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COVID-19: Epidemiology and Public Health Aspects

INTRODUCTION

On December 31, 2019, the World Health Organization (WHO) was informed of cases of pneumonia of unknown etiology detected in Wuhan City, Hubei Province of China. A novel coronavirus (2019-nCoV) was identified as the causative virus by Chinese authorities on January 7. Available evidence on the 2019-nCoV virus and previous experience with other coronavirus (MERS-CoV and SARS-CoV) and other respiratory viruses (e.g., avian influenza) suggests that there was zoonotic transmission associated with the 2019-nCoV.^[1] The outbreak was declared a Public Health Emergency of International Concern on January 30, 2020. The WHO has now characterized the outbreak as a pandemic.^[2] A nCoV is a new strain that has not been previously identified in humans.^[3] A corona of large, distinctive spikes in the envelope makes possible the identification of CoV by electron microscopy.^[4] On February 11, 2020, the WHO announced an official name for the nCoV disease: COVID-19. As on March 15, 2020, the initial outbreak in China had spread to 185 countries. Table 1 gives an overview of the current global situation with respect to the top ten affected countries.

EPIDEMIOLOGY

A study of the Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China (2019-nCoV) genome has revealed differences between 2019-nCoV and SARS or SARS-like CoV. A systematic comparison identified 380 amino acid substitutions between these CoV.^[6] The genomic characteristics are important to understand the pathogenesis of the virus [Figure 1].

The main route of transmission is via respiratory droplets or close contact with an infected person, including through fomites. Contact transmission includes contact with oral, nasal, and mucous membranes of the eye.^[7] There is now evidence that exposure to eye may be one of the routes for the virus to enter the human body.^[8] Human-to-human transmission also occurs, as indicated by infection in persons without exposure to wet markets but with exposure to people with respiratory symptoms and by infections among health-care workers.^[9] A review on the potential R_0 showed the average R_0 to be 3.28 and the median to be 2.79 which was more than the WHO estimates of 1.4–2.5.^[10]

In serial nose and throat swabs in several cohorts totaling more than 100 symptomatic COVID-19 patients with exposure in China and Singapore, the highest viral loads were detected within 3 days after symptom onset, with higher viral loads detected in the nose than in the throat, especially in the early stage of illness. Viral loads peaked between 6 and 12 days after symptom onset and were highest in those most

severely ill. Limited experience indicates that no vertical transmission (from mother to fetus or newborn before, during, or immediately after delivery) of SARS-CoV-2 has been reported; SARS-CoV-2 was not detected in samples of amniotic fluid, and all infants tested negative.^[11]

Duan *et al.* assessed the stability of SARS-CoV on surfaces and commonly used materials (including wood, glass, mosaic, metal, cloth, paper [filter and press], and plastic). Viral samples were placed on the surface of these materials and stored at room temperature (20°C [68°F]) over time. The results showed that viral infectivity for cells for samples placed on most of these materials persisted for approximately 60–72 h after exposure. By day 5, low levels of infectivity were detectable from viral samples placed on metal, cloth, and filter paper, but were undetectable in all the other samples.^[12]

Current evidence suggests that the incubation period for COVID-19 ranges from 2 to 14 days. It is possible that the virus may be detectable in the upper/lower respiratory tracks for many weeks after the beginning of the illness. There have been reports of asymptomatic infection with COVID-19.^[13]

CLINICAL MANIFESTATIONS

Frequently reported signs and symptoms of patients admitted to the hospital include fever (83%), cough (82%), shortness of breath (31%), and muscle ache (11%) at illness onset. Imaging showed 75% of patients had bilateral pneumonia.^[14] Approximately 20%–30% of hospitalized patients with COVID-19 and pneumonia have required intensive care for respiratory support.^[7] On admission, ground-glass opacity was the most common finding on computed tomography (56.4%).^[15]

Table 1: Confirmed cases and fatalities in the top 10 affected countries and India as on April 25, 2020^[5]

Country	Confirmed cases	Fatalities	Case fatality (%)*
USA	905,333	51,947	5.7
Spain	219,764	22,524	10.2
Italy	192,994	25,969	13.5
France	159,952	22,279	13.9
Germany	154,999	5700	3.7
UK	144,640	19,567	13.5
Turkey	104,912	2600	2.5
Iran	88,194	5574	6.3
China	83,899	4636	5.5
Russia	68,622	615	0.9
India	24,530	780	3.1
Global total	2,811,891	197,162	7

*Crude rates not adjusted for age, sex, existing comorbidities, etc.

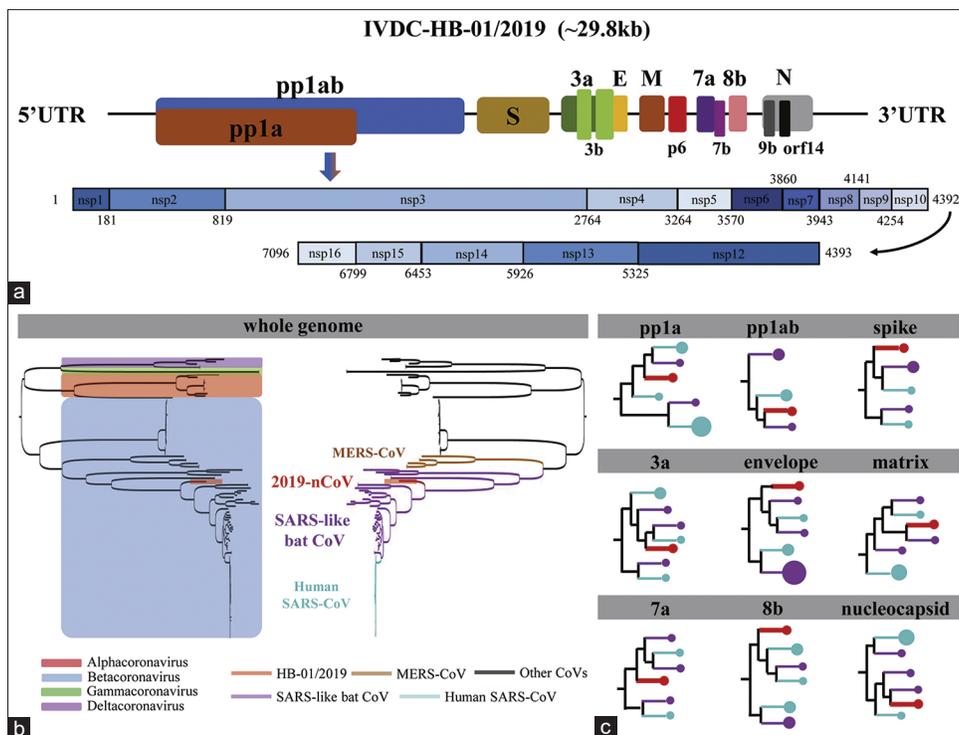


Figure 1: Genome composition and phylogenetic tree for 2019-novel coronavirus.^[6] (a) Schematic diagram of the genome organization and the encoded proteins of pp1ab and pp1a for the IVDC-HB-01/2019 (HB01) strain. The largest gene, namely the orf1ab, encodes the pp1ab protein that contains 15 nsps (nsp1-nsp10 and nsp12-nsp16). The pp1a protein encoded by the orf1a gene also contains 10 nsps (nsp1-nsp10). Structural proteins are encoded by the four structural genes, including spike (S), envelope (E), membrane (M), and nucleocapsid (N) genes. The accessory genes are distributed among the structural genes. The protein-encoding genes of the genome of 2019-nCoV were predicted by the online servers of GeneMarkS (<http://exon.gatech.edu/GeneMark/genemarks.cgi>) and ORFfinder (<https://www.ncbi.nlm.nih.gov/orffinder/>) with manual check. (b) Phylogenetic relationship based on the whole genome for the HB01 strain and other coronaviruses. All viral strains were classified by the genus and the type, which are presented on the left and right schematic phylogenetic trees, respectively. The four genera of the coronaviruses, including Alphacoronavirus (red), Betacoronavirus (blue), Gammacoronavirus (green), and Deltacoronavirus (violet) are blocked in the left phylogenetic tree. The MERS coronavirus (brown), the SARS-like bat coronavirus (violet), human SARS coronavirus (light blue), and the HB01 strain (red) are highlighted by lines of different colors in the right phylogenetic tree. (c) Schematic phylogenetic trees of individual genes for the HB01 strain. The coronavirus species were colored in the same way as (b). The amount of the strains in the phylogenetic clade is denoted by the area of the circles. Reproduced with permission from Elsevier

No specific treatment for COVID-19 is currently available. Clinical management includes prompt implementation of recommended infection prevention and control measures and supportive management of complications, including advanced organ support if indicated. Remdesivir, an investigational broad-spectrum antiviral with an inhibitory effect on SARS-CoV-2, and the only drug thought to have real efficacy against SARS-CoV-2, has begun clinical trials in the U.S. to evaluate its efficacy in treating laboratory-confirmed, hospitalized adult COVID-19 cases.

Additional drugs thought to have an inhibitory effect include chloroquine and lopinavir/ritonavir. Usual antiviral drugs (including oseltamivir [Tamiflu] and acyclovir) are ineffective. The current advice is that steroids should not be used.^[16]

PUBLIC HEALTH MEASURES TO CONTAIN AND PREVENT INFECTION WITH CORONA VIRUS

Effective public health measures include social distancing, contact tracing, and surveillance as also containment of the

disease by the public health authorities. Social distancing is an important tool to flatten the curve of the pandemic. A few examples of these are given as broad guidelines, at the workplace and protective measures for health care facilities.

Interventions at Community and Healthcare levels

Social distancing prevents illness, delays and lowers the epidemic peak, and prevents the health systems from being overwhelmed. The aim is to maintain at least 2 m (6 feet) distance between individuals. Tables 2 and 3 give examples of physical distancing and other protective measures at different levels.

Containment of the corona virus pandemic

The basic principles of contact tracing, testing, quarantine, isolation, treatment and public health hygiene (cough etiquette, hand hygiene, physical distancing) are the cornerstone for containing this pandemic. The WHO has a guideline in place for surveillance of human infection with coronavirus disease.

Case definitions for global surveillance of human infections with COVID19 are as follows.^[17]

Table 2: Interventions at various levels**Action to be taken by individuals without respiratory symptoms in the Community**

Avoid crowds and gatherings
 Physical distancing: Maintain at least a 2 m distance from anyone
 Frequent hand hygiene - wash with soap and water for at least 20 s
 Use alcohol based hand rub with >60% alcohol
 Observe cough etiquette - cough into tissue to be then properly disposed of or cough into your elbow
 Refrain from touching your mouth and nose
 Postpone all nonessential travel
 Don't greet by handshakes. The traditional Indian Namaste would be a useful alternative

Interventions at Workplace

Explore options for working from home
 Have a policy on number of people using an elevator at the same time
 Explore staggered working - alternate days, different timings
 Ensure that a given workstations are at least 2 m away from each other
 Use video conferencing instead of face to face meetings
 Postpone all workshops during the time of the epidemic
 Have a temperature screening at the workplace
 Shut down all nonessential work areas
 Consider site closure if community transmission is happening
 Wear a mask when physical distancing is an issue

COVID: Coronavirus disease

Suspect case

(A) A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease (e.g., cough, shortness of breath), AND with no other etiology that fully explains the clinical presentation AND a history of travel to or residence in a country/area or territory reporting local transmission of COVID-19 disease during the 14 days prior to symptom onset OR.

(B) A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case (see definition of contact) in the last 14 days prior to onset of symptoms OR.

(C) A patient with severe acute respiratory infection (fever and at least one sign/symptom of respiratory disease (e. g., cough, shortness breath) AND requiring hospitalization AND with no other etiology that fully explains the clinical presentation.^[17]

Probable case

A suspect case for whom testing for COVID-19 is inconclusive.

Confirmed case

A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

Coronavirus disease 2019 containment strategy in India

The Government of India has a robust containment plan for COVID-19. It focusses on surveillance and contact tracing through the integrated disease surveillance program. Early diagnosis is through a network of laboratories.^[18] As a part of the containment strategy the Government of India has

strengthened cluster containment to stop transmission, morbidity, and mortality due to occurrence of an unusual aggregation of health events pertaining to COVID-19 that are grouped together in time and space and reported to a health agency, as depicted in Table 4.

The surveillance would include contact listing, mapping the containment and buffer zones, contact tracing through active surveillance as also testing and hospitalization where needed. Any discharge after hospitalization would be governed by two consecutive samples testing negative and the patient to be free of symptoms. In addition to the above surveillance protocol, the government's strategy toward social distancing includes closure of theaters, schools, colleges, and workplaces wherever needed. Cancellation of mass gatherings, avoidance of public places, and cancellation of public transport are other tools to prevent the COVID-19 from spreading.

The Indian Council of Medical Research (ICMR) has recently come out with guidelines for testing for the nCoV.

Indian Council of Medical Research Revised coronavirus disease 2019 testing strategy in India

In an evolving strategy, the ICMR had the following initial strategy (March 17 notification). The guidelines were as follows:^[19]

1. All asymptomatic people who have undertaken international travel: They should stay in home quarantine for 14 days. They should be tested only if they become symptomatic (fever, breathing, etc.). If the test result is positive, they should be isolated and treated as per standard protocol
2. All contacts of laboratory-confirmed positive cases: They should stay in home quarantine for 14 days. They should be tested only if they become symptomatic (fever, breathing, etc.). If test result is positive, they should be isolated and treated as per the standard protocol
3. Health-care workers managing respiratory distress/severe illness should be tested when they are symptomatic.

Later, on April 4, the ICMR added antibody testing to its strategy. The antibody testing flowchart is shown in Figure 2.^[20]

On April 17, the ICMR released the guideline for testing in hot spots using a mix of reverse transcription polymerase chain reaction (RT-PCR) (within 7 days of illness) and antibody testing (after 7 days of illness, to be confirmed by RT-PCR if negative).

The ICMR also recommends testing of all patients with severe acute respiratory illness as also asymptomatic direct and high-risk contacts of a confirmed case (to be tested between day 5 and day 14 of coming in contact).

Lockdown as a means of flattening the curve

Recently, as a part of the containment strategy, the Government of India instituted a nation-wide lockdown effective March 25, 2020, which was then extended on April 14, to last till the May 3. The lockdown is expected to flatten the curve and

Table 3: Protective measure for health-care facilities**For patients with respiratory symptoms**

Wear a medical mask while waiting in triage or waiting areas or during transportation within the facility
 Wear a medical mask when staying in areas dedicated to suspected or confirmed cases
 Do not wear a medical mask when isolated in single rooms but cover mouth and nose when coughing or sneezing with disposable paper tissues
 Dispose them appropriately and perform hand hygiene immediately afterward

For health-care workers

Wear a N 95 mask when entering a room where patients suspected or confirmed of being infected with 2019-nCoV are admitted and in any situation of care provided to a suspected or confirmed case

Table 4: Scenarios for determining containment and buffer zones

Scenario	Containment zone details
A small cluster in closed environment such as schools, hostels or hospital	Zone determined by mapping of persons including cases and contacts. A buffer zone of additional 5 km radius will be defined
Single cluster in a residential colony	Administrative boundary of the colony and a buffer zone of 5 km radius. Risk assessment to guide buffer zone
Multiple clusters in communities within an administrative jurisdiction	Administrative boundary of the urban district and a buffer zone of neighboring urban districts
Multiple clusters separated in different administrative jurisdictions	Administrative boundary of city and an additional area in the periurban areas based on risk assessment
Cluster in a rural setting	3 km of containment zone and additional 7 km of buffer zone

reduce the number of fresh cases as also mortality arising from fresh cases.

A recent paper on the potential impact of the lockdown on the number of cases has mathematically modeled the impact of a lockdown and has suggested various scenarios for duration of lockdown which will have a maximal impact. Figure 3 depicts the modeling done by Singh and Adhikari.^[21]

However, the increase in cases took a different turn after it turned out that many members from a congregation in Delhi (March 1 to 15) tested positive for COVID-19 and indeed travelled to different parts of India during March. This led to a spike in cases contributing to quite a bit of the increase in cases after March 28. The Government of India's contact tracing mechanism has helped in tracking more than 9000 of the contacts to ensure quarantine, testing, and treatment where required.

Figure 4 depicts the actual progress of the positive cases in India till date. It can be observed that this is at quite a variance from what has been projected in the Oxford modeling. The key aspect to be observed is that the cases while increasing have not grown at an exponential rate but show a linear increase indicating that the lockdown measures have been successful in keeping the increase to manageable proportions. It is expected that if the current trajectory continues in terms of containment and increasing the time taken to doubling of cases, India should be able to flatten the curve in the next 4–6 weeks. The daily number of cases as seen in the Figure 4 is not increasing in an exponential manner.

THE CONTROVERSY AROUND IMMUNITY PASSPORTS AND THE VALUE OF ANTIBODY TESTING

The WHO has addressed the suggestion of providing

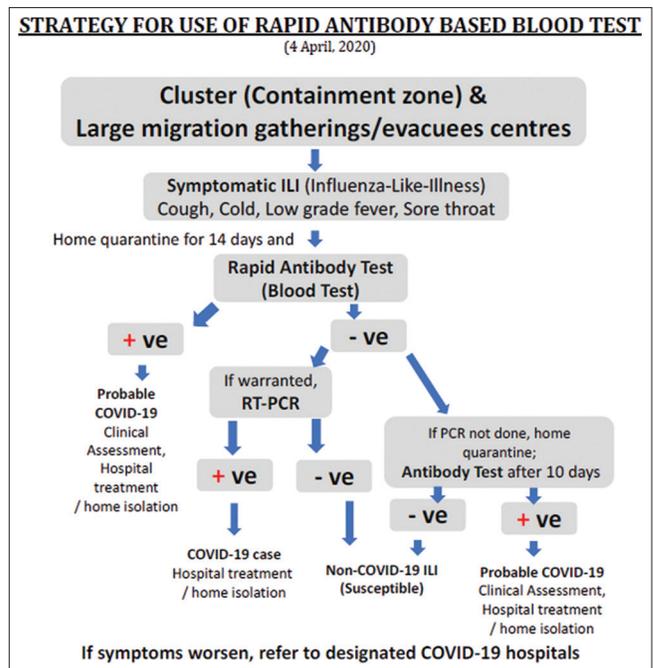


Figure 2: Indian Council of Medical Research guideline on use of rapid antibody-based blood test

immunity passports to those who would have antibodies to the COVID-19. The WHO brief is important in the context of some countries and business organizations mooting immunity passports as a criterion for return to work.

In a scientific brief,^[22] dated April 24, the WHO has said that while some governments have suggested that the detection of antibodies to the SARS-CoV-2 could serve as the basis for an “immunity passport” or “risk-free certificate” that would enable individuals to travel or to return to work ; there is

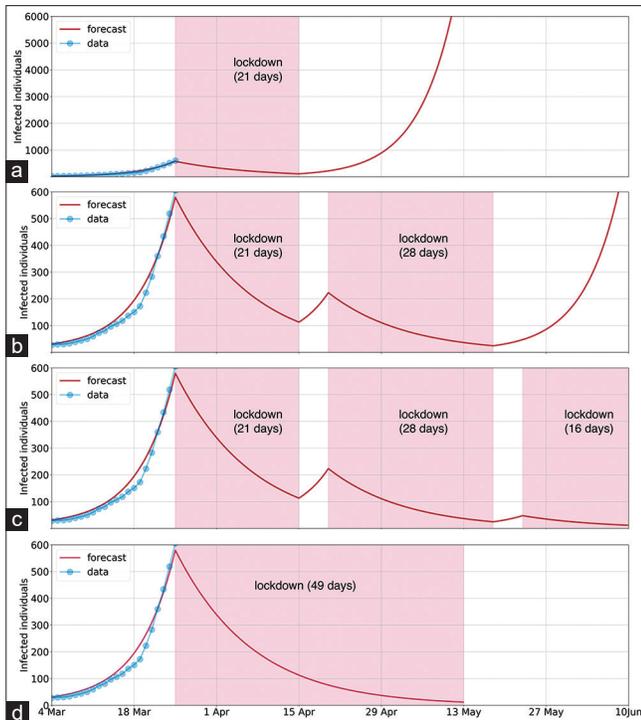


Figure 3: Mathematical modeling of the lockdown and its impact on potential coronavirus disease-2019 cases. Forecast of the coronavirus disease-2019 epidemic in India with mitigatory social distancing. Each of the four panels shows the variation in the number of infectives with lockdowns of various durations. The 3-week lockdown starting 25 March does not prevent resurgence after its suspension as shown in panel (a). Neither does a further lockdown of 28 days spaced by a 5 days suspension, shown in panel (b). The protocols in panels (c and d), comprising three lockdowns with 5 days relaxations and a single 49 days lockdown reduce case numbers below 10. This forecast is based on all cases being symptomatic so $\alpha^- = 1$. The fit parameter is $\beta = 0.0155$ and we set $\gamma = 1/7$

currently no evidence that people who have recovered from COVID-19 and have antibodies are protected from a second infection. In fact, they may ignore public health advice and increase the risk of continued transmission.

Inaccurate immunodiagnostic tests may falsely categorize people in two ways. The first is that they may falsely label people who have been infected as negative, and the second is that people who have not been infected are falsely labeled as positive. Both errors have serious consequences and will affect control efforts. These tests also need to accurately distinguish between past infections from SARS-CoV-2 and those caused by the known set of six human CoV. Four of these viruses cause the common cold and circulate widely. The remaining two are the viruses that cause MERS and SARS. People infected by any one of these viruses may produce antibodies that cross-react with antibodies produced in response to infection with SARS-CoV-2

Key questions

As the world gears up to control the pandemic, there are still a few concerns about the nCoV.

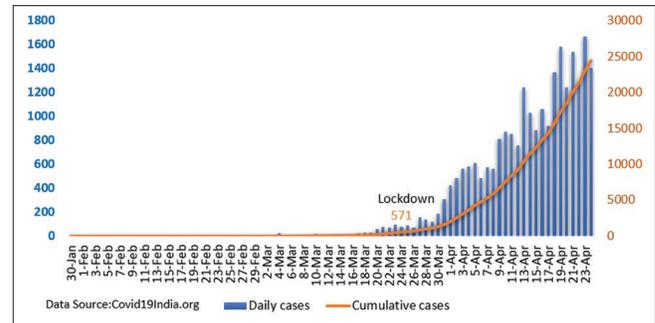


Figure 4: The progress of coronavirus disease-2019 positive cases in India

1. How will this virus behave in future? Will it mutate?
2. Will there be a second wave of the viral outbreak in winter? How virulent would that be?
3. A vaccine is a good distance away. Will we get one within the next 12–18 months?
4. While the antiviral drug remdesivir is undergoing trials, is there a cure in sight?
5. How can public private partnership forge innovation for cures and vaccine development?
6. How long does any immunity to the COVID-19 last?

CONCLUSION

While the COVID-19 has affected millions of people around the world, an early lockdown strategy in India has prevented a runaway increase in cases and deaths. With a CFR of around 3%, a manageable number of overall cases and an increase in testing capacity – currently India's overall testing is >400 tests/million population and increasing daily with some parts of the country doing significantly more testing with the overall tests done till date standing at 579,957,^[23] it is expected that the overall strategy along with rigorous contact tracing and associated measures will help India flatten the curve. We need to understand that any lift of the lockdown needs to be gradual with hotspots and other containment zones being eased only after confirmation of no fresh transmission in these areas.

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Conflicts of interest

There are no conflicts of interest.

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