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ASSESSMENT, DIAGNOSIS, TREATMENT AND FUTURE OF COVID-19 PANDEMIC

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ABSTRACT

The epidemic of this era, novel corona virus named COVID-19 by WHO (World Health Organization) is spreading its wings throughout the world. Several countries such as America, India, Italy, China, different parts of Europe, Iran and all other countries in the world have suffered enormous consequences. The newly discovered novel coronavirus is similar to some of the β- coronaviruses found in bats, but different from previously known SARS- CoV and MERS- CoV. High sequence identities and similarities between 2019- nCoV and SARS- CoV were identified. The safety measures recommended by various national and international agencies are followed in phased manner by the Government of India which has allowed India to be an unanimous leader as compared to other countries in responding against the COVID-19 situation for slowing down the exponential growth of COVID-19. This review article discusses some of the basic steps taken by India, the current status and the future way forward to emerge from this situation.

KEYWORDS: COVID-19, Corona virus, Treatment, Measures.

INTRODUCTION

COVID-19 is the infectious disease caused by the most recently discovered coronavirus. This virus and disease was unknown before the outbreak began in Wuhan, China, in December 2019. The first known patient for COVID-19 was observed in the month of December 2019 in Wuhan, China. Slowly the infection spread across the world impacting 216 countries.

COVID-19 is a spherical or pleomorphic enveloped particles containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections. Some coronaviruses also contain a hem agglutinin-esterase protein (HE).[1],[2] Coronaviruses are a large family of viruses that can contribute to disease in animals and humans. In humans, several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recently discovered coronavirus causes coronavirus disease COVID-19. Viruses of the coronaviridae family possess a single-strand, positive-sense RNA and have been identified in various avian hosts and mammals, seven of which could cause illness ranging from the common cold to more severe diseases such as MERS-CoV and SARS-CoV.[3]

Several researchers are engaged in identifying the DNA structure and sequencing pattern of novel Corona virus 2019. Yi-Lin Lu et. al. identified that the novel corona virus 2019-nCoV has large amount of similarities with SARS-CoV.[4] COVID-19 is like the coronavirus responsible for SARS-CoV with >79% sequence identity; but it is more distant from MERS-CoV (only 50% homology).[5]

Life cycle of corona virus

Corona virus infection can be briefly described in following four stages[6],[7]

1. Attachment and entry
2. Replicase protein expression
3. Replication and transcription
4. Assembly and release

Spread

When someone who has COVID-19 coughs or spits they release droplets of infected fluid. Most of these droplets fall on nearby surfaces and objects, person gets infected if they touch mouth or eyes or ears or nose after touching these surfaces or objects. Like touch If someone stands close to the infected person [within 1 meter] and inhale the droplets spread because of coughing or sneezing of the infected individual.[8]

The COVID19 spreads by following ways

1. Face-to-face contact with a probable or confirmed case within 1 meter and for more than 15 minutes;
2. Direct physical contact with a probable or confirmed case;
3. Direct care for a patient with probable or confirmed COVID-19 disease without using proper personal protective equipment; OR
4. Other situations as indicated by local risk assessments.
5. Through respiratory droplets produced when an infected person coughs, sneezes or talks.[9]

Most persons infected with COVID-19 experience mild symptoms and recover. However, some experience more serious illness and may require hospital care. Risk of serious illness rises with age: people over 40 seem to be more vulnerable than those under 40. People with weakened immune systems and people with conditions such as diabetes, heart and lung disease are also more vulnerable to serious illness.[10] Symptoms may appear 2-14 days after exposure to the virus.

Symptoms[11],[12]

- Fever
- Cough
- Shortness of breath or difficulty breathing
- Repeated shaking with chills
- Muscle pain
- Headache
- Loss of taste or smell
- Sore throat
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

Isolation of virus

Bronchoalveolar-lavage fluid samples were collected in sterile cups to which virus transport medium was added. Samples were then centrifuged to remove cellular debris. The supernatant was inoculated on human airway epithelial cells.[9],[13]

Testing

WHO has listed the two diagnostic tests for emergency use during the Covid-19 pandemic which are `Genesig Real-Time PCR Coronavirus (COVID-19)´[14] and `Cobas SARS-CoV-2.[15] Qualitative assay for use on the cobas® 6800/8800 Systems.

Treatment

Researchers successfully isolated the sequence of Corona virus and various trials were undergoing in China for checking efficiency of drugs. Remdesivir (which is a monophosphoramidate prodrug) and Favipiravir interfere with synthesis of viral mRNA targeting RdRp which were developed for treatment of Ebola however have shown potential for treatment against COVID-19.[11] Many of the hospitals are utilizing the well-known anti-malerial drug Hydroxychloroquine along with combination with other drugs such as azithromycin during treatment yielding better control over the eroding condition of patients.[16],[17],[18]

Approved nucleoside analogues (Favipiravir and Ribavirin) and experimental nucleoside analogues (Remdesivir and Galidesivir) may have potential against 2019-nCoV. Nucleoside analogues in the form of adenine or guanine derivatives target the RNA-dependent RNA polymerase and block viral RNA synthesis in a broad spectrum of RNA viruses, including human coronaviruses. Favipiravir (T-705), a guanine analogue approved for influenza treatment, can effectively inhibit the RNA-dependent RNA polymerase of RNA viruses such as influenza, Ebola, yellow fever, chikungunya, norovirus and enterovirus[19], and a recent study reported its activity against 2019-nCoV (EC50 = 61.88 μM in Vero E6 cells). Patients with 2019-nCoV are being recruited in randomized trials to evaluate the efficacy of Favipiravir plus interferon-α (ChiCTR2000029600) and Favipiravir plus Baloxavir marboxil (an approved influenza inhibitor targeting the cap-dependent endonuclease) (ChiCTR2000029544). Ribavirin is a guanine derivative approved for treating HCV and respiratory syncytial virus (RSV) that has been evaluated in patients with SARS and MERS, but its side effects such as anaemia may be severe at high doses[19] and whether it offers sufficient potency against 2019-nCoV is uncertain.[20],[21]

The majority of existing observational studies have not suggested clinically significant associations between prenatal azithromycin exposure and major congenital malformations. As shown by Damkier et al., the associations reported by a few studies might well be attributable to maternal confounders.[18],[22] To date a single study suggested an approximately

1.5-fold increase in the rate of spontaneous abortions which needs further confirmation. Therefore, azithromycin can be used for the treatment of critical infections during pregnancy when clinically indicated. Azithromycin is compatible with breastfeeding from the RID perspective, since its measured and simulated RID is low and it has been used in higher doses for the treatment of infections in infants. The suggested association between macrolide use during breastfeeding and IHPS needs further confirmation. However, the infant should be monitored for early signs of IHPS.[23]

Usage of Lopinavir-Ritonavir combination was evaluated and recommended for treatment of COVID-19 symptomatic patients.[24] A combination of three drugs that can successfully treat mild to moderate cases of COVID-19 has shown positive results and entered in Phase II clinical trials. The drugs are, Interferon beta-1b, Lopinavir-Ritonavir [an HIV drug] and ribavirin [an oral hepatitis C drug].[13]

Recently government of India have approved to manufacture and market Favipiravir in India for treatment against COVID-19 basis of various positive results in initial treatment of COVID patients.[25],[26] Ministry of Russia has included Avifavir for treatment of COVID19.[27]

VACCINES UNDER DEVELOPMENT

Researchers all over the globe are working tirelessly to develop a vaccine against COVID-19. Table 1 contains some of the vaccines under development.[28]

Table 1: Vaccines under development.

Candidate	Sponsor	Stage
Bacillus Calmette-Guerin [BCG] live-attenuated vaccine	University of Melbourne and Murdoch Children's Research Institute; Radboud University Medical Center; Faustman Lab at Massachusetts General Hospital	Phase 2/3
AZD1222	The University of Oxford	Phase 2/3
mRNA-1273	Moderna	Phase 2
BNT162	Pfizer, BioNTech	Phase 1/2
Inactivated vaccine	Wuhan Institute of Biological Products; China National Pharmaceutical Group [Sinopharm]	Phase 1/2
BBIBP-CorV	Beijing Institute of Biological Products; China National Pharmaceutical Group [Sinopharm]	Phase 1/2
CoronaVac	Sinovac	Phase 1/2
GX-19	Genexine	Phase 1/2
Gam-COVID-Vac	Gamaleya Research Institute, Acellena Contract Drug Research and Development	Phase 1/2
bacTRL-Spike	Symvivo	Pre-clinical

Candidate	Sponsor	Stage
Covaxin	Bharat Biotech; National Institute of Virology	Pre-clinical
PittCoVacc	UPMC/University of Pittsburgh School of Medicine	Pre-clinical
Measles vector vaccine	University of Pittsburgh's Center for Vaccine Research	Pre-clinical
NVX-CoV2373	Novavax	Pre-clinical
Ii-Key peptide COVID-19 vaccine	Generex Biotechnology	Pre-clinical
Recombinant vaccine	Vaxart	Pre-clinical
Self-amplifying RNA vaccine	Imperial College London	Pre-clinical
Plant-based COVID-19 vaccine	Medicago	Pre-clinical
DNA-based vaccine	Takis Biotech	Pre-clinical
Ad26.COV2-S	Johnson & Johnson	Pre-clinical
AdCOVID	Altimmune	Pre-clinical
T-COVIDTM	Altimmune	Pre-clinical
Protein subunit vaccine	University of Saskatchewan Vaccine and Infectious Disease Organization-International Vaccine Centre	Pre-clinical
LUNAR-COV19	Arcturus Therapeutics and Duke-NUS Medical School	Pre-clinical
Recombinant vesicular stomatitis virus [rVSV] vaccine	Merck; IAVI	Pre-clinical
Adenovirus-based vaccine	ImmunityBio; NantKwest	Pre-clinical
Molecular clamp vaccine	CSL; The University of Queensland	Pre-clinical
AAVCOVID	Massachusetts Eye and Ear; Massachusetts General Hospital; University of Pennsylvania	Pre-clinical
Recombinant vaccine	Sanofi, Translate Bio	Pre-clinical

SAFETY MEASURES

Preventive measures taken till date by government and institutions for avoiding COVID spread

- Suspension of active VISAs for travellers except diplomatic individuals, medical staff and UN or international organizations.
- Individuals with travel history to be kept under quarantine for 14 days.
- Temporary restrictions of schools, educational institutions, private organizations.
- Temporary restrictions on shopping centres, food chains, retail stores except hospitals and essential services.
- Restrictions on air, sea and road travel and vehicle movement to limit non-essential movements.
- Temporary restrictions on sport activities and competitions and events causing large people congregation.

- Restrictions on activities in pilgrim spots, temples, churches and mosques etc.

Following are the Do´s and Don'ts for people

Do´s

- Maintain personal hygiene and physical distancing.
- Practice frequent hand washing. Wash hands with soap and water or use alcohol-based hand rub. Wash hands even if they are visibly clean.[29]
- Wash hands after disposal of mask.
- Cover your nose and mouth with handkerchief/tissue while sneezing and coughing.
- Throw used tissues into closed bins immediately after use.
- Maintain a safe distance from persons during interaction, especially with those having flu-like symptoms.
- Sneeze in the inner side of your elbow and not to cough into the palms of your hands.
- Take temperature regularly and check for respiratory symptoms in case of sickness.
- Contact state or government authority in case of symptoms for any fever/flu-like signs/symptoms, please call State helpline number.
- Wear masks in case of medical or respiratory symptoms or if treating or coming in contact with COVID positive individual.

Don´ts

- Shake hands.
- Have a close contact with anyone, if you're experiencing cough and
- fever.
- Touch your eyes, nose, ears and mouth.
- Sneeze or cough into palms of your hands.
- Spit in Public.
- Travel unnecessarily, particularly to any affected region.
- Participate in large gatherings, including sitting in groups at canteens.
- Visit gyms, clubs and crowded places etc.
- Spread rumours or panic.

Present status

As per data provided by WHO on 10th July 2020 total number of confirmed cases across the globe stands 12,064,828 and deaths 550,384 categorizing the COVID-19 as very high risk at

global level.[30],[31] As on date 09th July 2020 active cases in India are 269789 cured & discharged are 476377 and deaths are 21129.[32]

In very short time, a localised outbreak of COVID-19 started from Wuhan China evolved into a global pandemic with three defining characteristics:

- Speed and scale: the disease has spread quickly to all corners of the world, and its capacity for explosive spread has overwhelmed even the most resilient health systems.
- Severity: overall 20% of cases are severe or critical, with a crude clinical case fatality rate currently of over 3%, increasing in older age groups and in those with certain underlying conditions.
- Societal and economic disruption: shocks to health and social care systems and measures taken to control transmission have had broad and deep socio-economic consequences.

Strategy followed by government to tackle the situation[33],

Find: Find the personnel with symptoms of COVID-19

Test: Perform testing on identified subject for confirmation of COVID-19.

Isolate: Isolate the subject in order to prohibit the community transfer.

Care and mitigate the risk: Take care of every individual in hospital until the symptoms are treated and the testing is indicating negative test results twice for the subject.

Quarantine contacts: Perform contact tracing for the infected individual based on his routine before identifying COVID-19. Isolate the subjected individuals or families in dedicated shelters and perform testing to check the spread.

Control transmission: Take immediate precautionary steps to avoid community transfer of the disease.

Usage of mobile apps such as `Ayush Sanjivani´ for various measures to promote immunity by usage traditional Ayurvedic medicines comprising of Tulsi leaves, Dalchini, Sunthi, and Krishna Marich[34],[35] and `Arogya Setu´ for tracking and identifying the spread of COVID-19 through self-assessment.[36]

To meet the following objectives

- Mobilize all sectors and communities to ensure that every sector of government and society takes ownership of and participates in the response and in preventing cases.
- Control sporadic cases and clusters and prevent community transmission.
- Suppress community transmission.

- Reduce mortality
- Develop safe and effective vaccines and therapeutics that can be delivered at scale and that are accessible based on need.

Coming out of this situation,

China appeared to manage the coronavirus outbreak effectively, putting in place early travel bans within the country itself. As early as January 23, Chinese authorities declared a nationwide travel ban, which, some experts suggest, may have averted over 700,000 COVID-19 cases within the country.[37]

Since mid-February 2020 the main province of China indicated progress towards containment of COVID-19 spread. The steady decline in China was obtained with various levels of controls. COVID-19 spread was controlled to maximum extent by China to start routine operations post vigorous lockdown steps at start of April.

Following are some recommendations to be followed to avoid the risk of transmission of COVID-19 as well as other emerging pathogens,

- Anyone visiting live animal markets, wet markets, or animal product markets should practice general hygiene measures,

- Including regular hand washing with soap and water after touching animals and animal products,
- Avoiding touching eyes, nose, or mouth with hands, and
- Avoiding contact with sick animals or spoiled animal products.

- Any contact with other animals possibly living in the market [e.g. stray cats and dogs, rodents, birds, bats] should be avoided.
- Attention should also be taken to avoid contact with potentially contaminated animal waste or fluids on the soil or structures of shops and market facilities.
- The consumption of raw or undercooked animal products should be avoided. Raw meat, milk, or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices.

People working in animal markets shall take above preventive measures in addition to following measures,

- Avoid contact with sick animals or spoiled animal products.

Any contact with other animals possibly living in the market [e.g. stray cats and dogs, rodents, birds, bats] should be avoided. Attention should also be taken to avoid contact with potentially contaminated animal waste or fluids on the soil or structures of shops and market facilities.

- The consumption of raw or undercooked animal products should be avoided. Raw meat, milk, or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices.

UNICEF has recommended following points to consider for prevention of COVID-19 in schools which can be applied to all educational institutions[22],

- Sick students, teachers and other staff should not come to school. Establish procedures if students or staff become unwell.
- Schools should enforce regular hand washing with safe water and soap, alcohol rub/hand sanitizer or chlorine solution and, at a minimum, daily disinfection and cleaning of school surfaces.
- Schools should provide water, sanitation and waste management facilities and follow.
- Environmental cleaning and decontamination procedures.
- Schools should promote social distancing such as,
  - Staggering the beginning and end of the school day
  - Cancelling assemblies, sports games and other events that create crowded conditions
  - When possible, create space for children's desks to be at least one metre apart
  - Teach and model creating space and avoiding unnecessary touching
- Update or develop school emergency and contingency plans. Work with officials to guarantee schools are not used as shelters, treatment units, etc. Consider cancelling any community events/meetings that usually take place on school premises, based on risk.
- Prepare and maintain handwashing stations with soap and water, and if possible, place alcohol-based hand rub [hand sanitizers] in each classroom, at entrances and exits, and near lunchrooms and toilets.
- Plan for continuity of learning,
  - Use of online/e-learning strategies
  - Assigning reading and exercises for home study
  - Radio, podcast or television broadcasts of academic content
  - Assigning teachers to conduct remote daily or weekly follow up with students
  - Review/develop accelerated education strategies.

- Monitor attendance of school staff and students.

Follow correct procedures

- Wash hands properly[38],
  - Step 1: Wet hands with safe running water
  - Step 2: Apply enough soap to cover wet hands
  - Step 3: Scrub all surfaces of the hands – including backs of hands, between fingers and under nails for at least 20 seconds
  - Step 4: Rinse thoroughly with running water
  - Step 5: Dry hands with a clean, dry cloth, single-use towel or hand drier as available

- The correct procedure of wearing triple layer surgical mask.[38,39]
  - Perform hand hygiene
  - Unfold the pleats; make sure that they are facing down.
  - Place over nose, mouth and chin.
  - Fit flexible nose piece over nose bridge.
  - Secure with tie strings [upper string to be tied on top of head above the ears –lower string at the back of the neck.]
  - Ensure there are no gaps on either side of the mask, adjust to fit.
  - Do not let the mask hanging from the neck.
  - Change the mask after six hours or as soon as they become wet.
  - Disposable masks are never to be reused and should be disposed off.
  - While removing the mask great care must be taken not to touch the potentially infected outer surface of the mask
  - To remove mask first untie the string below and then the string above and handle the mask using the upper strings.
  - Disposal of used masks: Used mask should be considered as potentially infected medical waste. Discard the mask in a closed bin immediately after use.

Safety measures to be followed by government and private institutions

- Identify the personnel who has recent travel history to COVID-19 impacted areas and evaluate them for symptoms related to any medical condition.
- Provide enough space to work [in case if options such virtual office or work from home is not available].

- Provide healthcare facilities for quarantined personnel and patients.
- Technical expertise and health emergency workforce:
  - Issue advisories for government and private institutions for better containment of situation.
- Provide adequate facilities for healthcare service provider [Hospitals, sanitizers, medical aides, medicines, recent knowledge on research].
- Accelerating research, innovation, and knowledge sharing: Identify the improvement opportunities through public campaign for taking preventive steps to contain the situation and to identify the easier and novel approaches to stop the spread.
- Coordinated global supply chain management: Ensure uninterrupted supply of essential health commodities such as vaccines, therapeutics and diagnostics and other essential goods such as food and water.

Proposals for travel

- WHO has published guidance on adjusting public health and social measures for the next phase of the COVID-19 response. `Immunity Passport´ or `Risk Free Certificate´ may serve as a basis of personnel evaluation for allowing travel in the globe. The evaluation to measure the antibodies specific to COVID-19 is underway. The development of immunity to pathogen may take 1-2 weeks. World health organization is presently monitoring the progress on antibody measurement.[40]

- **Avoid myths and rumours, some of them are mentioned below**

- Claims regarding cure of COVID-19 in any form such as allopathic, Ayurvedic or homeopathic medicine. Unless until proven medically and clinically these claims shall not be supported.
- Adding pepper to soup or other meals avoid COVID-19. There are no scientific evidences for such claims hence these shall be avoided.
- Novel corona virus is transmitted through flies. There are no evidences to report this.
- Injecting the bleach or sanitizers or disinfectant inside the body.
- Drinking ethanol, methanol or any other drinks.
- Novel corona virus does not transmit in hotter areas or after exposing to sun.
- Cold weather and snow kills novel corona virus.
- Taking hot batch does not prevent COVID-19.
- Corona virus affects only old people.

CONCLUSION

It is quite clear that this unprecedented situation has taught man a number of lessons to make a better life out of the present one, and has also taught us to live with the situation until we have a definitive remedy for COVID-19. With the world facing an unmatched threat, there is an opportunity to emerge with stronger health systems, and improved global collaboration to face the next health threat. With scientists and researchers making extensive efforts in finding cure for COVID-19 its certain that we are heading towards a better future and emerge out as better human being with a better healthcare system which will always be ready to tackle such situation in future.

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