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Study and overview of the novel corona virus disease (COVID-19)

Krishna Mohan Agarwal^a, Swati Mohapatra^b, Prairit Sharma^a, Shreya Sharma^c,
Dinesh Bhatia^{d,*}, Animesh Mishra^e

^a Mechanical Engineering Department, Amity University Uttar Pradesh, Noida, 201301, India

^b Department of Microbial Technology, Amity University Uttar Pradesh, Noida, 201301, India

^c Department of Biotechnology, Amity University Uttar Pradesh, Noida, 201301, India

^d Department of Biomedical Engineering, North Eastern Hill University, Shillong, 793022, Meghalaya, India

^e Department of Cardiology, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, 793018, Meghalaya, India



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ABSTRACT

In December 2019, a new disease with pneumonia-like symptoms was spreading throughout Wuhan in China which was entitled as novel coronavirus disease or COVID-19 caused by the virus SARS-CoV-2. Within a span of a few days, this disease became a global threat and was termed as a pandemic by the World Health Organization (WHO) on March 11, 2020, since then the disease has affected more than 1.5 crore people worldwide and around 6.9 lakh people in India as of July 5, 2020. The origin of the COVID-19 disease has been traced back to the bats, but the intermediary contact is unknown. The disease spreads by respiratory droplets and contaminated surfaces. In most cases, the virus shows mild symptoms like fever, fatigue, dyspnea, cough, etc. which may become severe if appropriate precautions are not adhered to. For people with comorbidities (usually elderly) the disease may turn deadly and cause pneumonia, Acute Respiratory Disease Syndrome (ARDS), and multi-organ failure, thereby affecting a person's ability to breathe leading to being put on the ventilator support. The reproduction number (R_e) of COVID-19 is much higher than its predecessors and genetically similar diseases like SARS-CoV and MERS-CoV. This paper discusses the epidemiological characteristics of the SARS-CoV-2 virus, its phylogenetic relationship with the previous pandemic causing viruses such as SARS-CoV-1 and MERS-CoV and analyzes the various responses to this global pandemic worldwide, focusing on the actions taken by India and their outcomes.

1. Introduction

The current global pandemic is caused by the “novel coronavirus disease (2019-nCoV) or severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) popularly known as COVID-19 disease” originated in the city of Wuhan in Hubei Province, China, during December in 2019. The virus quickly spread throughout the world. Many countries reacted too late to implement preventive measures leading to a sudden upsurge in the number of cases worldwide. Genomic analysis of the virus SARS-CoV-2 was found to be phylogenetically similar to other bat originated coronaviruses like SARS-Cov-1 and MERS-CoV, thereby confirming that bats are the primary reservoir of the virus, however, the intermediate source of origin and its transfer to humans is not yet known [4,42]. As of July 5,

2020, there is no clinically approved antiviral drug treatment or vaccine available to be used against COVID-19, however, in the month of July 2020 certain organizations worldwide are claiming to be working on a vaccine to treat the novel coronavirus. Drugs like Remdesivir (GS-5734) and Dexamethasone are being evaluated in late-stage clinical trials but have not been approved anywhere. The transmission of COVID-19 is confirmed to be through human to human interactions [21], the maximum amount of viral load shedding is done by symptomatic carriers, however, there are confirmed cases of asymptomatic carriers also transmitting the disease [4].

* Corresponding author.

E-mail address: bhatiadinesh@rediffmail.com (D. Bhatia).



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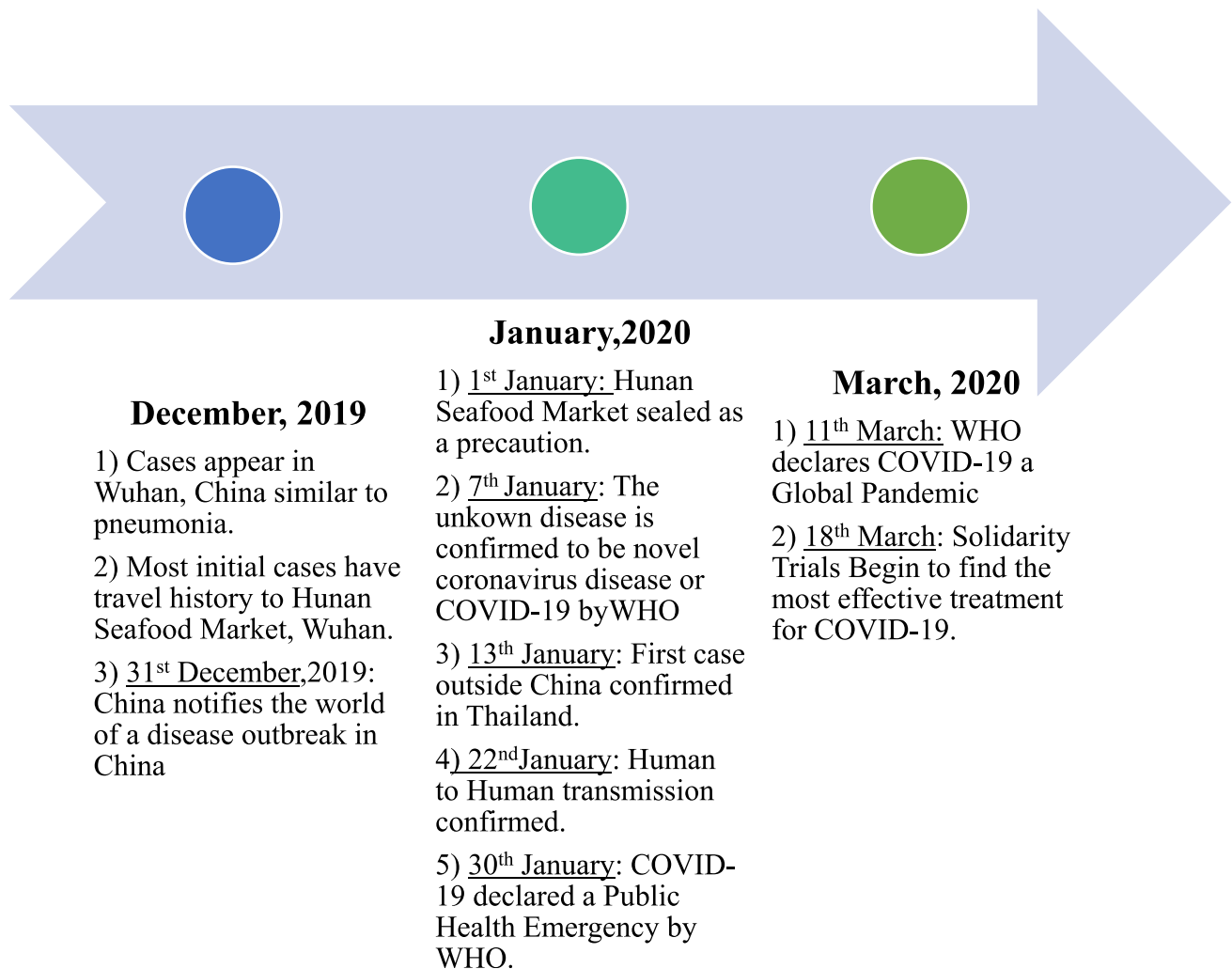


Fig. 1. Timeline depicting the major events that lead to the declaration of COVID-19 as a Global Pandemic.

2. Epidemiology of the novel coronavirus

During December 2019 in Wuhan, the capital city of Hubei Province China, strange cases of severe pneumonia had been identified and started spreading. Most of the initial cases found had a travel history to the Hunan wholesale seafood market which also sold live animals. In China, the intelligence system which was established after the SARS outbreak in 2003 was immediately alerted and samples of the patients were sent to labs for aetiological inspection. This was followed by China notifying the world of an outbreak on December 31, 2019, subsequently, on January 1, 2020, the Hunan seafood market was sealed, on 7th January roughly a week after China's notification of a possible outbreak the disease was confirmed to be the novel coronavirus disease or COVID-19 which has more than 95% homology with bat coronavirus and almost 70% similarity to the SARS CoV-1 virus [8,43].

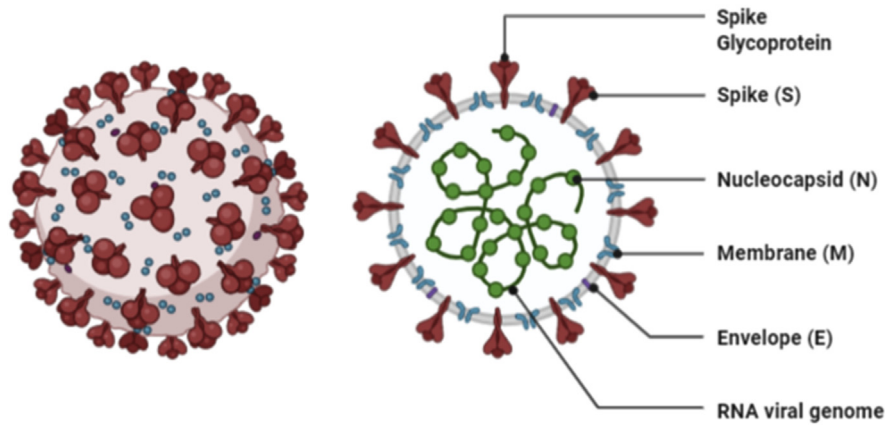
Environmental samples collected from the Hunan seafood market were tested positive with traces of COVID-19, indicating it as the origin of the virus [9,43]. In the ensuing days, more cases started to appear in China, some of which with no travel history to the Hunan seafood market, confirming that human to human transmission was taking place. The period of January being the month of Chinese New Year incited transmission of the virus with people migrating within China as well as internationally. Cases were reported from Thailand, South Korea, Japan and those infected had a travel history to Wuhan. To contain the spread, the entire city of Wuhan was placed under lockdown on January 23,

2020, shortly after this the lockdown was extended to other parts of Hubei province. Flights were barred from China and screening of passengers with temperature monitors was started at airports. Soon local transmission was observed in diversified countries outside of China [12, 13,40] and it was found that asymptomatic carriers could also carry out load shedding of the virus following which almost all international travel came to a halt [4,10,11].

2.1. The structure of SARS -CoV- 2

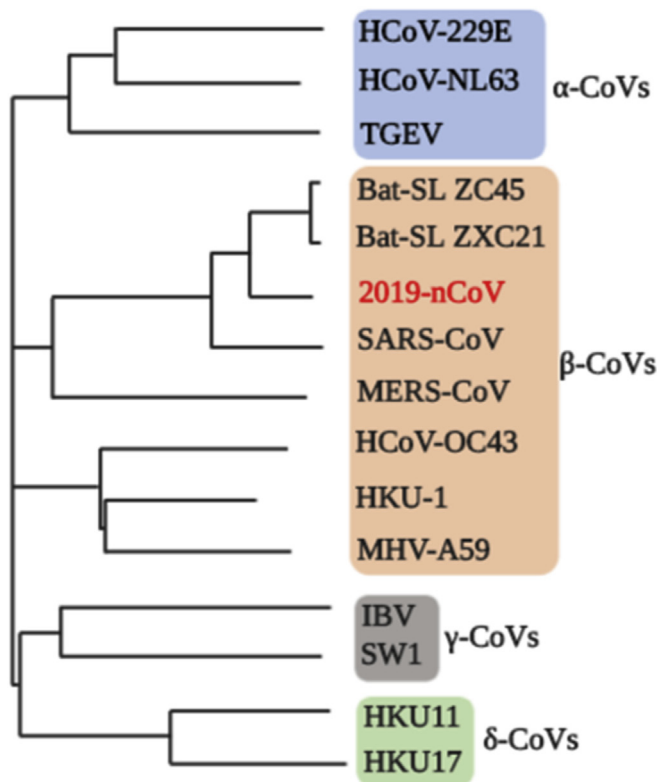
The size of coronaviruses ranges from 60 to 140 nm in diameter, its linearly stranded and positive-sense RNA genome is quite large, ranging from 26 to 32 Kb in size [18,43]. These spherical or pleomorphic viruses have envelopes that contain helical nucleocapsid of nucleoproteins(N) which is associated with the RNA genome. Embedded in the envelope is a 2 nm trimer of spike glycoprotein (S) that facilitates the virus's attachment to the receptor of host cells. Its envelopes also consist of integral membrane (M) and envelope (E) proteins. Coronaviruses that belong to the genus Beta-coronavirus have additional membrane glycoprotein hemagglutinin esterase which forms 5–7 nm long spikes (N.J., et al., 2019) these spike-like projections on its surface give it a crown-like appearance under the electron microscope, hence the name coronavirus [37]. The common cold which has a mild effect on our respiratory system is also a form of coronavirus.

Structure of SARS-CoV-2



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Fig. 2 1. A): Structure of the coronavirus [1].



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Fig. 2 2A. The phylogenetic tree of representative Coronaviruses, with the new coronavirus, 2019-nCoV highlighted in red [5].

2.2. The phylogenetic relationship of the coronaviruses

The crossover of animal beta coronaviruses with humans has resulted in severe life-threatening diseases in the past. The first case was witnessed in the years 2002–2003 when a new coronavirus whose origin was traced back to bats, crossed over with humans via an intermediary host “palm civet cats” in Guangdong Province, China [17,43]. The

disease was referred to as SARS (Severe Acute Respiratory Syndrome). The second instance was the MERS-CoV (Middle Eastern Respiratory Syndrome coronavirus) in 2012, where a similar bat originated virus was transmitted via an intermediary host the dromedary camels which emerged in Saudi Arabia [19,20]. (see Figs. 1 and 2.1)

Whole Genome sequencing of the current coronavirus illustrates that it belongs to the subfamily Coronavirinae in the family of Coronaviridae

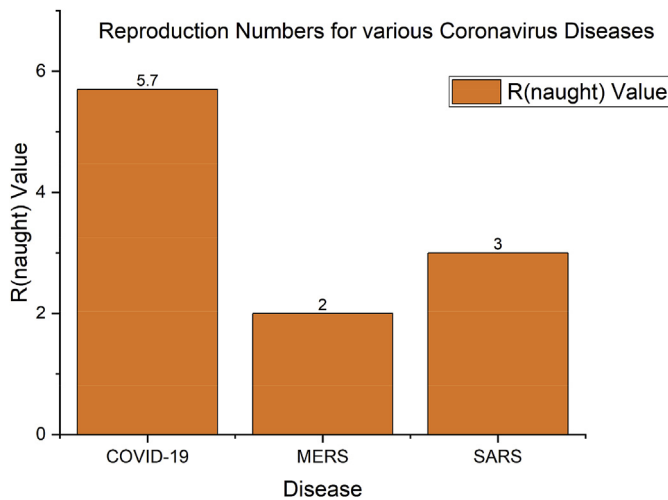


Fig. 2.3A. Reproduction Numbers for various coronaviruses Data Collected from Ref. [20] (Middle East respiratory syndrome coronavirus (MERS-CoV), 2020) [33].

of the order Nidovirales. This subfamily comprises of four genera *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus* (Fig. 2.2A). The phylogenetic analyses depict that the SARS-CoV, MERS, and SARS-CoV-2 all belong to the same genus of Betacoronavirus [5].

SARS-CoV-2 showcases a similar genomic structure to other betacoronaviruses. As per the data available in the research domain resembling other coronaviruses, its genome has 14 open reading frames (ORF) which code for 27 proteins. The ORF1 and ORF 2 are present at the 5' terminal of the genome and codes for 15 non-structural proteins that are considered essential for virus replication [30,47] Its 3' terminal of the genome codes for various structural proteins like the spike protein (S) that give it a unique structure, the envelope protein (E), membrane protein (M) and nucleocapsid (N), this region also has additional codons for certain accessory proteins [30,47].

Sequence analysis conducted by researchers depicts that the SARS-CoV-2 virus has a typical genome structure of the Coronaviruses and belongs to the cluster of beta-coronaviruses which includes Bat-SARS-like (SL)-ZC45, Bat-SL ZXC21, SARS-CoV, and MERS-CoV. Based on the phylogenetic tree of Coronaviruses, 2019-nCoV is more closely related to bat-SL-CoV ZC45 and bat-SL-CoV ZXC21 (isolated from horseshoe bats in China in the year 2015–2018) and is more distantly related to SARS-CoV and that they belong to a different clade from MERS-CoV, as evident from the phylogenetic tree in the (Fig. 2.2A) [5,33].

This explains that the SARS-CoV-2 although from the same genus of SARS and MERS has a different viral evolution from them, involving bats as a wild reservoir [35].

2.3. Pathogenicity and transmissibility of Covid-19 and other coronaviruses

Genomic analysis of the various beta-coronavirus suggests that the human cell receptor source used to enter a host cell is the same in the SARS-CoV-2 and SARS-CoV is called angiotensin-converting enzyme 2 (ACE2), whereas the human cell receptor used by the MERS-CoV is dipeptidyl peptidase 4 (DPP4) [35].

The SARS-CoV-2 virus binds to the angiotensin receptor 2 or ACE2 receptor found in the respiratory tract. The Basic Case Reproduction rate or BCR ranges within 2–6.47 which suggests that one person can infect 2 to 6 people [6]. The incubation period for this virus ranges from 2 days to 14 days with an average of 5 days for the onset of symptoms [27]. The average period from the commencement of symptoms to the state of breathlessness was 5 days, the need for hospitalization was 7 days and

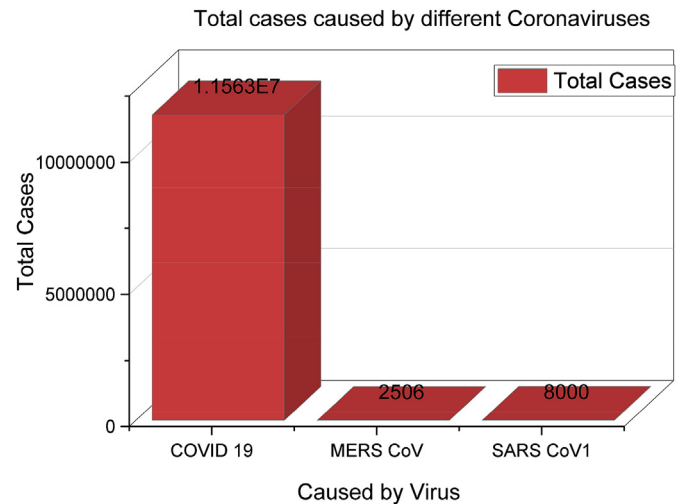


Fig. 2.3B. A comparison of total cases caused by different pandemic causing coronaviruses as of July 5, 2020. Data Collected From Ref. [20,38] (Middle East respiratory syndrome coronavirus (MERS-CoV), 2020).

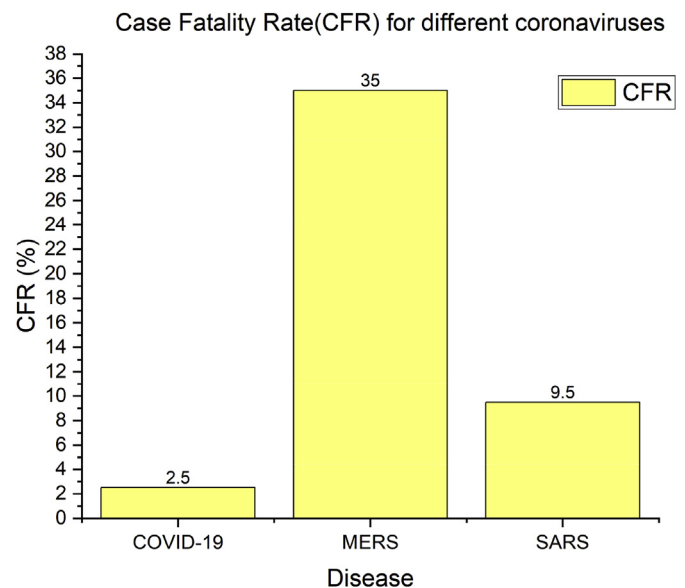


Fig. 2.3C. Case Fatality Rates for different coronaviruses Data collected from [20,33].

Acute Respiratory Distress Syndrome (ARDS) was 8 days [4].

The transmission of COVID-19 occurs mainly through respiratory droplets generated during coughing and sneezing mostly by symptomatic patients however, studies suggest that asymptomatic patients also possess the ability to transmit the virus [4]. The highest amount of viral load is found in the nasal cavity as compared to the throat [48]. These respiratory droplets may spread from 1 m to 2 m and get deposited on various surfaces, where they can remain viable for days. Infection is acquired either by inhalation of droplets or touching a contaminated surface and then touching the nose, mouth, or eyes. There is currently no evidence of transplacental transmission nonetheless neonatal disease due to postnatal transmission is elucidated [28]. Traces of viral load have been found in the stool of infected patients where the virus can be alive until 30 days. It has been also suggested contamination of sewage water and subsequent transmission due to aerosolization or fecal-oral route [43].

COVID-19 and the other deadly beta-coronaviruses are phylogenetically similar but their effects on the population are different in terms of

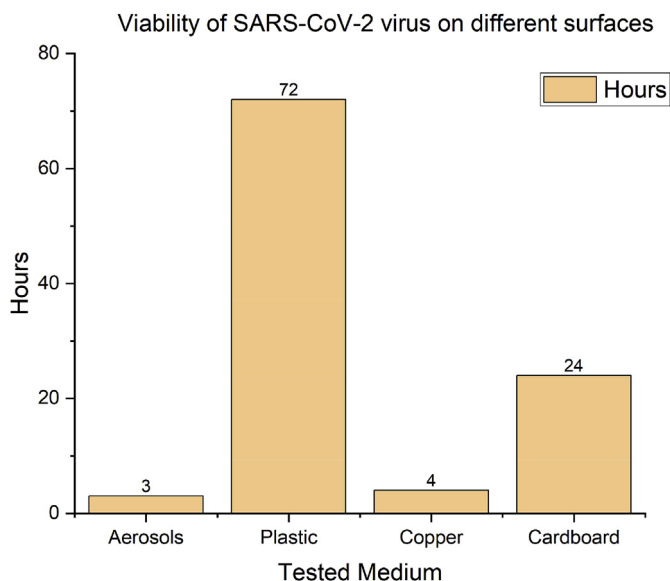


Fig. 2.3D. This Graph depicts the viability of the SARS-CoV-2 virus in different mediums and surfaces.

their reproduction number (R_0) and fatality rate (See Figs. 2.3A, 2.3B and 2.3C)

From the above data, we can infer that the R_0 of COVID-19 is much higher than that of SARS or MERS, hence the total number of cases is also exponentially higher than those of other similar viruses. On the other hand, SARS and MERS are much deadlier than COVID-19 with their fatality rates at 9.5% and 35%, respectively. A greater number of people succumbed to the virus with the ratio of those infected.

Other than the varying R_0 and fatality rate the three viruses are quite similar in their mode of transmission and general effect on the health of an individual suffering from these diseases. All three diseases had bats as their primary reservoir and were crossed with humans via an intermediary host (which is not yet confirmed in the case of COVID-19). The disease is transmitted by human to human contact, generally through respiratory droplets. The viruses cause ARDS (Acute Respiratory Disease Syndrome) in their worst cases forcing the patient to be put on ventilators to aid in their breathing.

According to a research which tested the viruses viability in different mediums and surfaces such as aerosol, stainless steel, copper, and cardboard providing essential information that these surfaces can be easily disinfected within a minute using certain chemicals like sodium hypochlorite, 70–90% ethanol and or hydrogen peroxide (Fig. 2.3D) [16].

2.4. Symptoms and effects of COVID-19

An infected COVID-19 patient can have two major states of infection, the asymptomatic state, and the symptomatic state. The symptomatic stage can develop into Acute Respiratory Disease Syndrome (ARDS) then raising infection can lead to multi-organ failure which can be fatal to the patient. An asymptomatic patient does not exhibit any symptoms of the disease due to high immunity but is still capable of infecting others, this state is extremely dangerous for the community and transmission of the virus. It is impossible to identify an asymptomatic patient without conducting an RT-PCR (Real-time polymerase chain reaction) test which can be difficult for a government institution to conduct on a large scale and limits its ability to identify the amount of spread of the virus in the community [4]. Symptomatic patients exhibit varying levels of severity of the disease, most patients display mild symptoms only like fever, cough, sore throat, headache, myalgia or severe symptoms like ARDS or organ failure (Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), 2020).

Illness Severity in COVID-19 Patients

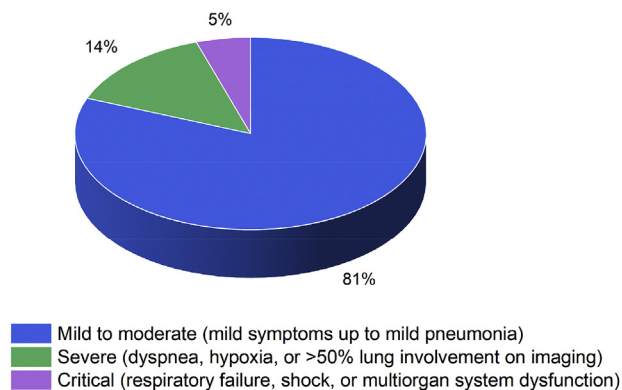


Fig. 2.4A. A Visual Representation of a cohort of >44,000 patients in China and their varying illness severity. Source: (Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), 2020).

Table 1

Table comparing Underlying health conditions with CFR, having comorbidities puts patients at risk of death due to COVID-19. Source: (Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), 2020).

Underlying Health Condition	Case Fatality Rate
Cardiovascular Disease	10.5%
Diabetes	7.3%
Chronic Respiratory Disease	6%
Hypertension	6%
Cancer	6%

ARDS is a type of respiratory failure mainly defined by the onset of inflammation in the lungs especially in the alveoli that helps in gas exchange and maintains the stability of the flow and surface tension of the lungs. In the case of COVID-19, an extreme rise in inflammatory cytokines, monocytes, neutrophils, etc. leads to vasodilation [43] which leads to the symptoms including shortness of breath, rapid breathing, and bluish skin coloration. (Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), 2020) Patients with ARDS are prescribed to be put on mechanical ventilators to aid in their breathing, therefore, the exponential rise in cases has led to an increase in the demand of such ventilators.

From (Fig. 2.4A) it is evident that most patients exhibit mild severity of illness (81%) and only (5%) exhibit critical severity of illness, from this study it was also found that the case fatality rate stood at 2–3% and most deaths (49%) occurred in patients with critical illness severity.

Amongst the most affected by SARS-CoV-2 are the people with underlying medical conditions like cardiovascular diseases, diabetes, respiratory diseases, hypertension, and cancer. Age is another strong risk factor for severe illness, complications, and death. The graph below depicts that the older an individual is, the higher is the case fatality rate (CFR), The (Table 1) illustrates that certain health conditions lead to an increased CFR.

2.5. Prevention

At the time of writing this paper, neither vaccine nor approved drug treatment for COVID-19 is discovered, prevention of the disease is therefore crucial to avoid the transmission. Although certain aspects of the virus pose serious hindrances in prevention aspects, such as no onset of symptoms until an average of 5 days during the 14 days incubation period or in some cases no symptoms, while at the same time the patient is shedding viral load similar to the symptomatic patient and prolonged

duration of the illness and transmission even after clinical recovery. Keeping these aspects in mind there some guidelines suggested by major institutes in a bid to prevent the spread of the virus.

At the community, level to slow the spread initially avoid large gatherings, defer non-essential travel for work or recreation, it is recommended to wear masks whenever heading out of the house for essential work the mask need not be surgical like N95 a simple mask made of cloth would suffice. Further covering of hands with disposable or washable gloves would also stop the spread of the virus. Practice hand hygiene frequently; washing hands with soap for a minimum of 20 s or using an alcohol-based sanitizer with a minimum of 60% alcohol. Practicing social distancing by standing at least 6 feet apart from others and avoiding encountering people having fever, cough, or sneezing. Avoid touching your face or mouth with dirty hands. (Coronavirus disease (COVID-19) advice for the public, 2020).

2.6. The various diagnostic tests for SARS-CoV-2

The increase in diagnostic tests for the detection of the SARS CoV-2 virus is an important factor in controlling the spread of the virus. Numerous patients who are impinged with viral infection are asymptomatic and the most recurrent carries of the virus, hence the major contributors in spreading the disease. This makes the identification of infected patients the foremost phase in battling the SARS- CoV-2.

Since this virus began spreading various studies have been conducted for the development of in vitro diagnostic tests (IVD). This paper focuses on the recent advancements in the field of development of diagnostic tests for COVID 19 [46].

This viral infection can be identified using two different procedures genetic and serological tests, the genetic tests easily detect viral cases that are active but cannot identify any former infections [15].

(1) Serological Tests

These tests are blood centered and help in ascertaining whether the tested person has been exposed to an infection in the past. The antigens present on the virus are recognized by the immune system of the infected person as a foreign body which initiates the formation of specific antibodies against the antigen to aid in fighting the infection. Since SARS-CoV-2 is a novel coronavirus the antibodies formed against this are specific and act as biological markers for the disease. These include tests like ELISA (Enzyme-Linked Immunosorbent Assay), IFA (Immunofluorescence Assay), and Western Blotting [46].

Serological tests identify the existence of IgM and IgG antibodies which act as specific biomarkers of the disease and can be detected using various Immunoassay Techniques. The IgM antibodies can be detected 10–30 days following the infection and the IgG antibodies can be detected 20 days after the infection. The IgM antibodies are produced earlier than the IgG antibodies, but they perish after quite a few days, IgG antibodies live for an extended period and protect against the virus. These tests are explicitly advantageous in identifying people who previously had the infection and have recovered from it [46].

The serological tests provide quick results and are much cheaper in comparison to a genetic test. These serological tests are often paired with genetic tests such as RT-PCR to enhance the sensitivity of detection and to yield confirmatory results [46].

(2) Genetic Test (RT-PCR)

The Reverse Transcriptase polymerase chain reaction (RT-PCR) is the most extensively employed detection analysis for SARS-CoV-2. This test requires nasal and throat swab which is used to directly detect the presence of the virus rather than the antibodies [14].

This test detects the virus's genetic material (RNA) which is present in the patient before the formation of antibodies or visibility of symptoms. With this test, one can detect the presence of the virus at an early stage.

The test proceeds by converting the RNA of the virus to cDNA by a process called "Reverse Transcription" [14].

The RT-PCR targets the Orf1b (Open Reading Frame gene) and N (Viral Nucleocapsid) regions of the virus after its genome was decoded. (WHO) The N-gene assay gives the initial results and the Orf1b assay confirms the diagnosis (frontier). RNA separated and isolated from the samples collected undergoes reverse transcription to form cDNA, which is then amplified in Real-Time Polymerase Chain Reaction thermal cyclers. Probes consist of a reporter dye at 5' end of cDNA and quenching dye at 3' end of the cDNA. The fluorescent signals produced by the reporter dye are absorbed by the quencher dye, thus not emitting any signals. It is during the process of amplification, the probes bonded to the templates are cut by the Taq enzyme which has a 5'-3' exonuclease activity, this separates the reporter dye from the quencher generating fluorescent signals. The PCR instrument automatically draws a real-time amplification curve based on the fluorescent signal change thus giving the final quantitative detection of the SARS-CoV-2 virus at the nucleic acid level. (COVID-19 Coronavirus Real-Time PCR Kit, 2020). RT-PCR can detect the virus in asymptomatic persons, the tests do give a false negative in about 30% of cases. Patients are, therefore, tested twice before being confirmed as non-infectious [14,32].

(3) Point of Care Testing (POCT)

The Rapid Antigen Detecting Test is conducted on swabbed nasal samples that detect antigens found on or within the SARS-CoV-2 virus. It is used to quickly obtain a diagnostic result. In India, this test is conducted on people that fall under the three categories; First, in people portraying influenza-like symptoms in a healthcare setting and presumed of having Covid-19 infection. Second, in asymptomatic patients who are hospitalized or seeking hospitalization, and fall under the high-risk groups; those undergoing chemotherapy, immunosuppressed patients including who are HIV positive, patients diagnosed with malignant disease, transplant patients, elderly patients (over age 65) with comorbidities. Third, in asymptomatic patients undergoing surgical/non-surgical interferences such as elective/emergency surgical procedures like neurosurgery, ENT surgery, dental procedures, and non-surgical intrusions like bronchoscopy and dialysis.

According to USFDA positive results from antigen tests are highly accurate, but there is a higher chance of false negatives, so negative results do not rule out infection. Thus, the negative results from an antigen test need to be confirmed with a PCR test before making treatment decisions or to prevent the possible spread of the virus due to a false negative. (M, 2020).

(3) COVID-19: India's Response and its Effects:

India had been lucky in the initial phase of the spread of the virus with only 3 cases being reported between 30th January and March 1, 2020 in Kerala. The affected being students who had returned from Wuhan. They were successfully treated and discharged by 20th February [38]. India at the same time in a bid to prevent the virus infecting the local population had from February 4, 2020 banned all inbound flights from China and carried out the screening of passengers arriving from South East Asian countries (Govt bans airlines from boarding passengers from China to India, 2020). However, European countries were being allowed unrestricted travel until 2nd March. When two new cases were reported in Delhi [38] these were Indians who had recently been to Italy where COVID-19 cases were on an exponential trajectory and what would later turn out to be one of the most severely affected European countries. Subsequently, more cases started to appear most of which could be traced back to Italy as the origin, by the end of the week there were 48 COVID-19 confirmed cases in India. Following this many states in India started implementing preventive measures and ordered the closing of schools and colleges, issued public advisories to prevent the spread. Till March 24, 2020, most metropolitan states in India were under

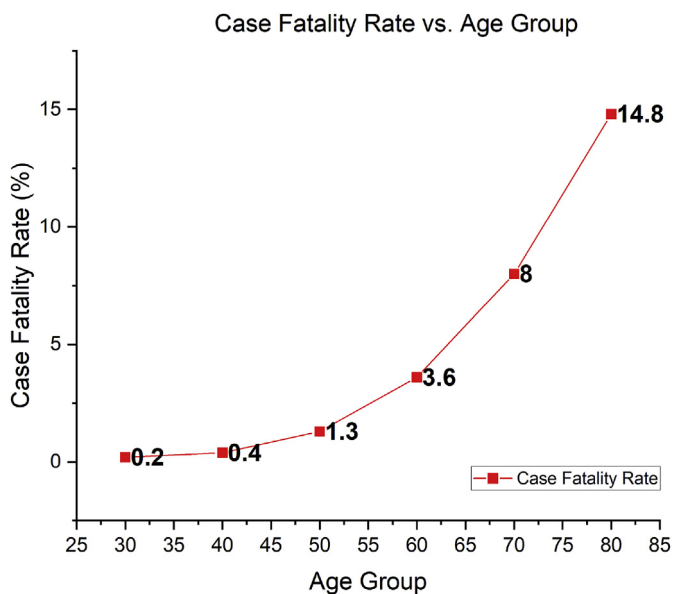


Fig. 2.4B. A comparison of age group and CFR average CFR for all cases is 2.5%. Higher age translates to more risk of death due to COVID-19. Source: (Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19), 2020).

lockdown-barring public gatherings, malls, movie halls, restaurants, and limited public transport. On 25th March, the Government of India implemented a nationwide lockdown to contain the spread. (Annexure to Ministry of Home Affairs Order No: 40-3/2020-D, 2020) (See Figs. 2.4B and 3A)

Following the guidelines from major health institutions and after a week of exponential growth in the number of cases, the Government of India on 25th March imposed a lockdown barring all non-essential work and started what is now known as one of the most stringent lockdowns [34](See Fig. 3B). At the beginning of the lockdown, there were a total of 519 confirmed cases in India and after 67 days of a stringent lockdown, we saw 1.9 lac confirmed cases. Subsequently, after 35 days of Unlock (the name given to a much more relaxed lockdown which allowed

opening up of restaurants, malls, and salons, etc.) we saw a total of more than 6.9 lac confirmed cases in India till July 5, 2020. Total deaths due to COVID-19 stands at 19,707 [38].

We now assess the impact of the lockdown in India on the spread of the virus during the period of 102 days of lockdown. This is reviewed through the perspective of the fundamental ideas on imposing a nationwide lockdown by the health officials who demanded a lockdown as a necessary action against coronavirus.

1. To Flatten the curve so as not to overwhelm the Healthcare infrastructure:

Flatten the curve is a statement used during healthcare emergencies, its basic concept is to limit the spread of the virus such that at any given time during a pandemic the total number of patients required to be hospitalized is less than the maximum capacity of the state's health infrastructure.

When compared to other countries India's doubling rate is a lot less due to early implementation of the lockdown which has helped in bringing down the doubling rate from an initial of five days to nearly thirteen days. Currently, the rate of growth of confirmed cases is at 3.54% [44] and the doubling rate is at 20.11 days [38]. The low doubling rate has also kept the health infrastructure from reaching its maximum capacity thereby reducing potential deaths. This is evident from the fact that on July 5, 2020 India has 3rd highest number of confirmed cases, yet the total deaths stand at 19,700. Countries like Spain and Italy have much less confirmed cases, yet their death figures are at 28,385 and 34,861, respectively [38]. Thus in India, early implementation and stringency of lockdown have played a significant role in reducing total deaths due to COVID-19.

2. To reduce the number of new cases emerging daily and the number of active cases.

This measure is an indicator of the effectiveness of lockdown in containing the virus. It helps assessors realize if the peak number of cases has been achieved by looking at the growth rate of daily new cases; a negative growth rate means peak has been achieved [22,23].

Even after the 102 days of the lockdown, at present, this negative

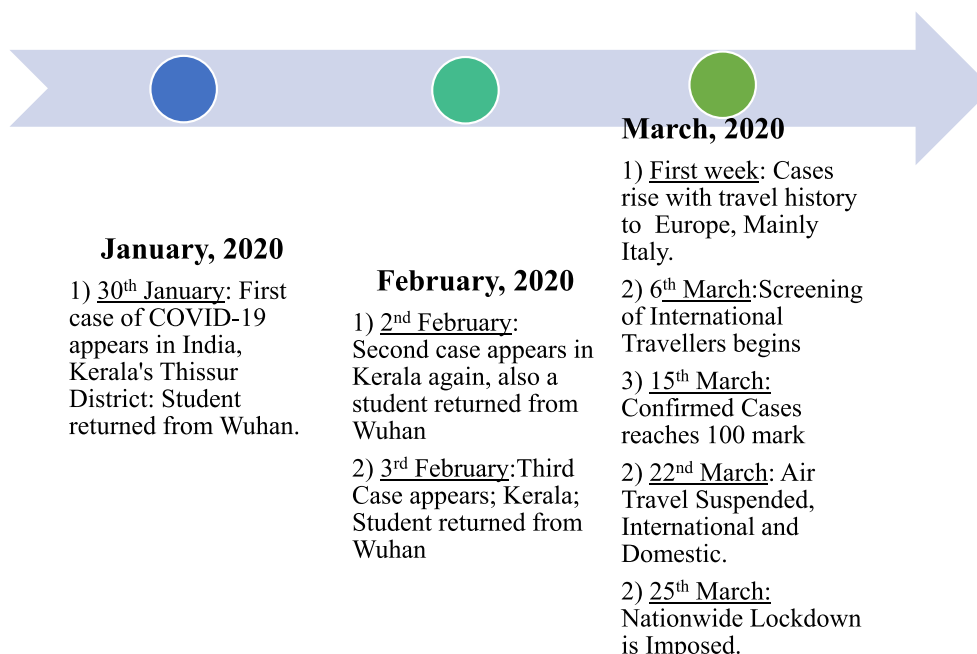


Fig. 3A. Timeline depicting the major events regarding the COVID-19 pandemic in India that lead to the declaration of Nationwide Lockdown.

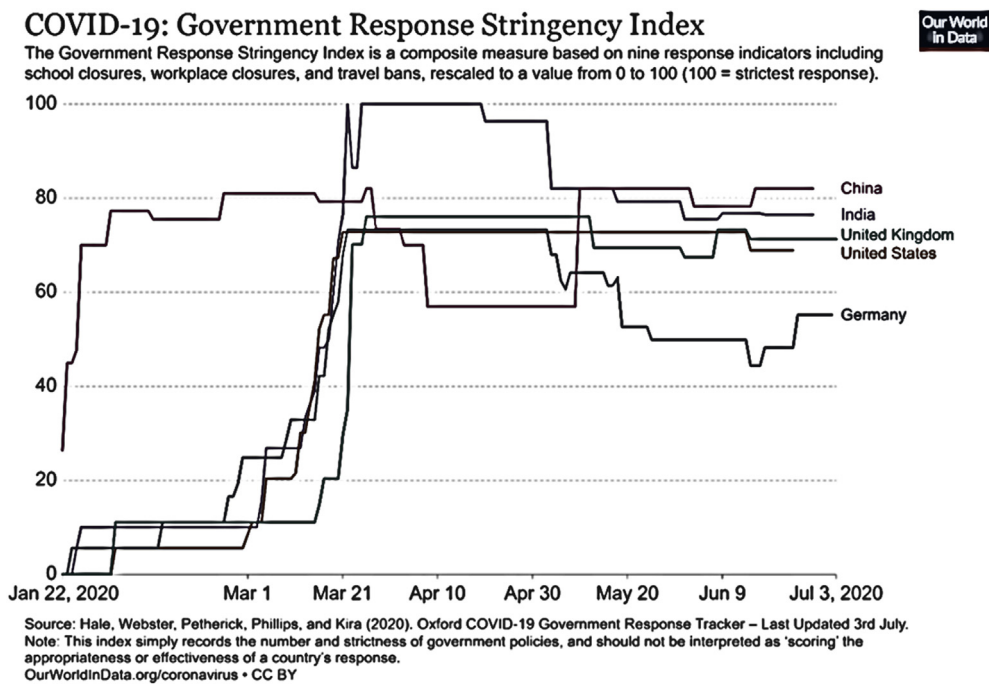


Fig. 3B. A graph of government response to the pandemic depicting the level of stringency, 100 being the maximum amount, from March 25th to April 19th India had the most stringent lockdown in the world. Source [38]. [34]

growth rate in daily confirmed cases has not been achieved except in smaller states like Uttarakhand and Himachal Pradesh and big states like Punjab and Kerala. But most big states; Maharashtra, Gujarat, Delhi, West Bengal, and Tamil Nadu are still reporting a growing number of daily cases indicating that the worst is far from over.

However, the recovery rate of infected patients in India has been on the rise continuously and currently stands at 60.85% [45], and some states like Delhi have a recovery rate of nearly 72% [45]. A higher recovery rate is an indicator of better healthcare facilities available.

3. Containing the virus's spread and preventing its spread to newer districts

When the total number of districts with COVID-19 cases is limited, resources like testing, sanitization, police and healthcare officials can be concentrated at those districts to try and contain the virus and assist those with serious illness however if the number of districts with cases surges, it translates to the distribution of these resources which in turn results in the rise of cases and the extent of virus spread becomes difficult to assess as well as contain without increasing the testing capacity (See Fig. 3 D). It shows that the number of districts without COVID-19 cases dropped significantly even after more than 3 weeks of lockdown, the main reason for such trends could have been the lack of testing in rural districts as well as the exodus of migrants from urban to rural neighborhoods who could have been carriers of the virus, indicating a much wider spread of the disease in urban neighborhoods [29,31].

4. Use this lockdown to boost the healthcare system's capacity.

The lockdown period acts as a pause button on cases requiring urgent medical attention this period can be used to ramp up the infrastructure of hospitals so that when the lockdown is lifted and cases rise medical attention could be given to every serious case thus aiding in preventing potential deaths. Till 15th May, India had made available 970 COVID only hospitals for critical patients along with 2300 COVID-19 health centers for patients with moderate illness, and 645,000 or (0.65 million) isolation beds for suspected cases and patients [26].

Till 12th June, there were 958 dedicated COVID Hospitals with 1,67,883 isolation beds, 21,614 ICU beds, and 73,469 oxygen supported beds. 2313 dedicated COVID Health Centers with 1,33,037 Isolation beds, 10,748 ICU beds, and 46,635 oxygen supported beds. 7525 COVID Care Centers with 7,10,642 beds Ventilators available for COVID beds - 21,494. (India may run out of ICU beds for COVID-19 patients by July end: Study, 2020). Since Unlock 1 was initiated on June 1, 2020 a significant rise in daily confirmed cases was seen, as expected. Early preparation to increase the capacity of health infrastructure had ensured that India could handle this surge [22,23].

(4) COVID-19 Response Strategies by other Countries

1. New Zealand:

On February 3, 2020, after an individual in the Philippines became the first person to die of COVID-19 outside China, New Zealand started banning the entry of foreigners coming from or via China. Any New Zealander returning from China had to isolate for 14 days [25]. At this point, there were no reported cases in New Zealand. Gradually as the virus spread flight bans were extended to Iran which became the place of origin for New Zealand's first case. Restrictions were also placed on people arriving from Italy, The Republic of Korea. From March 16, 2020, everyone coming to New Zealand - had to go into self-isolation upon arrival, this rule was exempted for people coming from largely unaffected Pacific island nations [25]. Then on 19th March New Zealand completely banned the entry of non-residents or non-citizens. Late March, in a bid to prepare the citizens for a continuously changing situation, New Zealand introduced a new four-stage alert system. Which was based on existing wildfire alerts, it would indicate the current risk and the necessary social distancing measures. At the start, the system was at level two, but on 25th March it had risen to level four which triggered a complete nationwide lockdown, with only essential services running and everyone is advised to remain at home [25,36]. At that time New Zealand had recorded only 102 cases and no deaths. During the lockdown, strategies were made to finesse an in-depth testing and contact tracing operation of all new COVID-19 cases. As a result, New Zealand was able to do nearly 10,000 tests daily which was quite enough for their population. On 8th June, The

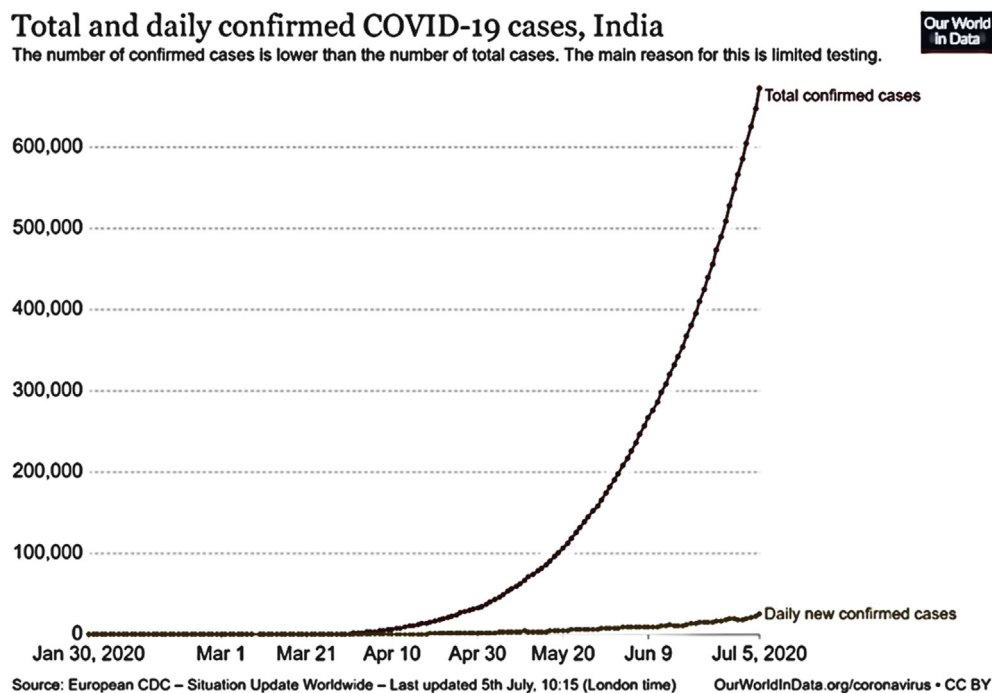


Fig. 3C. Graph illustrating a comparison between the total confirmed cases and the daily new confirmed cases in India. Source [38]

Prime Minister of New Zealand announced that no new community transmissions had been recorded for the past 17 days and all affected patients had fully recovered. The lockdown was lifted, and way of life is now almost entirely back to normal in New Zealand, with some social distancing [25].

2. United Kingdom:

On 31st January 2020 the UK received its first case of COVID-19 [2], unlike most countries the spread in the UK was fast with the first wave of infections. It wasn't until 6th February when the 3rd COVID case was detected in the UK [3] that the government decide to place people coming from South-East Asian Nations under a 14-day mandatory quarantine (COVID-19: guidance for staff in the transport sector, 2020). In-fact the UK never completely sealed their borders during this pandemic although it had made it mandatory for all incoming populace to self-quarantine for 14 days. By March 12, 2020, there were 590 confirmed COVID cases in the UK [38,39], it was on this day that the UK published its first advisory for their citizens asking people with cough and fever to self-isolate for 7 days. Schools were asked to cancel trips abroad and people above the age of 70 were advised to avoid cruises (Coronavirus: People with fever or 'continuous' cough told to self-isolate, 2020). With no respite in-site, the UK again updated its advisory on 16th March which recommended citizens to avoid non-essential travel and contact with others. Citizens were also recommended to avoid Pubs, Clubs, and theatres and try to work from home as much as possible. (Coronavirus: PM says everyone should avoid office, pubs and travel, 2020) On 23rd March Restrictions were placed on citizens with 3 weeks of lockdown. All non-essential activities were suspended, only essential work-related travel was allowed everyone was advised to stay at home unless there was an emergency. (Police can issue 'unlimited fines' to those flouting coronavirus social distancing rules, says Health Secretary, 2020) At that point, the UK had approximately 8000+ cases [38]. The Lockdown was further extended until 8th April and continued until the 1st of June. After 1st June, some relaxations in the lockdown were introduced, allowing some non-essential retail shops to open and primary schools to re-open as well although with mandatory social distancing norms (COVID-19: Non-essential shops to open from June 15 as the UK eases

lockdown, 2020). As of 5th July, the UK has 2,86,141 cases and 40,613 deaths [38].

3. Sweden:

As most countries chose to impose lockdowns to revert the spread of the COVID-19 disease, Sweden took the high road by deliberately choosing an alternative path of self-imposed social precautions without the state decree. At a time when countries were limiting the movements of their citizens with mandatory lockdowns. Sweden kept flights operational, did not seal national borders, no nationwide emergency was announced, no stay-at-home directives were issued, and offices functioned normally while work from home was endorsed. Almost everything from grade schools, hair salons, shopping malls to public transport, Movie Halls, libraries, restaurants, and cafes continued to remain open. The government of Sweden advocated social distancing norms along with citizens above 70 years of age is advised to stay at home. It also encouraged people to work from home as much as possible and abstain from any avoidable international travel or long-distance road travel in the country. The police had no orders to stop and inquire or penalize citizens even if some of them were found in violation of the advisories and restrictions. Result Sweden reported its first case on 15th February. Approximately after a month, Sweden had 1040 cases and three deaths due to the virus. From recorded data, it is revealed that the confirmed cases took 7–9 days to double initially. As the days progressed the doubling rate increased to 15 days and then a month, this indicated that Sweden was in-fact successful in slowing down the spread of the virus. A similar case was seen with the doubling rate of deaths, after reaching 1203 deaths on 8th April, deaths doubled in 15 days and subsequently more than a month [24]. The death count as of 5th July reveals that the doubling rate of death has slowed even further [38]. A reason for such a bold policy by Sweden might have been its trust in Sweden's health architecture which despite having an extremely high number of cases, was never overwhelmed by the disease, unlike what Italy faced. It was noted that despite the high case count, nearly 20% of all ICU beds remained vacant [24]. Sweden's massive investment in its health architecture over the past years has made the system one of the finest, and it has returned the reward in the ongoing COVID-19 pandemic. However, a high number

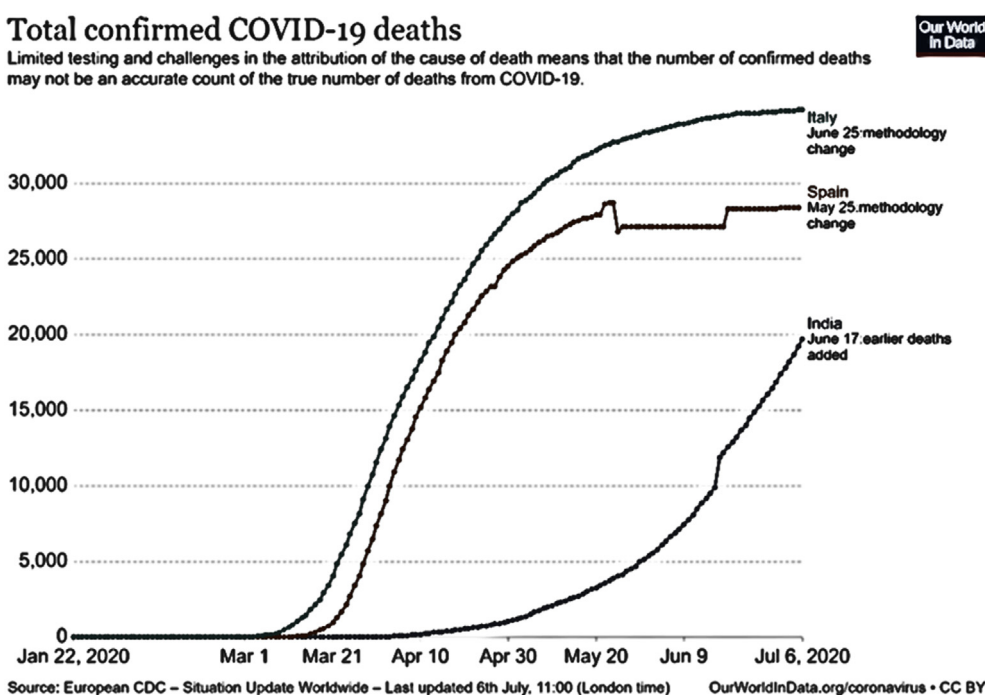
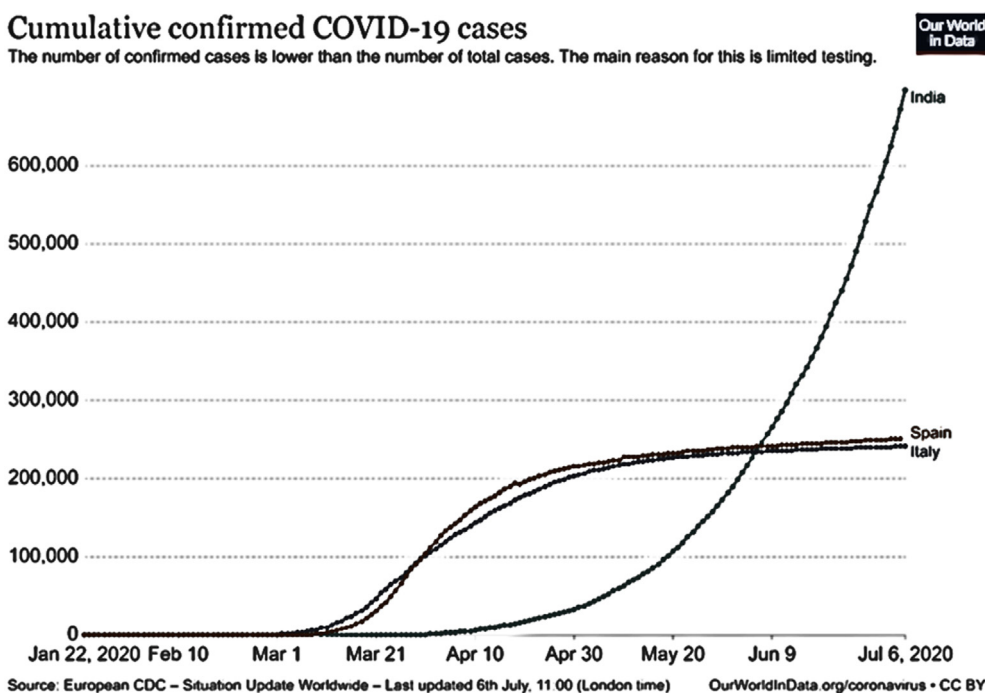


Fig. 3D. Two graphs comparing data of three countries; India, Spain, and Italy. The first graph compares the total confirmed cases of the three countries, India having a significantly higher number. The second graph compares total deaths due to COVID-19, here we see India has a reduced amount of deaths. From Our World in Data [38].

of old-age deaths have become a big concern. On 24th June, the most recorded deaths in Sweden lied in the 80–90 years age group at 2157, which was followed by 1331 deaths in the 90 years and above age group and 1141 deaths in the 70–79 years age group [24,41]. This illustrates the fact that the elderly had to bear the brunt of the disease. Although Sweden was able to slow the spread of the virus, it still had a very high case fatality ratio, particularly among the elderly. A high number of people who got infected died due to the disease as compared to other countries.

4. United States of America:

On 20th January 2020 the very first case of COVID-19 was recorded in the USA [7]. Following this, the government placed travel restrictions on people coming from China with 14-day mandatory quarantine for US citizens traveling back and a complete ban on any foreign national coming through China. In Mid-March after weeks of continuous rise in COVID cases in the US, many states gave orders for social distancing and mandatory lockdowns which included the closing of schools and non-essential services. But the US version of the Lockdown was one of the

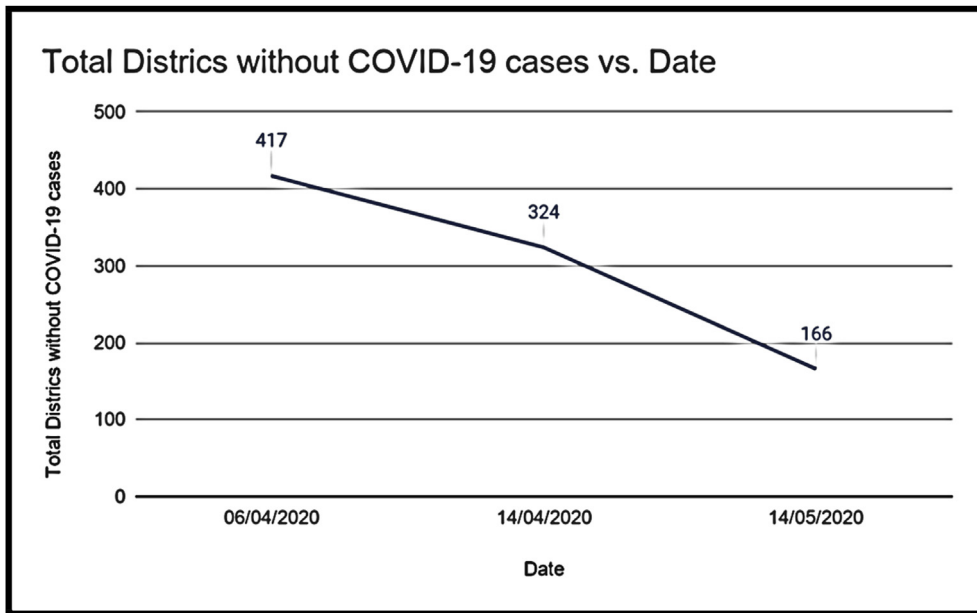


Fig. 3E. This graph depicts the No. of districts without confirmed cases vs date [26].

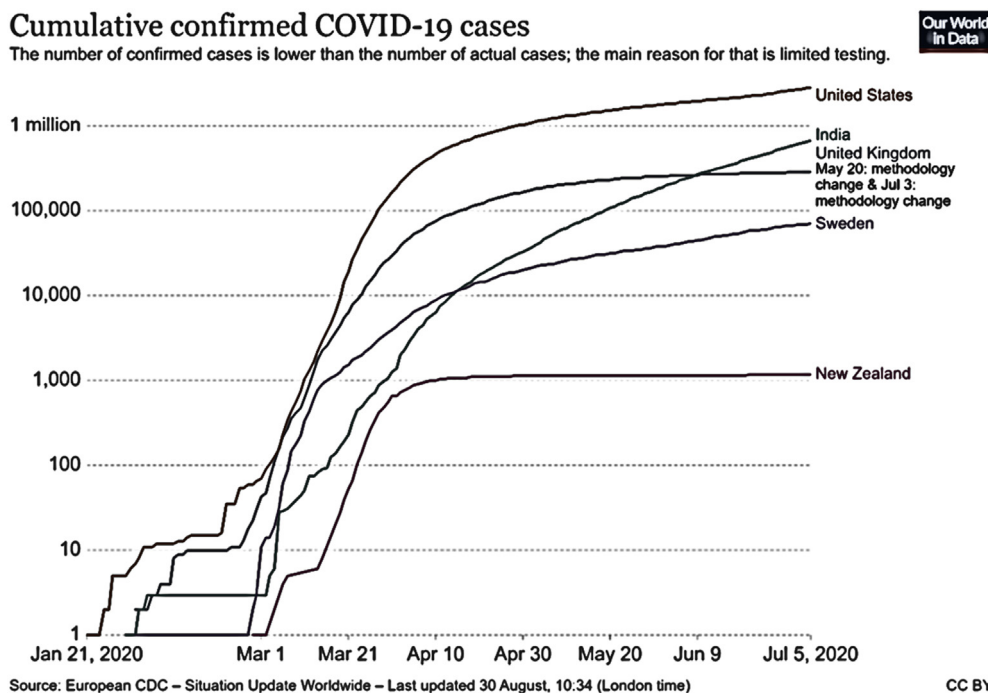


Fig. 4A. Comparison of confirmed COVID-19 cases of countries including India, New Zealand, Sweden, United Kingdom, and the United States of America. The graph highlights the high number of Cases in the USA and India in comparison to the lower number of cases in New Zealand. Source [38]

most lenient ones in terms of stringency index [34] USA government's response to COVID-19 was also one of the slowest responses, which is visible from the fact that the stringency index did not increase until 40 days since the first COVID case in the States. However, one should note that the Stringency Index does not signify the effectiveness of various government responses. In June, like other countries, the USA also started relaxations in the Lockdown which saw an alarming rise in the daily number of cases with a new record being set with a daily rise of 36,000 cases in a day. The United States of America is the worst-hit country by the pandemic with nearly 2.96 million Confirmed cases as of July 5, 2020 and 129,676 deaths [7,38] (see Figs. 3C, 3E, 4A, 4B and 4C).

3. Conclusion

SARS-CoV-2 upon whole-genome sequencing analysis is 95% homogenous to the bat coronavirus and almost 70% similar to the SARS-CoV-1. It belongs to the genus *β-coronavirus* of the subfamily coronavirinae. SARS CoV 2 is a respiratory pathogen which in its worst form of illness causes ARDS and hampers the patient's ability to breathe on his own and has to be put on Mechanical Ventilator Setup. In the past months, ventilators have become a scarce resource with increased hospitalization of patients with ARDS. Many countries and companies have taken this increase in demand as a challenge to manufacture ventilators

Cumulative confirmed COVID-19 deaths

Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.

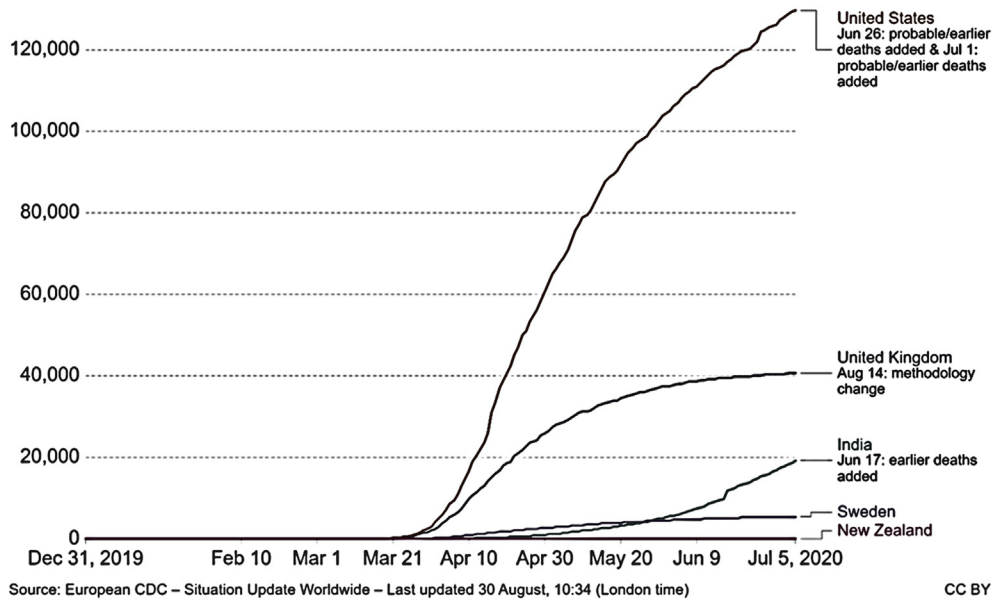


Fig. 4B. Comparison of confirmed COVID-19 deaths of countries including India, New Zealand, Sweden, United Kingdom, and the United States of America. The graph highlights the high number of deaths in the USA and the UK and comparatively low number of deaths in New Zealand and Sweden with the highlight being India which has a much higher case count but a much fewer number of deaths than others. Source [38]

COVID-19: Daily tests vs. Daily new confirmed cases per million

The figures are given as a rolling 7-day average.

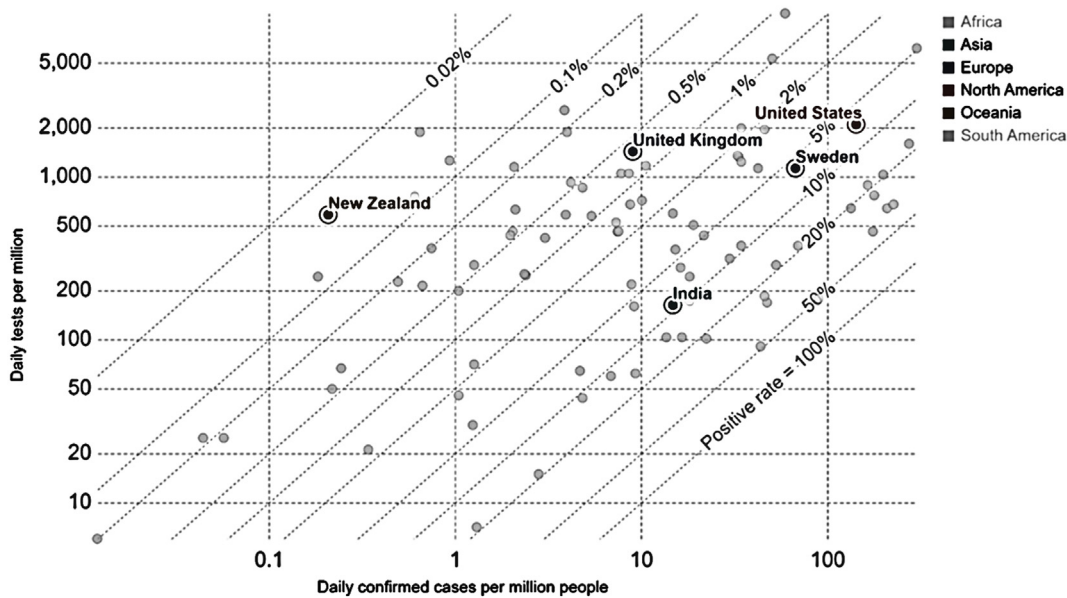


Fig. 4C. A graph showing a comparison between daily tests per million and daily confirmed cases per million and the corresponding Positivity Rate of countries including India, New Zealand, Sweden, United Kingdom, and the United States of America. The graph shows India has the highest amount of positivity rate and New Zealand has the lowest positivity rate. This highlights that the testing figures are quite low in India as compared to the size of the population whereas New Zealand has the highest. Source [38]

in the fastest time possible with minimum resources, to aid in the war against COVID-19. When news broke out COVID-19 disease was infecting people in China most states anticipated it to be an epidemic, even when

WHO declared COVID-19 a public health emergency on January 30th, 2020. Some states did not act accordingly until the middle of March when Italy had become the new hotspot of COVID-19. This lack of

response from states was probably since nobody ever imagined a disease could grip the entire world at such a fast rate and become a pandemic outbreak. However, experts believed a pandemic of such magnitude would have affected the human population sooner or later. Since more than 1.5 million such viruses exist in the wildlife which are unknown and as human populations rise uncontrollably and we continue to uproot trees to progress further into forests, to accommodate this growing overpopulation our interaction increases with wildlife that leads to zoonotic diseases such as COVID-19.

In the case of COVID-19, there is currently no vaccine and the best way for us to come out of this pandemic with minimal human casualties is aggressive social distancing and lockdowns. At the same time relaxation in lockdowns enhances the rate of cases and deaths as we saw after June 1st in India when relaxations were implemented, daily confirmed cases rose significantly. The current review highlights that even though India's lockdown strategy has been able to flatten the curve to a certain extent, it has essentially been unable to create a reversion in this trend or in isolating the disease. Therefore, substantial reforms in policies need to be implemented to seize the spread of COVID-19. This pandemic has resulted in the loss of a lot of lives, clearly indicating the lack of planning and understanding of various biological species that remain a threat to our civilization. Extensive research is still of paramount importance to develop the vaccine and ensure the process of interaction. Every State should be prepared beforehand to avoid such a significant rise in preventable deaths by assessing and studying about the COVID-19 pandemic carefully.

Declaration of competing interest

The authors have no interests to declare.

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Krishna Mohan: Agarwal has done his B. Tech. in Mechanical Engineering from KNIT, Sultanpur in 2000; M. Tech. in Energy from IIT, Delhi in 2007; pursuing a Ph.D. in Mechanical Engineering from Amity University, Noida, and MBA from Kurukshetra University. He is working as the capacity of Assistant Professor Grade III in Amity University Uttar Pradesh, Noida, India since August 2014. He has more than 18 years of teaching, research, and administrative experience. His broad research area lies in the field of Materials & Design (Microstructure and Mechanical Behavior of materials), Energy & Environment (Alternative Fuels for IC engines, Solar Energy), and Business & Management (Management Concepts and Human Resource Management), profkmagarwal@gmail.com



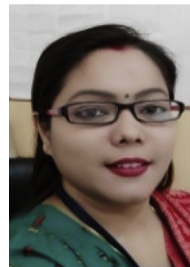
Dinesh Bhatia: pursued his Ph.D. in Biomechanics and Rehabilitation Engineering from MNNIT, Allahabad, India in 2010 with Bachelor's (2002) and Master's degree (2004) in Biomedical Engineering from Mumbai University. He completed his MBA (Dual Specialization) from IMT Ghaziabad in 2007. He is currently working as an Associate Professor in the Department of Biomedical Engineering, North Eastern Hill University (NEHU), Shillong, Meghalaya, India since August 2013. He was selected for the "Young Scientist Award (BOYSCAST)" in (2011–12) by the Government of India to pursue research in osteoarthritis (OA) for one year at Adaptive Neural Systems Laboratory, Biomedical Engineering Department, Florida International University, Miami, Florida, USA where he was leading a multidisciplinary team of researchers. He is also the recipient of the "INAE fellowship award" in 2011 by the Indian National Academy of Engineering. He was selected as one of the twelve young Biomedical scientists by the Indian Council of Medical Research (ICMR), Govt. of India to pursue a research fellowship (2014–15) in the field of sensory prosthetics at the University of Glasgow, Scotland, UK. He has attended Biomechanics and Human Gait training at Munich, Germany in March 2017 and training of use of rTMS, EEG, and EMG equipment(s) in disabled children in Ivanovo, Russia in September 2017. He delivered an Invited Talk on Gait and Osteoarthritis in Kuala Lumpur, Malaysia in August 2018. He has several research papers in reputed journals, conferences, seminars, and symposia with teaching and research experience of more than seventeen (17) years. He is an invited panel member of many professional bodies, editorial boards, committees, societies, and forums. He has worked on several funded projects from the Government of India on physically challenged, disabled, paralyzed persons, environment and waste management and few projects are still ongoing. He authored a book titled "Medical Informatics" published (2015) by PHI, "Current aspects in Stroke Rehabilitation" (2016) by ABS Publishers, "Smart healthcare monitoring for disease diagnosis" (2020) by Elsevier, and two books on ECG and EEG signal processing with Lambert Publishers, Germany (2019). He has published 06 books and 20 book chapters to date and supervised several UG, PG, and doctoral students. His research focuses on understanding muscle mechanics, joint kinematics, and dynamics involved in performing locomotion and routine tasks and undermining its effects during an injury or disease. His areas of interest are medical instrumentation, biomechanics and rehabilitation engineering, medical informatics, signal and image processing, marketing, international business, and environmental sustainability., bhatiadi nesh@rediffmail.com



Shreya Sharma: pursued B. Tech in Biotechnology from Amity University, Noida, Uttar Pradesh, India (2019). She completed her Major Project on the topic Heavy Metals Status of Water and Soil of Okhla Bird Sanctuary and Najafgarh Jheel under the guidance of Assistant Professor Dr.Pamposh Bhat at the Department of Environment Management, Guru Gobind Singh Indraprastha University, Dwarka, New Delhi, India (2019). She also worked upon Alanine Aminotransferase Enzyme Assay in Contrasting Nitrogen Responsive Rice Genotypes under the guidance of Dean of School of Biotechnology Prof.N. Raghuram at Guru Gobind Indraprastha University, Dwarka, New Delhi, India (2018). A nature enthusiast with a green thumb her research interests lie in the field of Microbial Molecular Biotechnology and its application in the field of Environmental Biotechnology, Medical Biotechnology, she is also very enthusiastic about the growing importance of Bioinformatics and its application in biological data analysis, Shreyasharma7942@gmail.com



Prairit Sharma: is currently a 4th year B. Tech (Mechanical Engineering) student from Amity University, Noida, Uttar Pradesh, India. His recent internship on the topic "Design of Physical Structure of ICU Ventilators for COVID-19" with INXEE Systems Pvt. Ltd. led him to research more about COVID-19 when he felt the lack of a compiled holistic guide to the Novel Coronavirus disease. Prairit during his engineering has researched topics like "Aerodynamics of Formula One cars" (2018) and completed projects like "Prototype Construction of an Arduino Controlled CNC Machine" (2019). His interests lie mainly in Design, manufacturing, Material Science, Fluid Mechanics, and Robotics. prairit@gmail.com



Swati Mohapatra: obtained her master's degree in Applied Microbiology from Kalinga Institute Industrial Technology, Bhubaneswar, and Ph.D. on the topic "Bio-prospecting and characterization of polyhydroxyalkanoates from Bacillus sp. isolated from rhizospheric soil" from Odisha University of Agriculture & Technology Bhubaneswar, Odisha, India in 2012 and 2016 respectively. She is currently working as an Assistant Professor in the Department of Microbial Technology, Amity University, Uttar-Pradesh, Noida. She has covered a wide area of expatriation in the field of Microbiology and having more than 6 years of teaching and research experience in the field of Microbiology and Biotechnology,

Her research work pertains to biopolymer & composite materials with its biomedical & agricultural applications. Dr. Mohapatra Awarded with "Young Scientist". She supervised 06 P.G and 01 ongoing Ph.D. students. She has published 32 scientific publications including research, review & popular science articles in different journals of national & international repute and book chapters in different books.

She is also the editor of the book 'Environmental and Agricultural Microbiology: Advances and Applications' to be published by John Wiley & Sons and editorial board member of 'Journal of Chemical Biology and Medicinal Chemistry'. swatimohapatraiit@gmail.com



Animesh Mishra: received his Post-Doctoral Degree DM Cardiology from G.B.Pant Hospital and associated MAMC, New Delhi, Delhi University in 2004. His specific interests lie in the Interventional Cardiology, particularly Heart Failure Management. He is currently a Professor in the Department of Cardiology, NEIGRIHMS, Shillong, Meghalaya, India with teaching and research experience of more than 23 years. He was the recipient of the Indian Society of Cardiology Fellowship (2011), and many other fellowships. He has several publications in reputed journals, books, and members of different Medical and professional bodies.