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Medical countermeasures for the COVID-19 pandemic management in India

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Abstract
The COVID-9 pandemic has created disaster throughout the world. Nations are struggling to combat this pandemic. As there is no "one size fits all" each country has to have a different approach depending on the resources available. Governments of several developing countries lack the healthcare capacity and resources making it difficult to provide protection to the frontline health workers and life-saving treatment to the patients. In this review, we highlight the challenges faced and medical countermeasures deployed in India to fight COVID-19. This review was prepared based on the literature search and data and information in public domain on the internet. A literature search was carried out on various articles/case reports in PUBMED/MEDLINE and the internet for the keyword's corona virus, SARS, COVID-19 and virus and India. COVID-19 has caused significant morbidity and mortality across all populations and India is no exception. In the first wave of pandemic the absence of proper diagnostic methods, protection kits and specific treatment made it extremely difficult to face the pandemic. The neglected facets of health care system were further highlighted by the second wave. However, with passing time and experience the healthcare system across the world geared up to take medical countermeasures to face the challenges of this pandemic. India had its own problems in terms of large population, diversified geographies, lack of preparedness and inadequate resource.

Keywords: Corona virus disease, SARS-CoV-2, pneumonia, acute respiratory distress syndrome, ARDS.

1. Introduction
The world has survived the two years long COronaVIrus Disease (COVID-19) since December 2019. The World Health Organization declared a pandemic in March of 2020asmillions of infected people had significant morbidity and mortality across the world. The infectivity of SARS-CoV-2 virus is very high with rapid transmission facilitated by absence of pre-existing acquired immunity. The emergence and re-emergence of COVID-19 infection was observed in India due to its large population and relatively free and fast national and international travel. The health care workers (HCW) faced high risk of infection while attending suspected or confirmed cases and during laboratory testing.(1) As a good-quality personal protective equipment (PPE) was the only preventive measure available, their shortage due to unprecedented demand created panic.(2)
Absence of sufficient evidence on effectiveness of potential therapeutic agents boosted development of drugs and vaccines using genomics and computational approaches.(3), .The exponential growth of scientific publications revealed genome sequence and protein structure of the virus. Several repurposed old drugs and new drugs are for COVID-19 treatments are under clinical trials. Current knowledge on SARS-CoV-2infection, pathology, prevention, and therapeutics has relatively improved potential drugs and vaccines. This review discusses the disease burden, clinical presentation, diagnostic challenges, medical countermeasures adopted and lessons learned during the COVID-19 pandemic in India.

2. Disease Burden
Kerala state of India documented first confirmed COVID case on 30 January 2020, shortly followed by cases in almost all parts of the country(4).The WHO disease containment

strategies were adopted as national guidelines to implement first 21 days lockdown on 25 March 2020to isolate 550 confirmed cases and screen all suspects (5).The local health authorities worked closely with administrative districts/ states machinery to innovate local/specific strategies. The Bhilwara model in Rajasthan proactively prevented the outbreak with complete recovery of most all patients (6). Immediately after the first case was detected public health actions such as cluster containment, contact tracing, quarantine, and isolation were implemented. Epidemiological approach of mapping the cluster was applied. The reservoir of infection was taken care by the District Public Health Team supported by Multidisciplinary Rapid Response Team. Strict enforcement of lock down ("ruthless containment") was implemented in the district. The State administration supported the daily need of the community with very well organised intersectoral co-ordination.

Initial cases were limited to few urban clusters transmitted by international passengers from countries at the stage of community transmission. Soon, the disease spread to close contacts of positive cases led to first wave. The co-morbid and elderly individuals were more susceptible to severe disease with high fatality. In spite of these measures, 11,000 new cases were recorded over next 60 days followed by 35,000 new cases per day on average. The immediate lockdown and swift containment measures across India reduced the spread of the disease and decline in growth rate of new cases of COVID-19.(7)

Healthcare workers and frontline staff were given the coronavirus vaccine. The norms were relaxed when daily infections in January 2021fell to fewer than 20,000 from a peak of over 90,000 in September. The second wave that followed reopening of most public places that allowed big social gatherings and rallies caught the officials and public off guard. It commenced in February 2021 with 11,000 cases in a day followed by average 22,000 cases daily for next 50 days and sharply soared to daily average of 89,800 cases. The rise in case numbers was faster and exponential throughout the country. (7)

The higher viral transmission rate and spread of infection among younger individuals <40 years of age led to more than 12 million cases across India. The viral mutation including highly transmissible UK variant led to infection among people taking all the precautions as well. Though COVID-19 deaths crossed 160,000, the case fatality rate one of the lowest.(7)

The better availability of testing kit in all states during second wave helped for speedy detection for vast population. The 60% active cases were concentrated in the state of Maharashtra. Even with a 0.1% infection fatality rate, more than half a million deaths were reported. The latest figures of number of active cases, discharges and death due to COVID-19 are provided on the website https://www.mohfw.gov.in/. (8)

3. Clinical presentation and diagnosis

The common symptoms associated with COVID- 19 are high fever, cough and difficulty in breathing. The involvement of lungs in severe cases cause severe pneumonia, acute respiratory distress syndrome (ARDS), and risk for life.(9)Even the asymptomatic individuals with international travel history or contact with a patient or quarantine was screened by government agencies. The health-care workers were monitored to check their health status and for the safety of their family as well as society.

Serological test

The diagnosis helped to understand disease transmission and to determine prevention and treatment strategies. Only the confirmed cases of COVID-19 either asymptomatic or symptomatic were known during scarcity of testing methods and kits.(10)However, early diagnosis and isolation of cases was critical, as transmission during the incubation period was high. The Centre for Disease Control and Prevention (CDC),(11) the World Health Organization (WHO),(12) and the Indian Council of Medical Research (ICMR)(13)recommended a few guidelines for the collection of the specimens from upper or lower respiratory tract of affected or suspected COVID-19 patients and testing. State or local health-care departments ensured the cooperation by affected or suspected individuals. The collection, storage, and shipment of the specimens were carried out as per the Biosafety level-3 (BSL-3) guidelines for the safety of the clinicians and researchers. Rapid IgG/IgM detection through immunoassay, Enzyme-linked immunosorbent assay (ELISA) and nucleocapsid and spike protein-based ELISA were used for SARS-CoV-2 detection.(14)

The rapid surge in COVID-19 cases demanded accurate and rapid diagnostic facility for large population. Such stress on diagnostic laboratory systems for manpower, resources and equipment may lead to hidden errors and mistakes. The quality management system (QMS) under Quality Council of India (QCI) ensure a high-quality laboratory practice to identify errors and prevent their recurrence. The QCI is a non-profit autonomous society responsible for accreditation and quality. The council has a National Accreditation Board for Testing and Calibration Laboratories (NABL) which is an autonomous society concerned with providing accreditation of technical competence to a testing, calibration, medical laboratory, proficiency testing provider and reference material producer for a specific scope following various international standards.(15)

To handle unprecedented demands of pandemic, the Indian Council of Medical Research (ICMR) setup or upgraded a network of existing diagnostic laboratories in addition to increased capacity at its Virus Research and Diagnostic Laboratories (VRDL). The guidelines on the various requirements for the setting up of diagnostic laboratories and expedited accreditation by NABL helped to add 818 laboratories to handle the emergency. Approvals from the Institutional Biosafety Committees and recommended accreditation of labs as per NABL, WHO and ICMR ensured accurate, reliable and efficient test results at par with the international standards. Initial ICMR approved Government centers were followed by NABL accredited private laboratories. (15)

The number of operational 1922 laboratories for COVID-19 diagnosis is steadily increasing across India. The Clinical and Laboratory Standards Institute (CLSI) guidance documents for laboratories is freely accessible on their website. The Department of Biotechnology of the Government of India has also laid out interim guidelines on laboratory biosafety to handle COVID-19 specimens. The non-propagative diagnostic laboratory work such as nucleic acid amplification tests(NAAT) and sequencing should be conducted at biosafety level (BSL) 2 laboratories and

propagative work such as virus culture, isolation or neutralization assays at a containment laboratory with inward directional airflow (BSL-3 laboratories) laboratories.(15)

Initially ICMR recommended the use of RT-PCR probes from the USA followed by approval of commercial kits and US FDA EUA/CE IVD-approved kits for diagnostic purposes. The kits with 100% concordance including 20 non-US/FDA/EUA/CE/IVD kits were fast-tracked through emergency use authorization by the drug regulator for routine use.(16) The identification of viral nucleic acid in the specimen through RT-PCR required significant time, trained personnel and well-equipped laboratories.(17) Latest advanced quantitative reverse transcriptase PCR (qRT-PCR) and digital droplet PCR (ddPCR) are a way more sensitive technique of CoV detection in terms of dynamics and accuracy.(18) A clustered regularly interspaced short palindromic repeats (CRISPR) based detection methods for the detection of SARS-CoV-2 is also now available.

In August 2021, India achieved COVID-19 sample Testing milestone of 500 million of which last 100 million samples were tested in 55 days. Enhanced production of diagnostic kits resulted in reduction of costs and improved availability of testing kits. Currently the number of COVID-19 testing laboratories is more than 2800.(19)

Chest computed axial tomography (CT)

The chest CT was preferred due to its non-invasive and less labor-intensive procedure. It was especially useful where laboratory testing was not available or the results were delayed. As it is not recommended for routine screening, it was ordered to assess progress of the disease. (14)

Blood test

Blood profiles and biochemical assays advised for preliminary screening revealed leucocytosis, leukopenia, lymphopenia, increased CRP, lactate dehydrogenase (LDH), and erythrocyte sedimentation rate (ESR).(20)SARS-CoV-2 infection also altered liver function test along with abnormal procalcitonin, a predominance of monocytes in sputum, high level of activated prothrombin, troponin, decrease in pro-albumin, and albumin.(14)

4. Vaccine development and manufacturing

India is considered as world leader in vaccine production. More than 50% of global demand for different vaccines needed for global immunization problems is supplied by Indian pharmaceutical companies. Vaccination is one of the most preferred and reliable means of protection against infectious diseases morbidity and mortality. However, development of an effective vaccine is complex and time consuming due to optimization, production, and clinical development. Clinical trial to determine the purity, capability, safety and efficacy of vaccine is quite challenging in case of SARS-CoV-2 due to early mutations in genes encoding surface glycoproteins of RNA viruses.(21), (22) Speedy development of effective and successful vaccine from conception to market usually takes minimum 2–18 months. (23)

Desperate efforts by all the stakeholders to develop and launch effective vaccines against SARS-CoV-2 using advanced molecular biology and biotechnology were witnessed. The Coalition for Epidemic Preparedness Innovations (CEPI) with global health authorities and scientists encouraged and supported development of vaccines against SARS-CoV-2. It is essential that the efficacy data of the vaccine is vetted independently. The first vaccine against SARS-CoV-2 was Sputnik V, approved by Russia on11 August 2020. Worldwide, large number of vaccines is in different stages of clinical trials.

Several COVID-19 vaccines were granted restricted use in emergency even before completion of Phase III clinical trials in India. Both pre-clinical and clinical data (complete data for Phase I and II, and partial data for Phase III) of these vaccines were thoroughly scrutinized by the regulators for safety and effectiveness and immunogenicity response. Although the vaccines have demonstrated favorable safety profile with induction of significant antibody response, the extent of the protection to recipients is not known. Therefore, the regulators have allowed restricted emergency use in trial mode.

The indigenously developed Covaxin (Inactivated-virus vaccine) also completed the phase III trial in India. Both indigenous and imported COVID-19 vaccine candidates are under production and clinical trials in India.

Covishield has completed its Phase III trials in UK and abridging trial in India. Covaxin was approved in public interest with abundant precaution for restricted use in emergency situation while its clinical trials were ongoing.

A controversy around it was in limelight in context of efficacy of Covaxin against infections by mutant strains. The vulnerability of millions of people was defended by both manufacturer and drug regulator for "accelerated" authorization after the phase II trials. It was approved as per Indian regulatory laws under the clause "unmet medical needs of serious and life-threatening diseases in the country". Local pharmaceutical and biotech companies have also inked collaborative agreements with foreign-based vaccine developers for development and manufacturing of vaccines. These collaborations have variable shared responsibilities for clinical trials, development to large-scale production and distribution of vaccines (Table 1).(24)

Table 1: Potential vaccine candidates and their regulatory status in India.

Vaccine	Indian Company	Collaborator	Vaccine design	Regulatory status
Covaxin	Bharat Biotech Ltd, Hyderabad, India	National Institute of Virology of ICMR, India	Inactivated-virus vaccine	EAU Jan 2021
Covishield	Serum Institute of India (SII), Pune, India	University of Oxford, UK, and pharma giant AstraZeneca	Non-replicating chimpanzee adenovirus vaccine vector (ChAdOx1)	EAU Jan 2021
Sputnik V	Dr. Reddy's Laboratories, Hyderabad, India	Gamaleya National Research Institute of Epidemiology and Microbiology, Moscow, Russia	Inactivated human adenovirus Ad5 and Ad26 with Spike proteins inserts	EUA April 2021
ZyCoV-D	Cadila Healthcare, /Zydus Cadila, Ahmedabad, India	Department of Biotechnology, Government of India	Plasmid DNA vaccine	EAU August 2021

Janssen COVID-19 vaccine	Johnson & Johnson, India	Janssen Pharmaceuticals	Inactivated human adenovirus (Ad26) Spike protein	EUA August 2021
HGCO19	Gennova Biopharmaceuticals Ltd, Pune, India	HDT Biotech Corporation, USA	mRNA vaccine	Approval for Phase 2/3 clinical trials August 2021
Corbevax	Biological E. Limited, Hyderabad, India	Dynavax Technologies Corporation and Baylor College of Medicine, USA	Recombinant RBD protein-based vaccine, with adjuvant CpG 1018	Phase 3 CT ongoing

The federal government approved Cipla Ltd. to import Moderna vaccine with nearly 95% efficacy. The government is also preparing to use a local version of Novavax vaccine, produced by the Serum Institute of India (SII). The vaccine had more than 90% efficacy in a late-stage US-based clinical trial. The government has placed an order for 300 million doses of a corona virus vaccine from Biological E.

India has shipped about 66 million doses of vaccines to 95 countries in Latin America, the Caribbean, Asia and Africa as on May 2021. The recipient countries include UK, Canada, Brazil and Mexico. Both Covishield and Covaxin have been exported - some in the form of "gifts", others in line with commercial agreements signed between the vaccine makers and the recipient nations, and the rest under the COVAX scheme, which is led by the World Health Organization (WHO) and hopes to deliver more than two billion doses to people in 190 countries in less than a year.(25)

5. Treatment strategies

During the initial phase of first wave of COVID-19, due to unavailability of any clinically proven drugs, the management and treatment was mostly supportive. The only aim was reducing mortality and preventing spread. Worldwide, personal hygiene, social distancing, and quarantine practices are recommended to combat virus transmission. In India, treatment protocols and guidelines were released by the government agencies. Several repurposed drugs were being used, including antiviral (Remdesivir, Ribavirin, and Oseltamivir) and antimalarial drugs.(26),(27), (28) Several clinical trials were initiated to evaluate their safety and efficacy in treating COVID-19.(26), (28),(29)

All new and repurposed drugs have to undergo clinical trials before marketing in India. The New Drug and Clinical Trial Rules, 2019, provided waiver to local phase-III clinical trials to drugs approved and marketed in certain countries (as notified from time-to-time), subject national emergency or epidemics in public interest.

Two antiviral drugs, Favipiravir - influenza drug and Remdesivir- a broad-spectrum antiviral drug received EUA in June 2020 for treating mild to moderate COVID-19. Itolizumab was approved for treating moderate to severe acute respiratory distress due to COVID-19 in July 2020. The regulatory status of Emergency Use Authorization (EUA) for repurposed drugs in India is summarized in Table 2.

Table 2: Drugs for COVID -19 with Emergency Use Authorization in India.

Treatment	Approval time
Remdesivir, Favipiravir	June 2020
Itolizumab	July 2020
Pegilated Interferon 2b alpha	April 2021
Baricitinib, Casirivimab, Imdevimab	May 2021
Bamlanivimab	June 2021

Drug supply and shortage

Severe shortage for Remdesivir and Tocilizumab despite its questioned efficacy was observed during pandemic. After emergency use authorization to both; Remdesivir was excessively prescribed by Indian doctors. Despite efforts of seven manufacturers, black marketing at five times the official price 100mg vial of remdesivir for 24,000 rupees ($320; £232) was observed. The recommended six doses of 100mg were raised to eight doses by physicians. Tocilizumab (arthritis drug) and Propofol (sedative-hypnotic) faced severe shortages.(30) The regaining measures include ramping up production and increasing imports and monitoring a three-pronged strategy of supply chain management, demand-side management and affordability.

The government is monitoring supply of various 'protocol drugs' like Remdesivir, Enoxaparin, Methylprednisolone, Dexamethasone, Tocilizumab and Ivermectin. Besides, supply of other drugs like Favipiravir, Amphotericin and Apixamab is also being monitored. The Central Drugs Standard Control Organization (CDSCO) and the National Pharmaceutical Pricing Authority (NPPA) are coordinating with manufacturers to enhance production and getting data about current stock, current capacities, projected production for May 2021.

The increase of Remdesivir producing plants from 20 to 60 tripled its availability in just 25 days. The government initiated monitoring the supply of various essential drugs used in the treatment of COVID-19. The government has also enhanced the availability of Tocilizumab injection in the country by importing 20 times more than what was being done in normal times. Besides, production of Dexamethasone (0.5 mg) tablets and injection, Enoxaparin Injection, Methylprednisolone Injection, Ivermectin (12 mg) tablet, Favirpiravir, and Amphoterecin B Injection have been ramped up.

6. Research, innovation and development

Research, innovation and development of drugs, vaccines and diagnostics are critical countermeasures to combat COPVID-19 pandemic. Across the India most research institute were in pursuit of newer treatment and diagnostic modalities. Our Institute - Mahatma Gandhi Medical College and Research Institute, Pondicherry announced a

"call for innovative ideas to address unique challenges of Indian health care sectors for management of COVID-19" for cash prizes. The Chancellor of our University- Sri Balaji Vidyapeeth, Pondicherry encouraged COVID-19 research activities with allocation of huge grant of 20 million INR (280,000 USD).(31)

Almost 1297 COVID-19 related clinical trials have been registered with the critical trial registry - India (CTRI) as on 30th November 2021.(32) As discussed in the above sections several clinical trials were carried out with repurposed drugs and vaccines, which received emergency use authorization. In a review of 122 registered trials on COVID-19 extracted from the CTRI database it was found that 34.42% (n=42) trials were on allopathic drugs, 54.9% (n=67) were on traditional medicine and 10.65 % (n=13) were from miscellaneous therapy areas. Of the 42 allopathic drug trials, 28 were on repurposed drugs, used singly (n=24) or in combination (n=4). Of these 28 trials, 23 were to evaluate their therapeutic efficacy in different severities of the disease. There were 9 trials on cell- and plasma-based therapies, two phytopharmaceutical trials and 3 vaccine trials.(33)

Indigenous vaccines were developed within relatively short time period and have been used in the vaccination drive across country. Our Institute was one of the investigational sites for the indigenously developed whole virion inactivated SARS-COV-2 vaccine (Covaxin) clinical trial which was found to be highly efficacious against confirmed symptomatic COVID-19 disease in adults. The interim analysis demonstrated vaccination was well tolerated with no safety concerns.(34) Our Institute was also one of the investigational sites for Corbevax vaccine for a prospective, multicentre, phase II/III clinical study to evaluate the immunogenicity and safety of CORBEVAX vaccine for protection against COVID-19. Another indigenous COVID-19 vaccine developed was DNA SARS-CoV-2 vaccine (ZyCoV-D). It was found to be safe, well-tolerated and immunogenic.(35)

Large number of clinical trials on repurposed drugs (favipiravir, hydroxychoroquine, ivermectin, pegylated interferon alpha-2b, ozonised saline, intravenous immunoglobulin) for management of COVID-19 were carried out in India.(36), (37), (38), (39), (40), (41), (42), (43), (43) Moreover India also participated in several large international multicentric clinical trials on drugs for COVID-19 management.(44), (45), (46), (47), (48) The Solidarity international open-labelled, randomized, parallel-group, multiple-arm clinical trial was initiated by WHO to find an effective treatment for COVID-19. It was planned with a total sample size of 7000 participants, of whom 1500 participants are to be enrolled from India from 24 sites. The trial is being conducted in India with the support of ICMR.(49) Our Institute has been selected as an investigational site for a global multicentric, randomized, double-blind, placebo-controlled, phase III study to evaluate the efficacy and safety of proxalutamide (GT0918) in hospitalized COVID-19 patients.

In a secondary analysis of a randomized controlled trial, it was observed that cohort of moderately and severely ill patients with COVID-19, severity of illness, underlying comorbidities and elevated levels of inflammatory markers were significantly associated with death.(50) Clinical trials with monoclonal antibodies were carried to explore their utility in the cytokine storms and severe condition. COVINTOC was a multicentre, randomized, controlled, phase 3 trial conducted in 180 patients with moderate to severe COVID-19 who were randomly assigned (1:1 block randomization) to receive tocilizumab 6 mg/kg plus standard care (the tocilizumab group) or standard care alone (the standard care group). It was found that routine use of tocilizumab in patients admitted to hospital with moderate to severe COVID-19 is not supported. However, post-hoc evidence from this study indicated tocilizumab might still be effective in patients with severe COVID-19.(51) Itolizumab was found to be safe and effective immunomodulatory therapy for treatment of acute respiratory distress syndrome (ARDS) due to cytokine release in COVID-19 patients, with survival and recovery-benefit.(43)

Intravenous immunoglobulin was found to be safe and efficacious as an adjuvant with other antiviral drugs in the treatment of COVID-19.(43) PEG IFN-α2b was repurposed for COVID-19 and was found to induce early viral clearance, improved the clinical status, and decreased the duration of supplemental oxygen.(41) A randomized control trial in 60 patients (n = 30/group) with ozone as an adjuvant to the standard of care demonstrated improvement in clinical status and rapid reduction in viral load compared to SOC alone.(52)

Extensive research activities are carried out in alternative medicine to develop therapy for COVID-19 in India. The role of Pranayama and meditation alone or in combination with naturopathy and Ayurvedic agents is being evaluated in the prevention as well as treatment of COVID-19.(53),(54) There are several trials registered on patented products including AYUSH-64 patented by Central Council for Research in Ayurvedic Sciences. One of AYUSH-64 components, Glycyrrhiza glabra or Yashtimadhu, may interfere with viral entry as well as replication, thereby impacting the severity of infection.(33) A pilot clinical trial revealed that Neem (Azadirachta Indica A. Juss) capsules reduced risk of COVID-19 infection in healthy participants.(55) There are ongoing trials investigating the role of Tinospora cordifolia, (Guduchi), Withania somnifera (Ashwagandha) Turmeric (curcumin) to evaluate their role as preventive agents against COVID-19.(54), (56), (57)

Several homeopathic agents have been recommended by the Ministry of AYUSH, GoI, for the prevention of COVID-19. Of the 14 homeopathic trials registered in the CTRI, most (n=11) are of Arsenicum album 30 or Bryonia alba.(33) Our institute is an investigational site for a phase 2/3, prospective, randomized, observer-Blind, placebo-controlled study to evaluate the efficacy and safety of Homeopathic SARS-CoV-2 Nosode (BioSimCovex) against COVID-19 in healthy Individuals.

Kabasura Kudineer (KSK), a polyherbal formulation from India's Siddha system of medicine, has been traditionally used for clinical presentations similar to that of COVID-19. It was found that KSK significantly reduced SARS-CoV-2 viral load among asymptomatic COVID-19 cases and did not record any adverse effect, indicating the use of KSK in the strategy against COVID-19.(58), (59),

Extensive research was carried in diagnostic domain. The most preferred and widely used test for COVID-19 diagnosis is the conventional RT PCR. However, it is an expensive test and requires a well-equipped molecular laboratory with trained work force, which cans result into

acute shortages of diagnostic kits. Manufacturers of molecular testing kits and consumables also struggle to keep up with the increased demand. It has become important to come up with novel ideas to conserve the reagents used for molecular tests at the same time develop novel diagnostic methods that at cost effective and less labour intensive.(60)

Several novel techniques with increased sensitivity and specificity against the SARS-CoV-2 associated viral components or immune response against have been developed such as biosensor-based detection of antigens, fluorescent or colorimetric detection systems including CRISPR-Cas 13 based SHERLOCK kit, CRISPR Cas-9 based FELUDA test kit, CRISPR DETECTR kit, Next Generation Sequencing or microarray-based kits. These novel techniques are useful as a point of care detection methods but should be followed by RT PCR based detection for the confirmation of COVID-19 status.(61)

Introduction of rapid nucleic-acid-detection-based tests has increased pace of diagnosis of COVID-19 in India. TruNat, an indigenous testing developed originally for tuberculosis, has been explored and is now being used for COVID-19 testing in India. TruNat beta CoV test is a rapid microchip-based real-time PCR assay, which runs on TruNat machines. The benefit of TruNAT is that the virus is lysed during the testing process, reducing the risk of infection and contamination by the virus. It was declared as a comprehensive assay for screening and confirmation of COVID-19 cases by ICMR in May 2020, in India. About 480 labs are using RT-PCR-based tests, 134 labs are using TruNat tests, and 55 labs are using CBNAAT-based COVID-19 tests. Moreover, ICMR has validated about 63 antigen-based Rapid Test Kits approved for use in India.(62)

7. Lesson learned: Prepare for the ensuing wave

Adopt scientific and pragmatic pandemic response strategies:

Government health agencies should act rapidly when cases begin rise to prevent exponential growth in transmission. When cases are low, government should set up processes, task force sand institutional structures which provides timely and coordinated scientific advice to national decision-makers to guide a swift and timely response. Prepare a sustainable lockdown plan in consultation with key stakeholders that can be tolerated by the local economy and community.

All stakeholders should be made aware of their role and responsibility in the epidemic response. They should be empowered to develop processes based on latest evidence, and held accountable. These institutional processes and structures should be alert and reactive to current situations such as rise in cases or new virus strains. This will be facilitated with active monitoring.

Strategies for early detections of local outbreaks

Active surveillance systems should be deployed to detect outbreaks and monitor trends to enable rapid decision-making based on latest data. Fast action is critical to suppress a wave before it begins.

Robust and clear communication plan with the public

The public must be cautioned and prepared to return to distancing measures as and when numbers of cases begin to increase. All the stakeholders should be on same page and communicate same message. Strong and regular communication from trustworthy institutions can encourage the long-term use of masks in public spaces, social distancing (to different levels), testing upon onset of symptoms, and compliance to self-isolation. Strong and consistent communications that which is comprehensive helps in the public to take preventive measure during pandemic.

Vaccination plans for well-organized vaccine distribution and allocation

The regulatory approval process should be expedited to fast track COVID-19 vaccine approvals. An evidence-based vaccination plans should be established for successful distribution and administration of COVID-19 vaccines. The information flow about vaccine supply and inventory across different levels of government should be improved. The human resources and cold chain capacity should be increased by exploring public-private partnerships. Efforts should be made to reduce vaccine hesitancy through culturally sensitive and tailored risk communication and messaging. A robust pharmacovigilance infrastructure to collect, detect, assess, monitor, and prevent adverse effects should be established. Support from international community should be sought to improving vaccine financing (e.g. ACT-A Accelerator), manufacturing, donation, and surveillance. (63)

Digital platforms should be used to improve health surveillance

Digital technologies (AarogyaSetu app) have been used for contact tracing, syndromic mapping, and self-assessment of COVID-19 through a mobile application. These digital health technologies should be scaled up only after the technology has shown effectiveness and cost-effectiveness. While explore digital solutions, the use of these data and digital technologies should adhere to legal, ethical, and clinical standards of care.

Reinforce health services

Develop healthcare capacity to manage large number of COVID-19 cases, at the same time maintain other essential services. Increase the production of PPE, essential medicines and oxygen supply. Create plans for emergency field hospitals, which rapidly set up as required. Develop strategies to decrease the pressure on hospitals in advance and issue home-based care guidelines in collaboration with national medical institutions for the use of COVID-19 treatments. These guidelines and recommendations should assure quality, safety, efficacy, and cost-effectiveness of treatment.

8. Conclusion

After the first wave India affirmed triumph over COVID-19 wave and social restrictions are lifted, life began returning to normal. Unfortunately, it was hit by the second wave, which was more severe as compared to first wave. This demonstrated the lack of preparedness when cases are low. Similar trend was observed in the neighboring countries with a steep rise in cases. It is evidenced that the pandemics are here to stay, while when cases are low, all countries should make the most of their resources to prepare for a possible reappearance. There are several lessons that can be learned from India's experience for adopting effective medical countermeasures in the management of COVID-19.

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