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**Review Article**

# COVID-19 (CORONAVIRUS): A GLOBAL EMERGENCY OUTBREAK AND ITS IMPLICATIONS IN INDIA

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## ABSTRACT

Global outbreak of coronavirus disease 2019 (Covid-19) challenged the medical facilities and services worldwide with more than 200 countries affected by the pandemic. SARS-CoV-2, the seventh virus known to infect the human respiratory system, belongs to the genus *Betacoronavirus*. It affects the respiratory tract mainly by binding to the ACE-2 receptors chiefly found in lungs and heart. Major countries like the United States, Italy, France, and United Kingdom suffered great loss during the Covid-19 pandemic and large numbers of deaths were reported. At the same time, India too is combating against the virus. Covid-19 arrived in India from the global epicenter Wuhan in late January 2020 when a Kerala student tested positive for the virus. Maharashtra was the worst affected state with maximum number of positive cases and deaths in the country. First death due to Covid-19 occurred in Karnataka state that triggered the alarm of Covid-19 infection. Indian government is taking lots of efforts to control the transmission of the virus that spreads rapidly among humans. Strategies such as self-quarantine, social distancing and 40-days countrywide lockdown helped to slow down the virus which could have spread tremendously otherwise. Our review focuses on the implications of Covid-19 in Indian scenario along with report on active cases, death toll, cured cases, and strategies employed for the pandemic control.

**Keywords:** Covid-19, Coronavirus, India, SARS-CoV-2.

## INTRODUCTION

Coronavirus disease-2019 (Covid-19), also known as Severe Acute Respiratory Syndrome (SARS-CoV-2), is a deadly zoonotic, infectious, global emergency pandemic that affected more than 200 countries worldwide. The announcement of Public Health Emergency of International Concern (PHEIC) by WHO on January 30, 2020 had stipulated the severity of the disease (Mahase E. *et al.* 2020; Nishiura *et al*., 2020). Situation report-85 stated that 1,844,863 confirmed cases and 117,021 deaths were reported from around the world with 83,696 confirmed cases and 3,351 deaths reported from China alone (Covid-19 Situation Report–85, 2020). As of 16th April 2020, 10,477 active Covid-19 cases, 1489 cured/migrated cases, and 414 deaths were recorded in India (MHFW, Govt. of India, 2020). China was the first country to come up with critical cases of severe respiratory infection in December 2019 that was revealed to be a case of life-threatening viral condition (Nishiura *et al*., 2020). Wuhan is a city in Hubei province of China that is well known for its wholesale animal markets where different species of live wild animals and fish were easily available. According to the report submitted to China Center for Disease Control and Prevention (CDC) on December 30th 2019 emphasized the diagnosis of coronavirus by employing whole genome sequencing, culture and direct PCR in bronchoalveolar-lavage fluid of infected patients (Zhu *et al*., 2019).

Out of six investigated human infecting viruses, four (229E, OC43, NL63, HKU1) are known to cause the common cold and other two (SARS and MERS) are zoonotic and lethal. Severe acute respiratory syndrome (SARS) was identified in February 2003 and Middle East respiratory syndrome (MERS) was first identified in Saudi Arabia in 2012 (Su *et al*., 2016; Zhu *et al*., 2019). SARS-

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CoV-2 became the seventh known virus causing enormous death all over the globe. Genetic make-up analysis demonstrated that it was distinguished by the correlation of 88% genetic similarity with two bat-derived coronaviruses: bat-SL-CoVZC45 and bat-SL-CoVZXC21, and the distant genetic relationship with SARS-CoV (79%) and MERS-CoV (50%). Phylogenetic tree indicates that SARS-CoV-2 belongs to genus *Betacoronavirus* (Lu *et al.,* 2020). It is believed that Covid-19 infection proliferated through bats and pangolins to other animals and humans, as it shares genetic similarity with the viruses that are primarily found in bat (Lam *et al.,* 2020; Zhang *et al*., 2020). The virus might have evolved the ability to infect humans by the mutation of spike glycoprotein (Benvenuto *et al*., 2020)**.** On January 18$^{th}$ 2020, a 35 year old man was admitted to the hospital in Washington with 4-days history of cough and fever. This was the first ever case of Covid-19 reported in the United States (Holshue *et al*., 2020). Travelling of infected people from China to countries like Taiwan, Germany, Italy, Thailand, France, Australia, South Korea and Japan lead to the distribution of the virus around the world (Giovanetti *et al*., 2020). Gene sequencing of SARS-CoV-2 unleashed the way of medical treatment of infected patients. As a result, real-time reverse-transcription polymerase chain reaction (RT-PCR) was employed to diagnose the viral disease (Chinese Society of Radiology. 2020). Apart from RT-PCR, Chest CT scans were shown to be more specific and appropriate medical diagnostic tool for the identification of Covid-19. The potential of CT scan to recognize early stages of lung infection by the virus made it a convenient tool for the confirmation process. At present RT-PCR and chest CT scan are being used to confirm Covid-19 in the patients (Office of National Health Committee. 2020; Kanne, 2020; Pan & Guan, 2020). Chloroquine phosphate, a drug used to treat malaria has also been found effective in the treatment of Covid-19. It is one among the probable curative drugs attributed to its anti-inflammatory and anti-viral properties (Gao *et al*., 2020). It is important to know the viral transmission in the country as people are continuously exposed to the risk of contracting the virus without consciousness. Present review highlights the real viral outbreak situation in India.

## MATERIALS AND METHODS

This review was carried out with the help of various reference websites such as Google Scholar and Science Direct. We used the key words such as "India", "Covid-19", "Coronavirus" to get appropriate results with respect to Covid-19. The statistical data were retrieved individually through official websites of India state governments.

### Structure and mechanism of infection

Coronavirus is a spherical, enveloped structure having diameter of 60-140 nm and belongs to the genus *Betacoronavirus* (Lu *et al*., 2020; Cui *et al*., 2019). It is surrounded by spike-like spike protein (S-protein), envelope protein (E-protein), membrane glycoprotein (M-protein), and contains single-stranded ribonucleic acid as genetic material (Figure 1). The encircling spike-like S-protein (9-12 nm) is responsible for the solar corona-like appearance of the virus, and hence the virus is named coronavirus (Lu *et al*., 2020). The S-protein plays a crucial role in causing major human respiratory infection. The mutation of spike glycoprotein (S-protein) might be considered as one of the reasons for deadly human respiratory infection (Benvenuto *et al*., 2020). Angiotensin converting enzyme-2 (ACE-2) is the vital enzyme that converts the octapeptide angiotensin-2 to its metabolite angiotensin-(1-7) (Wang Q. *et al*. 2020; Zisman *et al*., 2003). The S-protein specifically binds to the ACE-2 receptor which is particularly expressed in human heart and lungs. Binding of virus to the ACE-2 receptor undoubtedly affects the human respiratory system (Turner *et al*., 2004).

### Viral spread in India

Covid-19 is believed to spread in two stages (Figure 1). First stage is characterized by the involvement of live animals which harbor the virus in their body that is transmitted to humans by contact. Second stage is characterized by rapid transmission of the virus by human to human contact (Kuldeep Dhama *et al*., 2020). After the viral outbreak in China, all other countries became alert and took immediate preventive measures that involved strict quarantine action at airports. India is the second most populous country in the world. It is also an immediate neighbor to China and hence more prone to the viral disease spread (US and World Population Clock, 2020). The country reported its first confirmed case on 30$^{th}$ January 2020 from the state of Kerala, which was directly linked to Wuhan, the epicenter of Covid-19 outbreak. A 76-year-old man who tested positive for SARS-CoV-2 was the first death from Covid-19 in India, reported from Kalaburagi, Karnataka (Update on state/ UT wise lockdown., 2020; Nagarjun Dwarakanath, 2020). Karnataka was the first state to report first Covid-19 death on 11$^{th}$ March 2020 in India. Reports of confirmed cases from other Indian states started to increase gradually. Government of India announced 21 days of lockdown in effect from 25$^{th}$ march 2020 with prescribed guidelines regarding management of essential services (Guidelines on the measures to be taken by ministries. 2020)**.** The lockdown was further extended till 3$^{rd}$ May 2020 (total duration 40 days).

As of 16$^{th}$ April 2020, majority of confirmed cases were reported from states such as Maharashtra-2916, Delhi-1578, Tamil Nadu-1242, Rajasthan-1023, Madhya Pradesh-987, Gujarat-766, Uttar Pradesh-735, and Telangana-647. Other states too reported increased cases of Covid-19 (Figure 3). Total 414 deaths and 1489 cured/discharged/ migrated cases were reported from the country (Figure 4 and Figure 5).

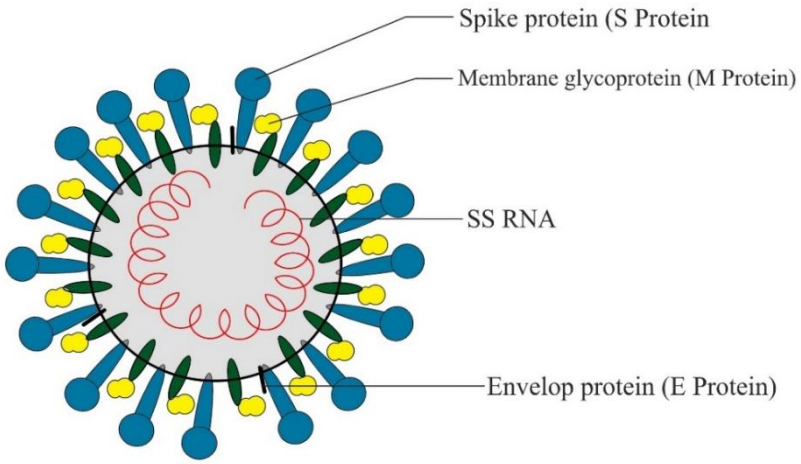


**Figure 1.** Structure of SARS-CoV-2.

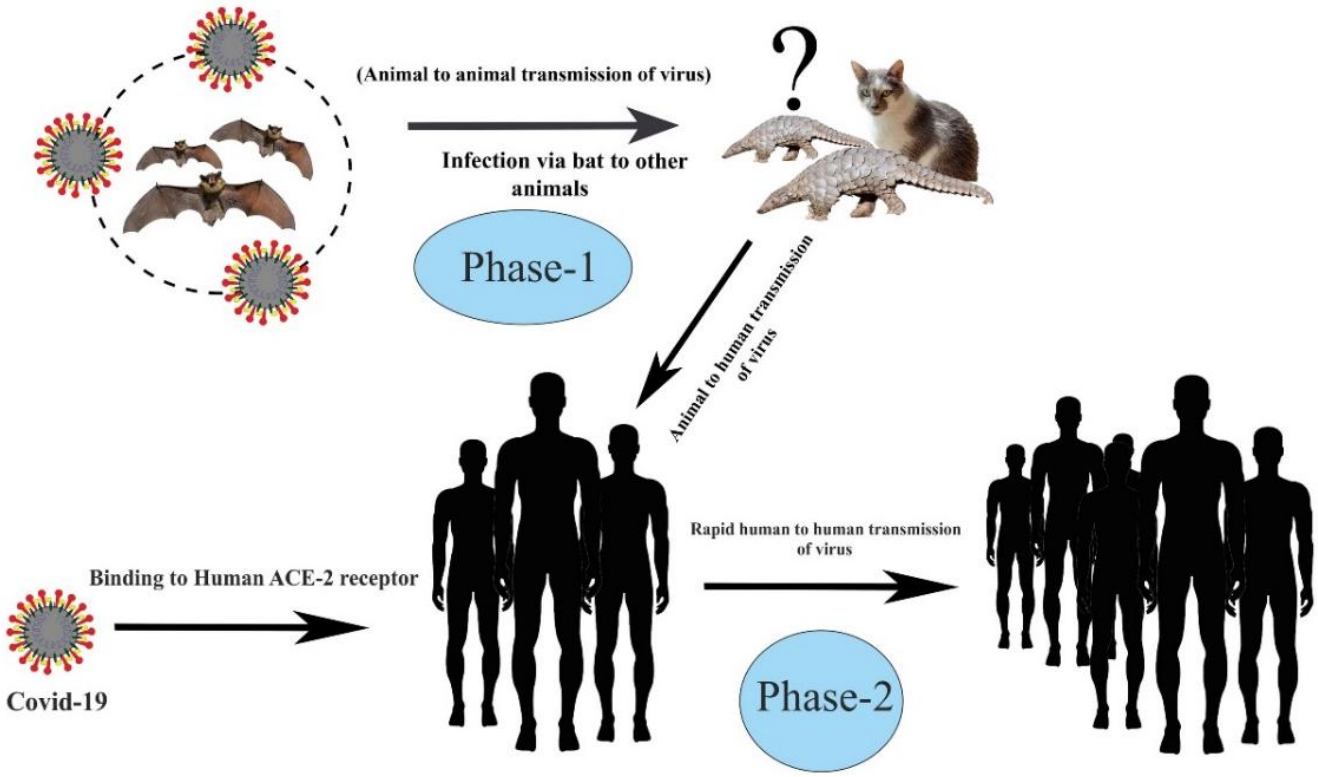


**Figure 2.** Two phase transmission of SARS-CoV-2 and binding of SARS-CoV-2 Human ACE-2 receptor.

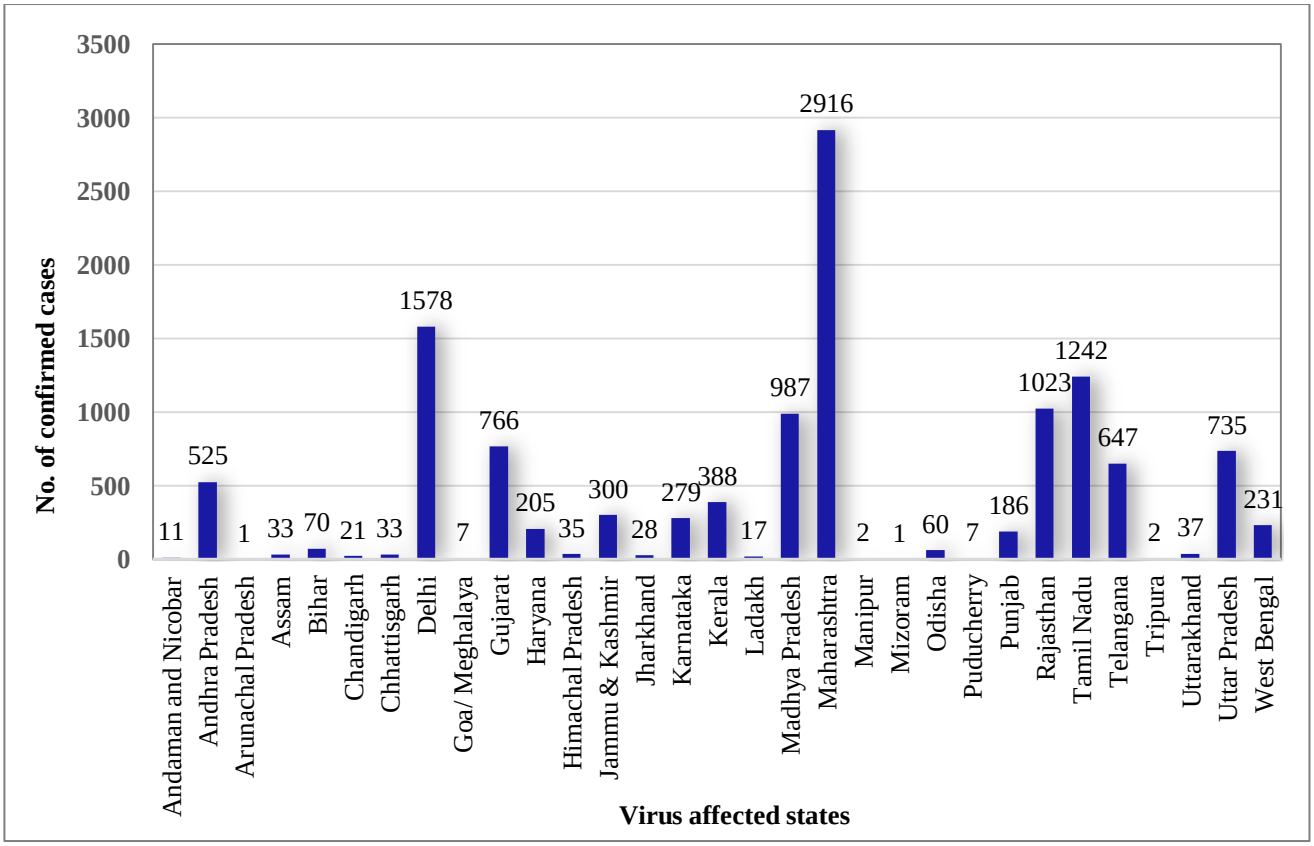


**Figure 3.** State wise Covid-19 confirmed cases in India.

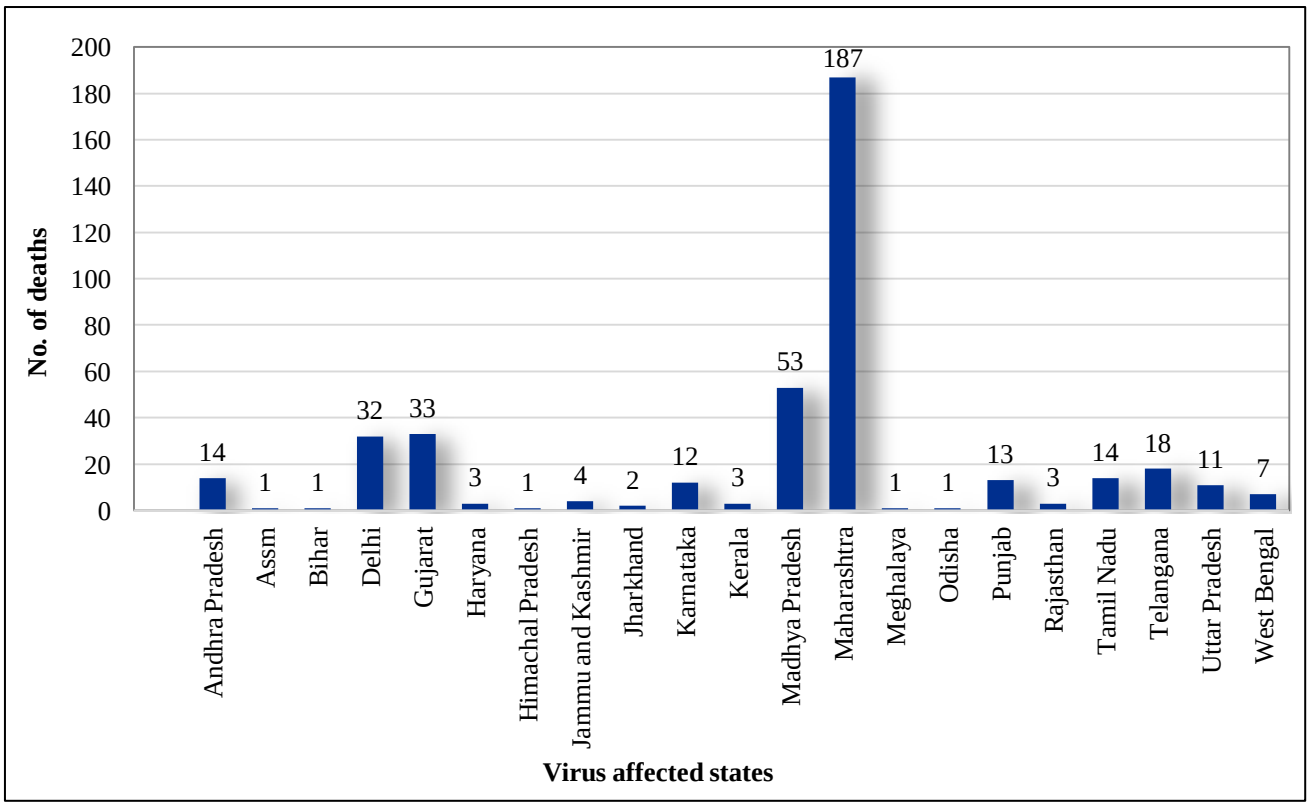


**Figure 4.** State wise number of Covid-19 deaths in India.

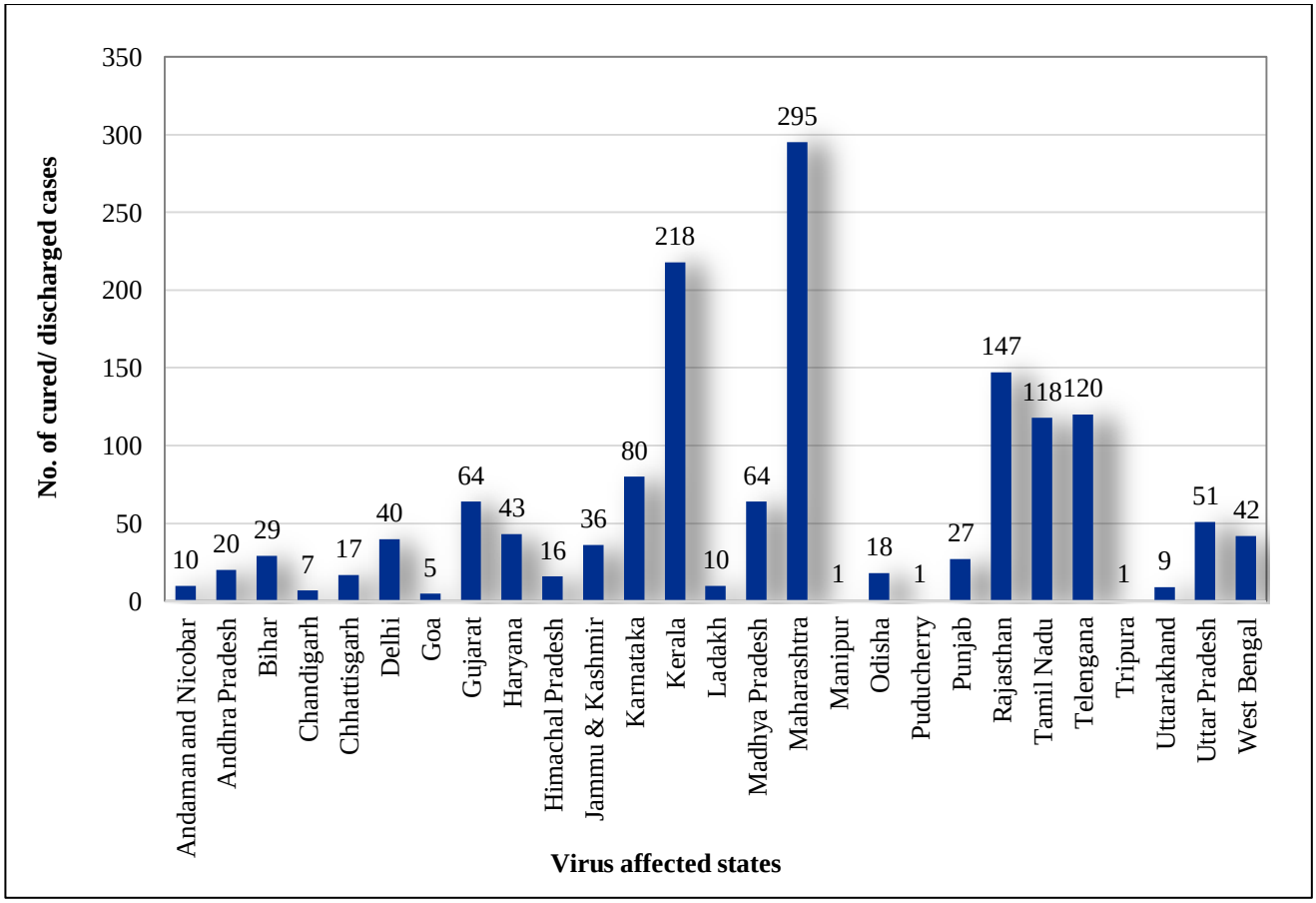


**Figure 5.** State wise number of cured/discharged cases.

**Clinical symptoms**

Clinical symptoms play a pivotal role in diagnosis of a disease. As the incubation period of SARS-CoV-2 usually ranges from 0-14 days and even more than 14 days in some patients, it requires time to manifest the symptoms. Infected people may or may not be symptomatic. Covid-19 infected people exhibit mild symptoms such as fever, sore throat, cough, phlegm and fatigue during initial stages (Bai *et al*., 2020; Bernheim *et al*., 2020). In severe cases patients exhibit headache, dizziness, vomiting, diarrhoea, shortness of breath (Dyspnoea), swollen lymph nodes (Lymphadenopathy), excess fluid accumulation between the pleura of the lungs (Pleural effusions), leucocytosis, lymphocytosis, round oval spots on the lungs (Pulmonary nodules), abnormal gas filled spaces in the lungs (Lung cavitation), bilateral disease, consolidation, greater lung involvement and crazy paving patterns (Bernheim *et al*., 2020; Shi *et al*., 2020).

Asymptomatic pneumonia was reported in some studies which makes it hard for the medical practitioners to diagnose the disease precisely (Bai *et al*., 2020). Apart from infected adults showing some of the above symptoms, few neonates born to the Covid-19 positive mothers were found to be infected but there is no direct evidence to confirm intrauterine vertical transmission of SARS-CoV-2 to the neonates. Pregnant women exhibited common symptoms, particularly diarrhoea, lymphopenia and elevated concentrations of AST or ALP (Chen H. *et al*., 2020). Hematological studies of the Covid-19 patient who was having 39 ºC body temperature revealed leucopenia with WBC count of $2.91\times10^9$ /L and showed elevated levels of C-reactive protein, erythrocyte sedimentation rate (ESR) and D-dimer (Lei *et al*., 2020).

**Diagnostic tools**

Very few diagnostic tools are available around the world to detect the novel Covid-19 disease. Some of them are as follows:

**Epidemiological diagnosis**

Coronavirus has the ability to survive on inanimate surfaces such as metals, textiles, plastic at favourable temperature of 30 ºC in active infectious stage for certain durations of time. Even though unfavourable conditions may kill/inactivate the virus, it is suggested to use disinfectants (0.1% sodium hypochlorite) and hand sanitizers (min. 70% ethanol) to clean the hands and surfaces (WHO. Annex G., 2014; Kampf *et al*., 2020). Tracing the travel history of the person exhibiting early symptoms of Covid-19 and his meetings with people from other infected parts of the world

can aid in the process of early detection. Human to human transmission is one of the rapid ways of expansion of the virus, the cough droplets from infected person and physical contact with the patients can cause viral transmission (Chan JFW. *et al*., 2020).

**RT-PCR detection**

Gene sequencing of SARS-CoV-2 was the main support for the development and manufacture of real-time reverse-transcription polymerase chain reaction (RT-PCR) diagnostic kit. Detection of viral nucleic acid using RT-PCR was the main objective of the diagnostic kit. It is the standard reference kit available in the market as of now, however the sensitivity of RT-PCR kit was found to be 60% in the early stages of infection ( Chan JFW. *et al*., 2020; Yang *et al*., 2020) with many actually infected persons testing negative for SARS-CoV-2 in initial diagnosis. The detection sensitivity highly depends upon the quality and quantity of the sample and sample collection site, as lower respiratory tract samples more likely to yield good result (Zou *et al*., 2020). In many cases the detection was either false positive or negative for positive patients which may be attributed to sampling error, clinical error, and/or manufacturing defects in the diagnosis kit (Fang *et al*., 2020; Zu *et al*., 2020).

**Computed tomography (CT) Scan detection**

As the sensitivity matters in the crucial detection of viral diseases, testing with RT-PCR diagnosis kit alone is not a recommended protocol. Due to the flaws in RT-PCR detection kits, clinical radiologists found alternative, highly precise diagnostic tool- CT-scan. A typical Covid-19 patient shows CT-scan characteristics of multifocal ground-glass opacities (GGOs), preferred posterior part or lower lobe predilection. CT scan was found to be 98% effective in the detection of early and progressive Covid-19 disease (Fang *et al*., 2020; Zu *et al*., 2020). However, it is necessary to confirm with both the detection tools in order to verify the disease.

**Treatment**

Treatment of Covid-19 infected patients is an infectious, laborious and time-consuming task due to the lack of specific anti-viral drug/vaccine against Covid-19 in pharmaceutical industries. A 35-year-old infected woman in China was given Lopinavir 400 mg/ Ritonavir 100 mg from the day 4 of illness and she displayed improved health condition (Cao *et al*., 2020; Kim *et al*., 2020). A similar drug therapy study reported that a 54-year-old patient in China was subjected to the administration of Lopinavir 200 mg/ Ritonavir 50 mg tablets from day 8 of infection. This accelerated the recovery from Covid-19 infection. Although clinical trial-based evidences are lacking on this drug use against Coivd-19, the patients might have recovered due to the natural healing process rather than drug administration or both (Lim *et al*., 2020).

An in-vitro study revealed that Remdesivir, a novel antiviral drug; and chloroquine, which is an efficient anti-malarial drug were found to be effective against Covid-19 (Wang M. *et al*., 2019). Patients treated with Hydroxychloroquine and Chloroquine for three to six days showed clearing of virus from nasopharyngeal passage but the study group also encountered two patients in whom hydroxychloroquine treatment was a failure. The same study group found the synergistic effect of hydroxychloroquine and azithromycin (Cortegiani *et al*., 2020; Gautret *et al*., 2020).

IFN-α, ribavirin, arbidol, chloroquine phosphate are some of the new drugs that were found to be highly potential against Covid-19 infection (Dong *et al*., 2020). Extracorporeal membrane oxygenation (ECMO) was suggested to be employed in critically ill patients to relieve the initial respiratory problems caused due to the infection (MacLaren *et al*., 2020). Treatment with combined anti-viral and anti-inflammatory drugs, inhibitors of ACEI and AT1R, and convalescent plasma therapy were also recommended by some study groups (Chen L. *et al*., 2020; Sun Meili *et al*., 2020; Stebbing *et al*., 2020; Aeturo Casadevall *et al*., 2020).

**Strategies to control Covid-19 in India**

The widespread transmission of Covid-19 in India is uncontrollable without successful implementation of preventive measures in infected areas. Home quarantine concept is one of the effective disease control measures executed via nation-wide lockdown in effect since 25$^{th}$ of March 2020 (Guidelines on the measures to be taken by ministries. 2020). However, home quarantine alone is not enough to prevent the rapid spread of the virus in the country. Government of India (Ministry of Health & Family welfare) announced some of the healthy practices following the recommendations of World Health Organization (WHO) and Center for Disease Control and prevention (CDC).

Airport quarantine of foreigners and citizens in 3 categories helped to control the invading virus as first line of defense in the country (Ministry of Health and Family welfare. 2020). Category A (High risk): Passengers with severe cough, fever and shortness of breath were considered to be high risk and were quarantined under medical observation. Category B (Moderate risk): Asymptomatic passengers with underlying health conditions such as diabetes mellitus, hypertension and asthma were quarantined for 14 days at government facilities and the responsibility of medical observation was taken by the state governments. Category C (Low risk): Asymptomatic passengers travelling from Covid-19 affected countries were home quarantined for 14 days and kept under medical observation. Ministry of Health and Family Welfare of India advised people to use disinfectants such as sodium hypochlorite, liquid bleach, sodium dichloro-isocyanurate (NaDCC), and chloramine to maintain cleanliness in the house.

**WHO and CDC recommendations**

Avoiding close contact with people and practicing social distancing to reduce the chance of viral spread. Using soap and hand sanitizers (60% alcohol) to maintain the personal hygiene. Washing hands for at least 20 seconds effectively kills the coronavirus. Avoiding touching the eyes, nose and mouth with unwashed hands. If any kind of sickness is felt, people are advised to seek immediate medical help and stay home as much as possible. People are advised to cover their nose and mouth while coughing. Use of face mask is mandatory for infected persons (Covid-19 guidance documents, 2020).

## RESULT AND DISCUSSION

Global outbreak of Covid-19 made more than 200 countries to suffer huge loss in terms of human resources and economy worldwide. The viral strain responsible for the outbreak was identified as SARS-CoV-2 which is related to the bat coronaviruses and belongs to the genus *Betacoronavirus* (Lu *et al*., 2020). It was confirmed by several research studies that it primarily affects the respiratory system in the human host. The strain had 79% genetic similarity with SARS-CoV and the respiratory infection might be attributed to the binding of the virus to human ACE-2 receptor (Turner A. J. *et al*., 2004). Fig. 2 illustrates the two ways of viral spread and the binding of spike protein to the ACE-2 receptor. The prolonged symptoms such as mild fever, cough and sputum production may be considered as indication of early Covid-19 infection. RT-PCR and Chest CT scan are the recommended diagnostic methods to confirm the presence or absence of the disease in the patient (Chan *et al*., 2020; Zu *et al.*, 2020). According to the situation report-85, the most populous country China was hit by the virus with over 83,696 confirmed cases and more than 3,350 deaths. The global epicenter later shifted to Europe with Italy and Spain being the worst hit countries with more than 20,400 and 17,400 deaths respectively. The United States of America had over 5,53,822 cases as of 14$^{th}$ April 2020 with death toll standing at 21,972 (Covid-19 Situation Report-85. 2020). India being the second most populous country in the world had 10,477 confirmed active Covid-19 cases and 414 deaths as of 16$^{th}$ April 2020 (Ministry of Health and Family Welfare, Government of India, 2020; Covid-19 Situation Report-85, 2020; State census, 2011). Considering the statistics of Covid-19 in India predominantly indicates that Maharashtra, Delhi, Tamil Nadu, Rajasthan and Madhya Pradesh were the top five most severely affected states having 2916, 1578, 1242, 1023, 987 confirmed cases respectively (Figure 3). Most of the positive Covid-19 cases in India had a history of travel to the infected parts of the world and many others were the persons who came in contact with these travelers. There were very little evidences of community transmission and mostly clusters of cases emerged from different parts of the country. Maharashtra, Madhya Pradesh, Gujarat, Delhi, and Telangana reported highest deaths in India (Figure 4). Maharashtra was the most severely affected state although it managed to sustain the health facilities and arrived with 295 recovered patients. Kerala, Rajasthan Telangana, Tamil Nadu, and Karnataka too reported 218, 147, 120, 118 and 80 Covid-19 cured cases respectively (Figure 5).

The incubation period of SARS-CoV-2 in the upper respiratory tract ranges from 2 to 14 days and as a result, increased number of novel cases is being reported from different parts of the country every day. As of 16$^{th}$ April 2020, India had 10,477 active cases of Covid-19 with 414 deaths and 1489 patients cured/ recovered/ migrated (Ministry of health and family welfare, Government of India. 2020). Cases per million people were only 9.1, which is one among the lowest in the world. The relatively low number of confirmed cases in India may be attributed to narrow testing methods and testing only the people who have travel history to affected countries/ areas and those who had contact history with Covid-19 positive patients. The lack of rapid and self-testing kits for detection of Covid-19 might result in many positive cases going undetected and unreported. However, the home quarantine/ countrywide lockdown were one of the main reasons that greatly reduced the spread of coronavirus and there was very little evidence of community transmission of the virus. The concept of social distancing emerged as a major contribution to the slowdown of SARS-CoV-2 transmission.

## CONCLUSION

The two-phase spreading of Covid-19 made its entry into India in 2$^{nd}$ phase i.e. human to human rapid transmission. India is one of the affected countries in the world struggling to control the spread of novel virus through various strategies. The lack of awareness about the pandemic and laid-back attitude of certain sections of population towards the disease made the task of viral control difficult in real situation and resulted in surge in the cases of Covid-19 in India with emergence of clusters of cases throughout the country and resulting in significant number of deaths. India still needs more sophisticated, rapid viral testing kits and potential medication for treating the infected patients in order to overcome this national emergency. Positive cases and death toll may increase if the situation isn't handled with caution by the Indian residents. Countrywide lockdown and social distancing measures greatly contributed in limiting the rapid spread of the disease.

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