835 confirmed cases and 29,957 deaths have been reported in the 180 countries of the World up to March 29, 2020.

EVOLUTION AND CLASSIFICATION OF CORONAVIRUS

Coronaviruses (CoVs) are the largest group of viruses belonging to the *Nidovirales* order, which includes *Coronaviridae*, *Arteriviridae*, and *Roniviridae* families [18]. CoVs belongs to subfamily *Coronavirinae* of *Coronaviridae* family. The subfamily *Coronavirinae* are further subdivided into four groups or genera, the Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus [18,19]. The alpha- and betacoronaviruses infect mammals, gammacoronaviruses infect avian species, and deltacoronaviruses infect both mammalian and avian species [20]. The alphacoronavirus and betacoronavirus are pathogenic to humans [21,22]. In the 21st century, two highly pathogenic human coronaviruses namely, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) emerged from animal reservoirs to cause global epidemics with alarming morbidity and mortality. In late December 2019, a new human pathogenic coronavirus (2019-nCoV) was recognized in China [21]. This new betacoronavirus was responsible for the outbreak of respiratory disease in Wuhan, China and has caused serious illness and death.

Coronaviruses are capable of adapting to new environments through mutation and recombination with relative ease and hence are programmed to alter host range and tissue tropism efficiently [20,23,24,25]. Large genetic diversity as well as the frequent recombination of genomes, and increasing activity at the human animal interface, the coronaviruses represent an ongoing threat to human health [22,26]. Coronaviruses are important pathogens for human and vertebrates also. They can infect respiratory, gastrointestinal, hepatic, and central nervous system of human, livestock, birds, bat, mouse, and many other wild animals [19,27,28,29].

STRUCTURE AND MORPHOLOGY OF CORONAVIRUS

Coronaviruses (CoVs) are the largest group of viruses that belongs to the order *Nidovirales*. All viruses in the order *Nidovirales* are enveloped, non-segmented, positive-sense RNA viruses. The subfamily *Coronavirinae* having the largest identified RNA genomes, contain approximately 30kb genomes [18]. In general, coronaviruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses, typically in range of 27 to 32 kb [20]. The genome of CoVs is a single-stranded positive-sense RNA with 5'-cap structure and 3'-poly-A tail [19]. At least four main structural proteins are coded by coronaviruses. These are spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins. Besides these four main structural proteins, different CoVs encode special structural and accessory proteins [19]. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N). The capsid is further surrounded by an envelope. Three structural proteins associated with the viral envelope include, the membrane protein (M), the envelope protein (E) and spike protein (S). The spike protein (S) mediates virus entry into host cells [20]. Some coronaviruses also encode an envelope-associated hemagglutinin-esterase protein (HE). Among the structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns [20].

OUTBREAK OF NOVEL CORONAVIRUS IN WUHAN DURING LATE 2019

In late December 2019 and early 2020, a novel human infecting coronavirus (nCoV) was identified to be the causative agent of a large and rapidly spreading outbreak of respiratory disease, including pneumonia, in Wuhan, China [19,30]. The new coronavirus was provisionally named as 2019-novel coronavirus (2019-nCoV). The new coronavirus disease was named as COVID-19 on 11 February, 2020 by WHO [31]. The viral genome of the new coronavirus has been sequenced and characterized. The 2019-nCoV is sufficiently divergent from SARS-CoV to be considered a new human-infecting betacoronavirus

[32]. The 2019-nCoV has spread to other countries and causing threat to human life of a large portion of population world-wide. The novel coronavirus (2019-nCoV) has reached to other countries through human carriers. WHO confirmed the first case of novel coronavirus outside of China in Thailand on 13th January 2020 and declared a Public Health Emergency of International Concern on 30th January 2020 [31,33].

CARRIER, SPREADING AND PATHOGENESIS OF 2019-nCoV

The new zoonotic human coronavirus (CoV) emerged in December 2019, with a cluster of patients having connections to a seafood market in Wuhan, China [34,35]. Soon after the first outbreak, secondary cases were reported [35]. Human-to-human transmission accelerated the spread of the outbreak. The coronavirus infection reached to other states of China and to other countries with the human carriers. Generally, the human-to-human transmission occurs with close contact [35]. The transmission primarily occurs when an infected person sneezes and through the respiratory droplets produced in a manner similar to spread of influenza and other similar respiratory diseases (Fig. 1). Extensive research throughout the world is in progress regarding the spread, transmission and origin of disease.

The important step in virus infection is the interaction of human cells with spike protein (S). The spike is also a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses [20]. Earlier, the structure, function, and evolution of coronavirus spike proteins were reviewed by Li [20]. According to author, the coronavirus spike contains three segments (i) a large ectodomain, (ii) a single-pass trans-membrane anchor, and (iii) a short intracellular tail. The ectodomain consists of a receptor-binding subunit S1 and a membrane-fusion subunit S2. During entry of virus, the S1 binds to a receptor present on the host cell surface for viral attachment, and S2 fuses the host and viral membranes. This process allows entry of viral genomes to host cells. Receptor binding and membrane fusion are the initial and critical steps in the coronavirus infection cycle. The CoVs changes genome by recombination, gene exchange, gene insertion, or deletion. The coronaviruses are capable of adapting quickly to new hosts through the processes of genetic recombination and mutation *in vivo* [22].

COVID-19 AS GLOBAL PANDEMIC

The first known case of the novel coronavirus was traced back to December 2019 in Wuhan, Hubei, China [36,37]. Within the next month, the number of coronavirus cases in Hubei gradually increased to a couple of hundred, before rapidly increasing in January 2020. These were mostly linked to the Huanan Seafood Wholesale Market, which also sold live animals; thus the virus is thought to have a zoonotic origin [38]. By mid-January 2020, the virus spread to other Chinese provinces, because of Chinese New Year migration and celebration, infections quickly spread throughout the country [39,40]. As the mode of transmission of the virus was unclear, it advised "against the application of any travel or trade restrictions on China". Based on Chinese National Health Commission; WHO stated that there was no infection among healthcare workers, and no clear evidence of human to human transmission by mid January [41]. On 24th February, Director WHO Tedros Adhanom warned that the virus could become a global pandemic because of the increasing number of cases outside China [41]. As on 30th January 2020, the WHO declared the outbreak to be a Public Health Emergency of International Concern [42]. Recently on 11th March 2020, the WHO officially declared the coronavirus outbreak to be a pandemic, following a period of sustained community-level transmission in multiple regions of the world [33,43]. The WHO requested countries to take immediate actions and scale up response to treat, detect and reduce transmission to save people's lives [44,45].

Currently, the novel coronavirus disease has spread to alarming situation in various countries. Indian government also announced official lockdown for 21 days (including some days of both March and April, 2020). There were 206 countries/ province, areas or territories suffering from COVID-19 cases [12,30]. According to WHO (WHO, 2020), up to mid 5th April 2020; a total of 1,245,207 confirmed COVID-19 cases with 67,910 confirmed deaths and 256,503 completely recovered cases were estimated world-wide (Fig. 2, Table 1). The number of coronavirus infected cases and deaths are still increasingly continuously.

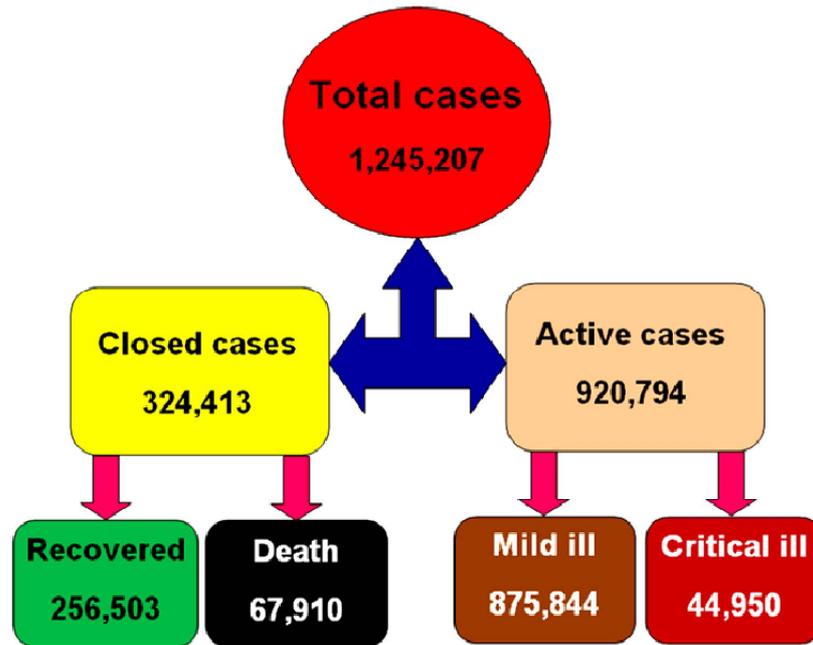


Fig. 2: Cladogram showing global scenario of pandemic COVID-19 by 5th April, 2020. Source: WHO.

Table 1. A glimpse of global pandemic coronavirus (COVID-19) up to 5th April, 2020.

Location	Total Cases	Total Deaths	Total Recovered	Location	Total Cases	Total Deaths	Total Recovered
World	1245207	67910	256503	Oceania	9796	36	2372
Europe	639940	48355	120147	Africa	9,311	427	889
North America	347117	9790	20030	South America	24106	841	2215
Asia	219648	8541	110766	India	3537	83	274

Source: <https://www.worldometers.info/coronavirus>.

Why COVID-19 is pandemic?

A pandemic (from Greek world pan "all" and demos "people") is a disease that has spread across a large region, for instance multiple continents, or worldwide. Pandemics can also occur in important agricultural organisms (livestock, crop plants, fish, tree species) or in other organisms. A widespread endemic disease with a stable number of infected people is not a pandemic. A disease or condition is not a pandemic merely because it is widespread or kills many people; it must also be infectious. For instance, cancer is responsible for many deaths but is not considered a pandemic because the disease is neither infectious nor contagious [46]. Throughout history, there have been a number of pandemics of diseases such as smallpox and tuberculosis. One of the most devastating pandemics was the Black Death (also known as The Plague), which killed an estimated 75–200 million people in the 14th century. Other notable pandemics include the 1918 influenza pandemic (Spanish flu) and the 2009 flu pandemic (H1N1). The ongoing pandemic (began as an epidemic in China in late 2019) of the novel coronavirus-2019 disease (COVID-19) was declared by WHO on 11th March 2020. The WHO designed and developed a note on phases of pandemic in 1999 and revised in 2005 that is applicable to the entire world and provide a global framework to preparedness and response planning against pandemic. The WHO has retained the use of a six-phased approach for easy incorporation of new recommendations and approaches. The first 3 phases correlate with preparedness, including capacity development and response planning activities, while the last 3 phases clearly signal the need for response and mitigation efforts [46].

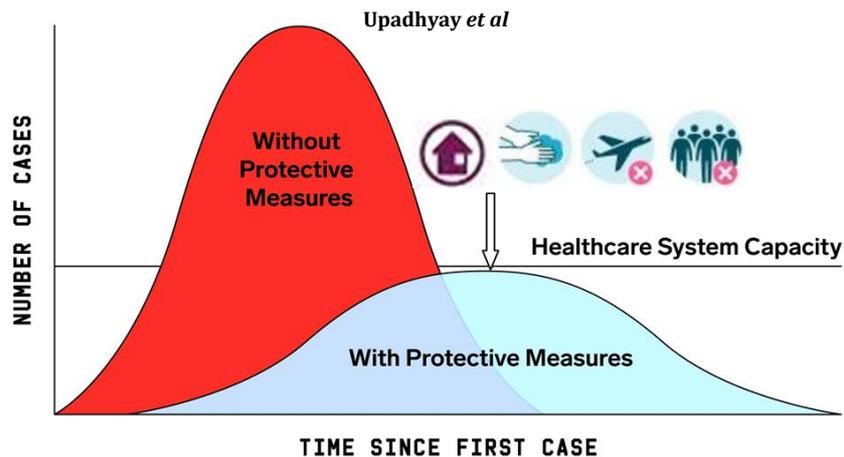


Fig. 3: The graph showing positive effect of protective measures in flattening number of COVID-19 cases.

WHO guidelines as preventive measures to COVID-19

The WHO and CDC suggested subsequent safety measures (such as: self quarantine, social distancing, cleanliness and hygiene) to avoid COVID-19 spreads as no any vaccine on hand to put off infection with newer novel coronavirus [47,48] and its effect on the rate of spreading have been assessed (Fig. 3). These suggested recommended steps to protect you and curtail mass spreading of COVID-19 are as given below:

- Keep away from large events and mass gatherings.
- Stay away from close contact (maintain a gap of 6 feet) with anyone or symptomatic.
- Remain distant yourself and others if COVID-19 spreading in community, particularly if having a top risk of serious illness.
- Wash your hands over and over again with soap and water for at least 20 seconds, or exercise an alcohol-based hand sanitizer
- Face your mouth and nose with elbow or tissue paper during sneezing and coughing and let it thrown into closed dustbin.
- Shun touching your eyes, nose and mouth from unclean hand.
- Spurn allotment dishes, glasses, bedding and other household items if symptomatic
- Clean and disinfect surfaces habitually touch on daily basis.
- Stay home, stay safe, work from home, avoid school and public areas if ailing, unless going to doctor.
- Keep away from public transportation if unwell.
- Offer mask and hand gloves.
- Avoiding eating raw or undercooked animal organs and contact to live animals may have touched by coronavirus carrier.
- People have a chronic medical condition check with doctor to protect by hand.
- If necessary the Government may impose legal or constitutional quarantines, travel bans and locked down on an unprecedented scale.

COVID-19 in India: Situation and precautionary strategies

Looking at the fondness in India, the earliest novel coronavirus case was reported in late January, 2020 from the South Indian state and patient having the travel history to Wuhan (China), the epicenter of Pandemic. Thereafter, up to first week of March, 2020 only 3 confirmed cases were identified from same state. All the 3 patents were taken in medical isolation ward and ultimately completely cured without any fatality [49]. During the first week of March, again the eruption of COVID-9 cases was notice, since then, the number of positive cases increasing continuously. In between the last week of March, the number of cases rose extraordinary and reached over 1500. The cumulative growth in the cases of COVID-19 is still going in India and more than 3537 cases were identified, over 83 deaths, and 274 completely recovered cases by mid 5th April, 2020 (Fig. 4).

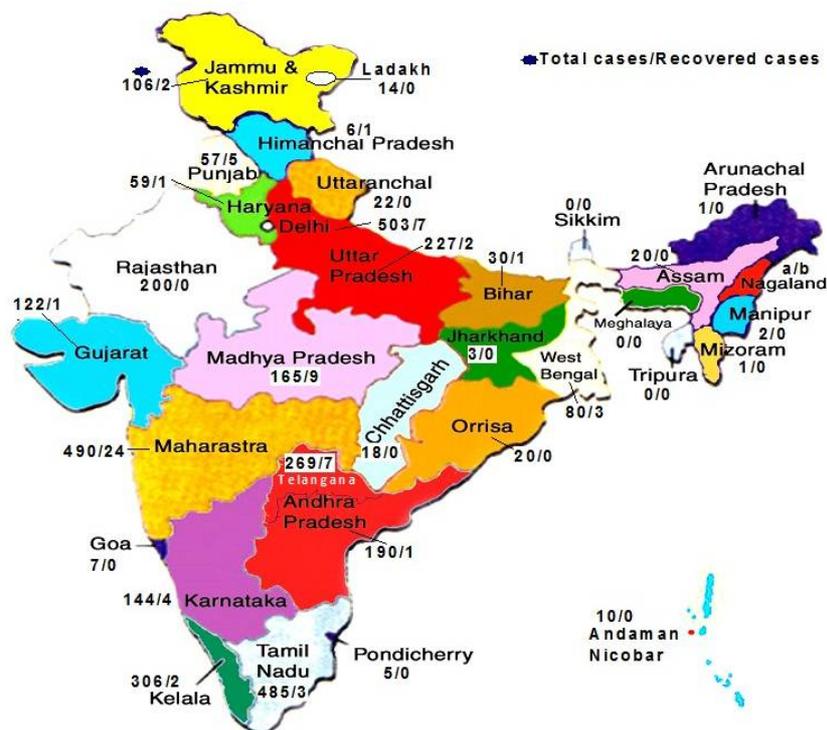


Fig. 4: The map showing state wise glimpse of COVID-19 in India by 5th April, 2020.
 Source: www.mohfw.gov.in.

The Director-General WHO declared the outbreak of novel coronavirus (2019-nCoV) by 30th January 2020 and constituted a Public Health Emergency of International Concern (PHEIC) after International Health Regulations (IHR) emergency committee. Since then, the Prime Minister’s Office (PM) Government of India along with Ministry of Health, Family and Welfare (MoHFW) closely monitoring situation of 2019-nCoV and intensifying preparedness and response efforts. The public health preparedness including surveillance, diagnostics, hospital preparedness, infection prevention and control, logistics and risk communication was being constantly reviewed by the national and state health authorities along with National Centre for Disease Control (NCDC) and has activated Strategic Health Operations Centre (SHOC) to command and control functions to public. Based on the human-to-human transmission based on current information through droplets or contact the MoHFW issued a travel advisory and counseling Indians to avoid non-essential travel to China. To tackle the situation, the GoI issued advisory to people coming from affected countries or having travel history, since 10th February 2020, being quarantined for 14 days on their arrival to India. As on 11th March 2020, WHO declared the novel coronavirus disease (COVID-19) as a global pandemic (an epidemic that has spread worldwide affecting a large number of people). On the same day, the Hon’ble Prime Minister of India, constituted a high-level Group of Ministers (GOM) to review, monitor and evaluate the preparedness and measures taken regarding management of COVID-19 in the country. The Government invoked powers under ‘Epidemic Diseases Act, 1897’ and declared COVID-19 a ‘notified disaster’ under the ‘Disaster Management Act 2005’.

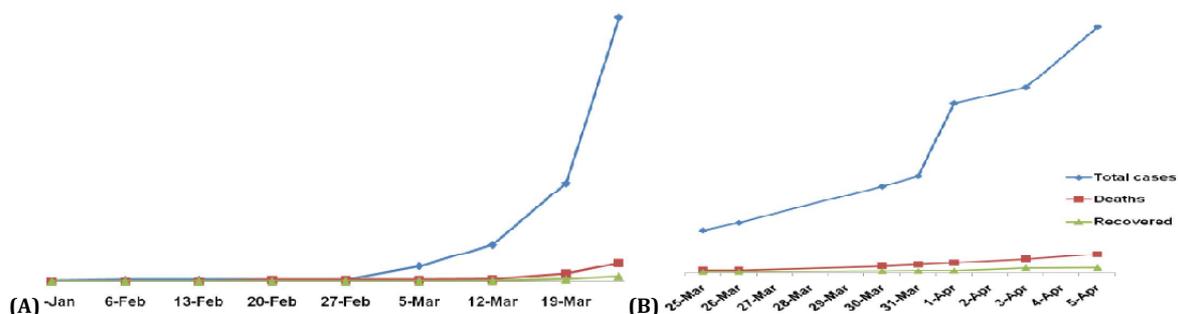


Fig. 5: COVID-19 scenario during pre-lockdown period (A) and lockdown period (B) in India.

The PMO, MoHFW and Cabinet Secretary were closely monitoring the situation round the clock and on 15th March 2020, all existing visas, except diplomatic, official, UN/International Organizations, employment, project visas, stand suspended until 15th April 2020. Thereafter, Hon'ble Prime Minister of India Shri Narendra Modi called for 'Janata Curfew' on 22nd March, 2020 from 7AM to 9PM, urging people to stay home except those in essential services, under the 'Essential Commodities (ECs) Act, 1955' up to 30th June 2020. In an order it was declared that all train services (except goods train) will be suspended and no scheduled international commercial passenger aircraft shall take off from any foreign airport for any airport in India till 31st March 2020. Later on the Hon'ble Prime Minister Mr. Narendra Modi, in exercise of the powers under 'section 6(2)(i) of Disaster Management Act, 2005', issued an order for State/UTs prescribing lockdown for containment of COVID-19 epidemic in the country for a period of 21 days with effect from 25th March, 2020 to 14th April, 2020. The comparative epidemiology of COVID-19 in India against pre-lockdown period and during lockdown was assessed (Fig. 5). The India's response to COVID-19 has been pre-emptive, pro-active and graded with high-level political commitment and a 'whole Government' approach to respond to the COVID-19 pandemic. The ICMR has issued guidelines for use of commercial kits for nasal/throat swab based diagnosis of COVID-19 and 104 out of 119 proposed labs in public sector are functional for COVID-19 or SARS-CoV2 test. Additionally, a total of 15 private labs in 7 states are also functional and test has been conducted with an efficiency of 96% across the republic of India.

CONCLUSION

It is too early to conclusively determine the path and mortality rates for COVID-19. We could learn from the experience on the outbreak of H1N1 flu pandemic in 2009 to understand the current global caseload better. Public health experts warn of a health catastrophe as the burden of COVID-19 swamps the capacity of health systems around the world. Developing countries such as India are especially vulnerable. The virus packs an insidious second punch that is hammering the global economy. As economists and development practitioners can attest, slow or declining growth poses extreme dangers to vulnerable populations, especially in developing countries. Governments across the world have imposed restrictions, extremely severe in some countries such as India, to slow the spread of the virus. Public health experts have led the calls for tough measures. Many economists have also supported these calls. But there are others, especially those working on economic issues, who worry that such restrictions could lead to severe economic and social consequences down the road. They believe that excessively harsh measures are disproportionate to the official data on the transmission of COVID-19, caseload, hospitalization and fatalities. The Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU) reports that 862,234 COVID-19 cases were confirmed as of April 1. Of these, 178,718 (20.7%) recovered and 42,404 (4.9%) died. The rest are active cases. The global case fatality rate (CFR) may be 4.9%, but there is wide variation across countries. Italy has a higher rate (11.4%), India is at 2.7%, the US at 1.8%, and Germany is at only 0.9%. It is clear that we do not know what the actual infection rate is. That is because not all who carry the virus are tested. For the most part, people are either asymptomatic or have mild symptoms. In such cases, testing is unlikely, especially in countries with limited capacity. With a new study linking BCG vaccination with scale of severity of COVID-19 globally, doctors in India said "large-scale epidemiological studies" need to be conducted before drawing any conclusion. According to the study led by a US-based researcher, a combination of reduced morbidity and mortality could make the *Bacillus Calmette-Guerin* (BCG) vaccination a "game-changer" in the fight against novel coronavirus. The BCG vaccine is part of India's universal immunisation programme and administered to millions of children at birth or soon after it. Large-scale epidemiological studies need to be conducted before we can draw any conclusion on this link. We found that countries without universal policies of BCG vaccination such as Italy, the Netherlands, and the United States, have been more severely affected compared to countries with universal and long-standing BCG policies," noted the researchers led by Gonzalo Otazu, assistant professor of biomedical sciences at NYIT. Jha of Fortis hospital, however, said the lockdown can only slow down the number of cases of infection but mortality as such will not be affected much. On a more positive note, clinical trials for an H1N1 vaccine started in July 2009, within three months of the first reported case. The US Food and Drug Administration (FDA) approved four H1N1 vaccines by September 2009. In October, the first vaccine was administered and by December 2009, 100 million doses of the vaccine were available for ordering. At that pace, we could have a COVID-19 vaccine this year. Clinical trials for a COVID-19 vaccine have commenced. That is cause for cautious optimism. Although several clinical trials are now underway to test possible therapies, the worldwide response to the COVID-19 outbreak has been largely limited to monitoring/containment.

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CONFLICTS OF INTEREST

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