



COVID 19: THE BATTLE CONTINUES

Microbiology

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ABSTRACT

COVID-19 Pandemic' is an 'Unimaginable Storm' in the 21st Century which has challenged the Global Health Community's Preparedness. The novel coronavirus infection – Covid 19, Being a 'Novel Coronavirus', there is currently 'NO HUMAN IMMUNITY' and, therefore, the 'PANDEMIC' was a matter of time. It is a reminder of the hazard that coronaviruses pose to public health. This review is an attempt at providing an outline on the current preparedness and strategic measures undertaken by India, Treatment and Prevention of COVID-19 and some Unresolved issues. Preventive measures are the only answers to halt the march of the COVID-19, as there is still no definitive treatment and vaccines are still in trial stages. Despite an army of Government officials, microbiologists and the entire medical fraternity working towards the containment of this novel coronavirus virus(COVID-19), it continues to spread at an alarming rate infecting multitudes and claiming hundreds of lives thus unfortunately the battle continues to contain and control.

KEYWORDS

INTRODUCTION

The month of December marked the dawn of an era of pandemic on the Chinese horizon, the world woke up with a start and witnessed the emergence of coronavirus disease 2019 (COVID-19). The year 2020 will always be remembered in history as the year of the deadly Wuhan coronavirus. The cases clinically resembled viral pneumonia while showing an epidemiological link to the Huanan Seafood Wholesale Market, where the sale of live animals was taking place. Based on the lessons learned during the previous coronavirus epidemics, China was able to recognize the outbreak within the first few weeks, sequence the viral genome and share the data internationally. This paved the way for the development of rapid assays, as well as vaccine development initiatives throughout the world.

The causative agent of the mystery pneumonia has been identified as a novel coronavirus through deep sequencing and etiological investigations carried out by at least 5 independent laboratories of China. The World Health Organization (WHO) announced an official name for the disease caused by the novel coronavirus as COVID-19 on 11th February 2020. On the same date, the International Committee on Taxonomy of Viruses announced 'severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)' as the name of the new virus because the virus is genetically related to the coronavirus responsible for the SARS outbreak of 2003. A majority of initial cases gave a history of direct or indirect contact with the Wuhan Huanan Seafood Wholesale Market, which is believed to be the place of origin of the outbreak of the COVID-19. On 31st January 2020, the WHO declared the outbreak a 'Public Health Emergency of International Concern. On 11th March 2020, the WHO declared COVID-19 as a pandemic. The sporadic renaissance of new coronaviruses (CoVs) is a stark reminder of the incessant threat of zoonotic diseases and their devastating health and economic impact.

INDIAN SCENARIO

According to the Ministry of Family Welfare, the current status update of SARS-CoV-2 (COVID-19) in India as on 02 September 2020, 08:00 IST is as follows

A cumulative total of 4,43,37,201 samples have been tested up to 01 September 2020. Number of samples 10,12,367 tested on 01 September 2020. The total no of active cases are 21.26% (801282), discharge are 76.98% (2,90,1908) and the deaths are 1.76% (66,333).

The Ministry website notes that: India has taken preemptive and proactive response to COVID-19 pandemic, motivated with high-level political commitment. The Indian Government is working to enhance preparedness and has already declared COVID-19 a 'notified disaster'. and is the largest country to have burden of the virus with no sign of flattening of the curve

Contributions of Microbiology fraternity

Microbiologists had a vital role to play as the pandemic struck the world. Beginning from the identification of the causative agent and

sequencing of the viral genome to deciphering the phylogenetic aspect. Furthermore, developing protocols for specimen collection and handling; strategies for testing; setting up the laboratory with BSL requirements; working towards novel and cost-effective diagnostic tests; establishing and supervising the infection prevention and control measures.

INDIA FIGHTS BACK

Prime Minister of India, exercising his powers under section 6 (2) (i) of the Disaster Management Act, 2005, issued orders of complete lockdown with effect from 25th March 2020. All travelers, returning from or having visited any COVID-19 affected region during their travel after 15th February 2020 were to be quarantined for a minimum of 14 days. Screening of passengers was done across all airports, seaports and border crossings.

Preparedness of healthcare Sector

Community surveillance, isolation wards, quarantine facilities, infection prevention, trained workforce and risk communications and community engagement for COVID-19 are being further strengthened for day-to-day operations. Since the lockdown, there has been mass production as well as the import of personal protective equipment, disinfectants, hand sanitizers, ventilators and other respiratory support systems.

COVID-19 and Universal Safety Precautions

Washing hands is the first line of defense against viruses such as coronavirus. Fear of the public for COVID-19 has significantly contributed towards maintaining the personal hygiene of the individuals. Governments and other organizations have succeeded in promoting the universal safety precautions such as washing hands, covering nose and mouth while coughing and sneezing, use of sanitizers, use of face masks, avoiding contact of fingers with mouth, nose and eyes, and social distancing techniques to a remarkable extent. Several cities and states across the world are currently short of hand sanitizers and face masks, which shows the public's interest in acquiring the universal precautions to a remarkable extent.6 Furthermore, in many countries, efforts are in place to demonstrate proper handwashing and mask usage techniques. Social distancing is a sage practice and an obvious action to be followed during outbreaks for preventing the spread of disease by confining the interaction of individuals and groups. Unfortunately, in India, social distancing measures and proper use of masks are still not in place as a result, hospitals were filled to capacity, and a rapid transmission was observed, which had led to a steep spike in newer infections.

A recent modelling study has predicted that if social distancing measures were implemented one week, two weeks and three weeks earlier in China, it could have reduced the number of new cases by 66%, 86%, and 95%, respectively. Furthermore, a New York Times model for the USA has suggested that aggressive social distancing measures could reduce COVID-19 cases from a possible peak of 9 million to 513 000 and cumulative deaths from 982 000 to 51 000 over

the next few months.¹⁰ Similarly, by adopting the community mitigation measures such as social distancing, countries like South Korea, which experienced a severe outbreak in its initial days, is now remarkably declining its epidemic curve.

Current preparedness and strategic Measures to halt COVID-19

The number of cases has now become significant and the focus has now shifted to testing with optimum capacity, preventing mortality and localizing the infection as the country has entered into the phase of unlocking step by step. A significant leap has been seen in the testing capacity throughout the country. As per the Press release on 22nd August, 2020 - in fight against covid 19 India scaled a new peak in daily testing a record of 10 lakhs test per day.

Whereas, viral diagnostics was earlier confined to a handful of government-approved Viral Research and Diagnostic Laboratories, but now total Operational (initiated independent testing) Laboratories reporting to ICMR are:

Government laboratories : 1019

Private laboratories : 595

- Real-Time RT PCR for COVID-19 : 819 (Govt: 464 + Private 355)
- TrueNat Test for COVID-19 : 673 (Govt: 521 + Private: 152)
- CBNAAT Test for COVID-19 : 122 (Govt: 34 + Private: 88)

Total No. of Labs : 1614

National Institute of Virology, Pune of the ICMR remains the apex laboratory for quality assurance for the testing for COVID-19.

In India, we follow the updated case definitions as released by the Government of India. The case definition has been updated time to time by the National Centre for Disease Control, Directorate General of Health Services Ministry of Health and Family Welfare (MOHFW), Government of India. The updated definition is as follows-

Suspectcase:

A patient with acute respiratory illness {fever and at least one sign/symptom of respiratory disease (e.g., cough, shortness of breath)}, 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

A patient/Health care worker with any acute respiratory illness AND having been in contact with a confirmed COVID-19 case in the last 14 days prior to onset of symptoms; OR

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; OR

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

Laboratory Confirmed case:

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

Updated definition of contact:

A contact is a person that is involved in Providing direct care without proper personal protective equipment (PPE) for COVID-19 patients

Staying in the same close environment of a COVID-19 patient (including workplace, classroom, household, gatherings).

Traveling together in close proximity (1 m) with a symptomatic person who later tested positive for COVID-19.

High Risk Contact:

Touched body fluids of the patient (Respiratory tract secretions, blood, vomit, saliva, urine, faeces)

Had direct physical contact with the body of the patient including physical examination without PPE.

Touched or cleaned the linens, clothes, or dishes of the patient.

Lives in the same household as the patient.

Anyone in close proximity (within 3 ft) of the confirmed case without precautions.

Passenger in close proximity (within 3 ft) of a conveyance with a symptomatic person who later tested positive for COVID-19 for more than 6 hours.

Low Risk Contact:

Shared the same space (Same class for school/worked in same room/similar and not having a high-risk exposure to confirmed or suspect case of COVID-19).

Travelled in same environment (bus / train / flight / any mode of transit) but not having a high-risk exposure.

Current patient testing criteria (Version 5, dated 18/05/2020)

To contain the spread of COVID-19 infection in India, ICMR has given its revised strategy for testing. ICMR recommends testing of all symptomatic (ILI symptoms- acute respiratory infection with fever $\geq 38^{\circ}\text{C}$ AND cough) individuals ,with a history of international travel in the past 14 days, with contacts of laboratory-confirmed cases, health-care workers/frontline workers involved in containment and mitigation of COVID-19, within hotspots/containment zones, among returnees and migrants within 7 days of illness; all patients of Severe Acute Respiratory Infection; asymptomatic direct and high-risk contacts of a confirmed case to be tested once between day 5 and day 10 of coming into contact and all hospitalized patients who develop ILI symptoms. The emergency procedure should not be delayed for the lack of test.

LABORATORY DIAGNOSIS

Specimen and collection

Diagnostic testing for COVID-19 is critical to tracking the virus, understanding epidemiology, informing case management and to suppressing transmission. The surveillance definitions provided by the WHO has been depicted in [Table 2]. The WHO recommends the collection of both nasopharyngeal and oropharyngeal swabs for the diagnosis of COVID-19 (As per the WHO guidelines 19th March 2020). Other respiratory specimens that can be collected include sputum, endotracheal aspirate, bronchoalveolar lavage or tissue from biopsy or autopsy. Paired serum for serological testing of antibodies against pan-coronavirus can also be collected (acute-1st week of illness and convalescent-2–3 weeks later). ICMR has approved a few rapid antibody detection kits for COVID-19, where a positive test indicates exposure to SARS-CoV-2; a negative test does not rule out COVID-19 infection. To contain the spread of COVID-19 infection in India, ICMR has given its revised strategy for testing

Transport of Specimen

For the transport of samples for viral detection, viral transport medium should be used. All samples should be transported to the laboratory at 2°C - 8°C , if ≤ 5 days and -70°C (dry ice), if > 5 days. All specimens to be transported in triple packaging consisting of a leak-proof primary receptacle covered with absorbent material, a secondary package of the sealed plastic bag and a rigid outer box with cushioning material. The package should be properly labelled and be accompanied by a duly filled requisition form and bills. Biosafety level 2 facilities are recommended for diagnostic testing.s

Various methods of testing

Real Time RT-PCR is the gold standard test for detecting cases of COVID-19. Average time taken is around 4-5 hours from receipt of sample to getting the result. In view of the specialized laboratory requirements, this test cannot be performed at every district level lab which do not have molecular virology facilities. However, wherever available, it is advised to use real time RT-PCR as the frontline test for diagnosis of SARS-CoV-2.

The TrueNat and CBNAAT systems have also been deployed for diagnosis of COVID-19 in view of availability of customized cartridges. These platforms have widespread availability even at district and primary health center level as these platforms are widely used for diagnosis of Tuberculosis and other infectious diseases. These platforms have a quick turnaround time (30 -60 minutes) but only 1-4 samples can be tested in one run, limiting the maximum numbers that can be tested to 24-48 samples / day only.

Availability of antigen-based detection tests is very limited all across the world.

Most of such tests have relatively moderate sensitivity but high

specificity. which does not require a specialized machine and can be interpreted with a naked eye. The test is a promising tool for quick diagnosis of SARS-CoV-2 in field settings.

Treatment and Prevention

The treatment strategies being tried currently include nucleoside analog (favipiravir and ribavirin), RNA polymerase inhibitors (remdesivir and galidesivir), protease inhibitors (lopinavir and ritonavir), immune modulators such as chloroquine and monoclonal antibodies (IFN alfacon-1). The initial clinical trial has shown that dexamethasone, a corticosteroid can be lifesaving for patients who are critically ill with COVID-19. According to preliminary findings, the treatment was shown to reduce mortality by about one third and one fifth among patients on ventilators and patients requiring only oxygen, respectively. Further research and large randomized control trials are needed to produce actionable evidence into these treatment strategies. As of 18th June 2020, there are 13 vaccine candidates in the clinical trial with nonreplicating viral vector platform-based vaccines ChAdOx1-S (University of Oxford/AstraZeneca), Adenovirus Type 5 Vector (CanSino Biological Inc./Beijing Institute of Biotechnology) and LNP encapsulated mRNA (Moderna/National Institute of Allergy and Infectious Diseases) being the front runners having entered phase two of trial. The Indian candidates include codon deoptimised live attenuated vaccines by Codagenix/Serum Institute of India; Indian Immunologicals Ltd/Griffith University and non-replicating viral vector platform with recombinant deactivated rabies virus-containing S1 by Bharat Biotech/Thomas Jefferson University are in pre-clinical trial.

Unresolved Issues

“Genomic Diversity makes the 'COVID-19 Pandemic' more overwhelmingly ravaging”

From a microbiological point of view, vaccine and an antiviral agent remain the first option to treat Covid-19. Currently, there is no specific effective treatment and only remdesivir is the most promising agent in mild to moderate cases. Low testing rates, deteriorating healthcare sector, reinfections after recovery from the virus and failure to implement policy of hospital infection control are the current challenges which India faces.

However, in the absence of a licensed vaccine/antiviral drug, the cases continue to rise and there is no flattening in the curve, Hand hygiene, Training and Initiating Behavior Change (social distancing and respiratory etiquettes), Use of Personal Protective Equipment, Environment Cleaning and Disinfection, are most powerful weapons against the covid-19 battle.

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