





An Overview of Novel Coronavirus SARS-CoV-2 Spanning around the Past, Present and Future Perspectives

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Abstract

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a new enveloped RNA virus known as Coronavirus (COVID-19) are most prevalent in humans and wild animals. All four species that is alpha, beta, delta and theta have been identified till date and are responsible for human disease; causing influenza like illness (ILI). This virus has similar lineage of Middle East Respiratory Syndrome coronavirus (MERS-CoV) and related Coronavirus (SARS-CoV). This outbreak initially presented as pneumonia-like illness in a group of people in Wuhan, China. The infection was said to be caused by seafood and unusual animals in the wholesale markets of this city. SARS-CoV-2 is highly infectious and has resulted in a rapid pandemic. As of now it has spread to 197 countries with total no of cases in the world being 3.76 million as of early march. The mortality till now is 7.11% . The cases have been increasing since its first discovery in China. In India also the number has been increased. Till now India has total of 39,980 cases and mortality is attributed to be 3.26%. As per data from Ministry of health and family welfare (MoHFW) death is more commonly seen in males with age >60years. Among these most of the deaths were related to other co-morbid conditions. This article will help the readers with an overview of novel Coronavirus spanning around the clinical features, diagnostic modalities, treatment strategies and infection control measures. It will also help in raising awareness among healthcare workers regarding COVID-19 and aid in early recognition of these patients. Moreover, this review will also focus on the most recent information for the effective management, prevention, and treatment of patients worldwide.

Keywords: COVID-19, Pandemic, Immunoinformatics, MERS CoV, Resilience, SARS CoV-2

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INTRODUCTION

COVID-19 pandemic is caused by Coronavirus, which was designated as SARS-CoV-2 initially. Coronaviruses are mostly responsible for causing respiratory diseases, from common flu like disease to more grave diseases leading to acute respiratory syndromes involving lower respiratory tract infection. Both these diseases are associated with high fatality leading to 11%, 34.4% and were first seen in 2003 and 2013 respectively¹⁻³.

The outbreak of SARS-CoV-2 was first detected in China's largest metropolitan city Wuhan in Hubei Province in December 2019. The published literature shows the beginning of these cases to the starting of December 2019. Initially these cases were called "pneumonia having no etiology". After investigation the causative agent was found to be a new virus belonging to Coronavirus (CoV) family. The case fatality associated with this novelCoV (nCoV) is 3.2%⁴.

Evolving Status of the 2019-nCoV and COVID-19

On February 11, 2020, the WHO Director-General, Dr. Tedros Adhanom Ghebreyesus, designated this virus as nCoV and called this disease as "COVID-19," that is "Coronavirus disease 2019". In the past two decades, other Coronavirus epidemics have also occurred in the world. Epidemic by Novel SARS-CoV too began from China and infected almost twenty four countries with 8000 patients and 800 causalities and the Middle East Respiratory Syndrome Coronaviruses (MERS-CoV) that initially was seen among Saudi Arabians caused disease in 2,500 patients and there was 800 causalities with sporadic cases occurring till date.

This contagious novel Coronavirus spread worldwide in short span of time. In a meeting on January 30, 2020, as per the International Health Regulations 2005, WHO called this outbreak as a Public Health Emergency of International Concern because it involves 125 countries with four countries reporting human-to-human transmission. Another landmark happened on February 26, 2020, when the United States reported about the first patient who was not imported from China. Due to its resemblance to other SARS viruses (SARS-CoVs) The International Committee on Taxonomy of Viruses (ICTV) designated it SARS-CoV-2.

Both SARS-CoV and MERS-CoV have

numerous common features that add to nosocomial transmission, especially its replication in the respiratory tract, and immunopathology. Regarding COVID-19, on February 28, 2020, WHO declared this virus as high level threat to cause epidemic. When this virus was found to be associated with 13 fold increase in cases of COVID-19 outside China and more than 118,000 cases in more than 100 countries till March 11 that included approximately 4,000 deaths, and then it was the time when WHO declared the COVID-19 as a pandemic⁵.

Pathogenesis and Virus-host Interactions

Following are the Hypotheses for COVID-19

SARS-CoV2 is from the beta Coronavirus family, it is a positive-sense, single-stranded RNA, enveloped virus that is 50-200 nm in diameter as shown in Fig. 1⁶. There are various surface proteins present on the surface of CoV. The most important of them is Spike Glycoprotein (S) which is known to bind to angiotensin-converting enzyme 2(ACE2) receptor on type II pneumocytes^{6,7}.

The second protein which is present on the surface is hemagglutinin-esterase (HE) dimer as shown in Fig. 1. After entering into type II pneumocyte cells through endocytosis, it multiplies rapidly within cytoplasm. After multiplication the cells get packed with virions and ultimately lyse the pneumocytes as shown in Fig. 2. Afterwards, the RNA from the SARS-CoV-2 acts as a pathogen-associated molecular pattern and is recognized by toll-like receptors on the host cell for attaching and infecting to other cell.

This process leads to excessive release of chemokines due to which neutrophil migrate along with activation of alveolar-capillary walls and destroys it. This leads to leaking of fluid into the alveolar sacs which is responsible for pneumonia like presentation in patients of COVID-19⁸. Another theory says that SARS-CoV-2 attacks 1 β chain of hemoglobin (Hb), due to which iron is released into the circulation. Thus hemoglobin loses the capacity to bind oxygen which is then not supplied to the organs for their proper functioning leading to hypoxia causing multi-organ failure. Alveolar macrophages get inflamed due to free iron toxicity. Body tries to compensate with increased Hb synthesis, increased ferritin production. The body in turn produces monocytes macrophages to engulf excess iron load. Excess Hb production

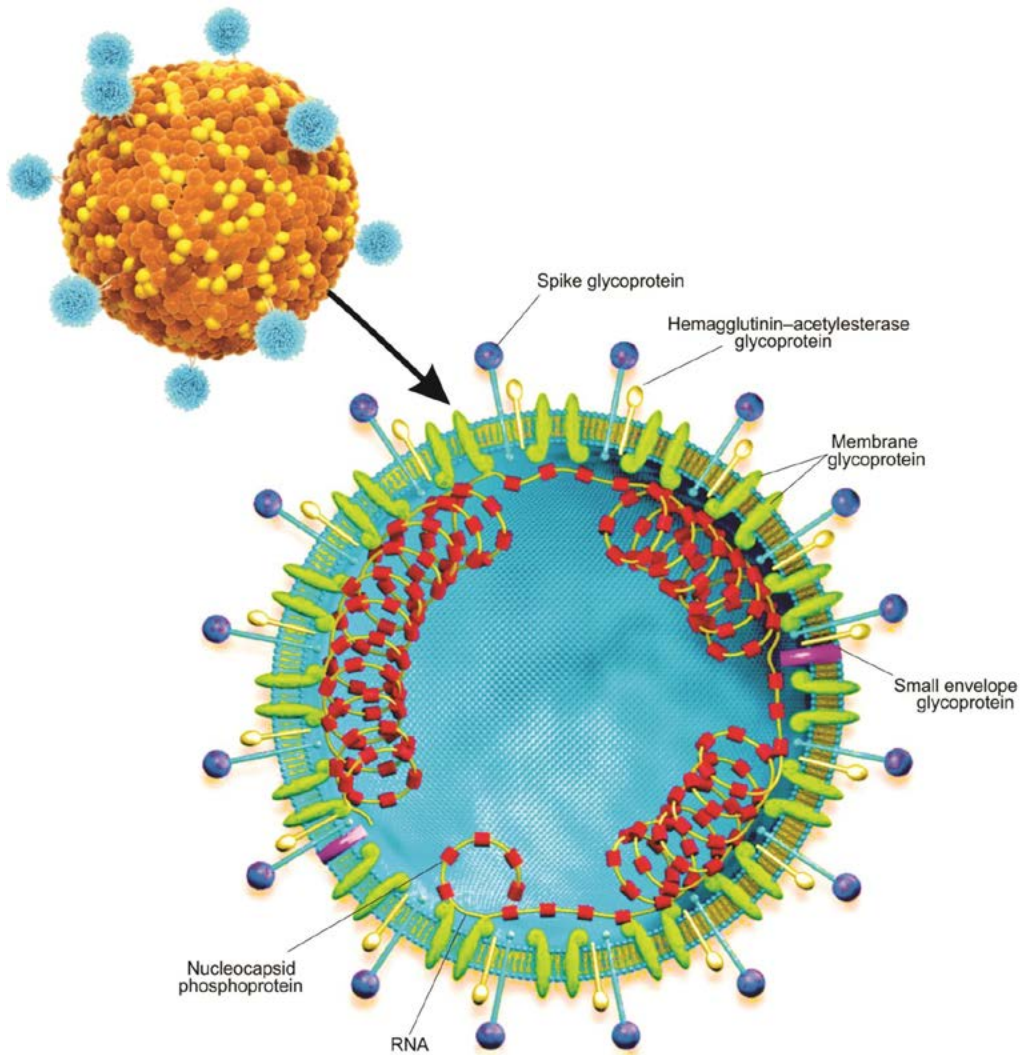


Fig. 1. 3D model of the SARS-COV-2 Virion and also showing its structure proteins and genome
Image modified from source [7]

leads to increase blood viscosity which leads to thrombosis. All together it leads to increase production of D Dimer, coagulation activation and disseminated intravascular coagulation leading to multi-organ failure⁹.

Genomic Organisation, Replication and Transmission

The electron microscopy reveals, spherical or pleomorphic shaped virions with club like projections formed by the spike proteins. It has Positive sense viral genomic m-RNA, comprising of 5' terminal cap structure and a 3' poly-adenylate tail structure as shown in Fig. 3. This genomic mRNA of CoV acts as an initial RNA of the

infectious cycle; as a template ;one for replication and transcription events; and lastly acting as a substrate for viral packaging into the progeny virus and releasing through apoptosis¹⁰. Virus attaches on the human epithelial cell, enters by fusion or by an endocytotic pathway. After entering the cytoplasm it uncoats itself, and releases the RNA genome. These RNA genomes integrate and replicate after entry. Replication is followed by translation of subgenomic mRNAs leading to production of structural and nonstructural viral proteins. The replicated RNA genome is organised into virions and released outside the cell¹⁰

Transmission

It is mainly by contact transmission, droplet transmission and in few cases airborne transmission may be considered as shown in Fig. 4; as in aerosol generating procedures performed in hospital such as intubation, bronchoscopy, CPR¹¹.

Impact of Weather Conditions on COVID-19 Outbreak

There are literatures which suggest that temperature does have an effect on this virus and it is said that this virus gets killed at 60°C after 30 minutes and in 5 minutes at 70°C. Studies are yet to be performed regarding relation of temperature and virus infectivity¹².

Community Acquired Human Coronaviruses

Following are the human Coronavirus which are responsible for infections in humans.

Historically, it was proven that the CoV infections in humans are related with upper respiratory tract infections, caused by number of CoV as mentioned in Table1.

Earlier reports investigated the three novels HCoVs viruses which were associated with respiratory diseases, the first one was HCoV-HKU1

Table 1. Showing types of coronaviruses

No.	Types of Coronaviruses	Example
1	α coronaviruses	229E, NL63
2	β coronaviruses	HKU1 , MERS-CoV, SARS-CoV and SARS-CoV-2 novel Human coronavirus
3	Delta coronavirus	Porcine Delta-coronavirus
4	Theta coronavirus	-

which caused pulmonary disease , second one was HCoV-NL63 which was associated with upper and lower respiratory tract diseases in all age groups and the third one was associated with acute pneumonia and it named MERS-CoV in April 2012. By these studies it seems that CoV was always there in nature as potential human pathogen^{5,31}.

Diagnosis and Infection Monitoring Strategies

Initial and precise diagnosis of COVID-19 is critical to control its spread and advance health outcomes.

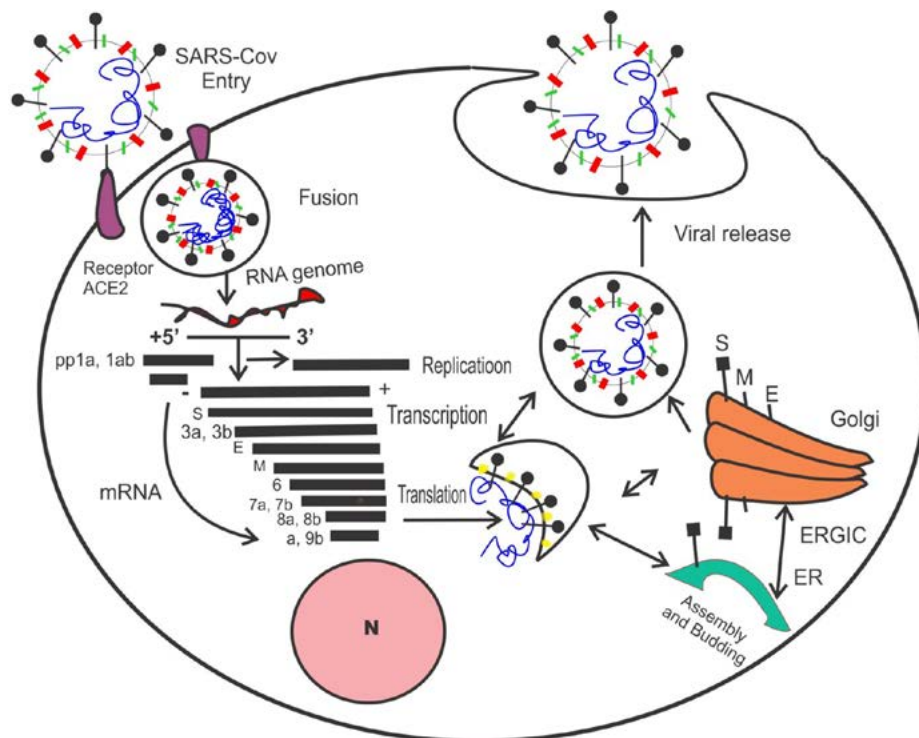


Fig. 2. Life cycle of SARS-CoV in host cells and its S protein structure
Image modified from source [8]

Table 2. Common presenting symptoms

SYMPTOMS	Reference
1. Fever, Cough, Shortness of breath or difficulty breathing, Chills, Repeated shaking with chills, muscle pain, myalgia, Headache, sore throat,	16, 17
2. Malaise, Gastrointestinal symptoms like diarrhea, abdominal pain, anorexia,	18
3. Loss of taste or smell.	19,20
4. Emergency warning signs Trouble breathing with constant pain or pressure in the chest Confusion and Fear, anxiety causing discoloration of lips or face	16

Diagnosis of COVID-19 can broadly be classified as:

Sign and symptoms

Laboratory confirmation.

Clinical Manifestations in people, as per research report asymptomatic individuals in 69% of cases and remaining 31% people with COVID-19 present with mild to acute symptoms¹⁴. Asymptomatic individuals are equally responsible for disease transmission¹⁵. These symptoms may appear 2-14 days after exposure to the virus:^{15,16}. Symptoms are shown in Table 2¹⁶⁻²⁰.

Recently some case reports suggest skin lesions in adult and especially in children,

it presents with covid toes²¹. Case reports also available where the virus is present in conjunctival swab²². Radiologically patients show bilateral pneumonic changes on CT²³. In severe cases these patient develop acute respiratory infection requiring oxygen therapy or mechanical ventilation.

These severe cases also land up in intensive units²⁴ with pneumonia. Centre for Disease Control and Prevention (CDC) has recently added emergency warning signs for COVID-19 where immediate and urgent medical attention is required¹⁶.

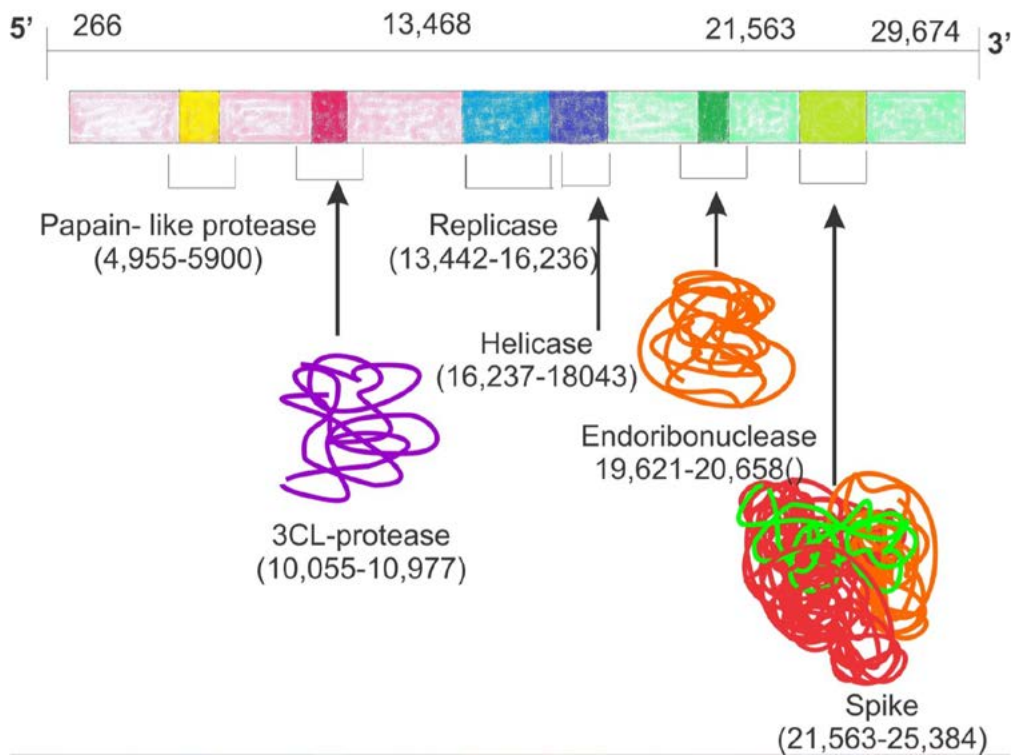


Fig. 3. Single Standard RNA genome of SARS Cov-2 (~30 kb length)
The image is modified from source [5]

Table 3. shows list of diseases presenting with similar sign and symptoms²⁶

Differential diagnosis Viral Diseases	Bacterial Diseases	Parasitic Diseases
ILI* caused by: Adenovirus Influenza Human metapneumovirus (HmPV) Parainfluenza Respiratory syncytial virus (RSV) Rhinovirus (common cold)	Bacterial pneumonia Atypical pneumonia Leptospirosis Rickettsia	Malaria

*ILI=Influenza Like Illness.

WHO has also laid down criteria for clinical syndrome associated with COVID-19 describing mild pneumonia, pneumonia, severe pneumonia, ARDS, sepsis and shock²⁵. There are many diseases which should be ruled out before confirming a case of COVID-19 (Table 3).

Laboratory Diagnosis

Laboratory findings in admitted cases include increase white blood cell count with lymphopenia, increased ferritin levels, D Dimer, lactate dehydrogenase, C Reactive protein, prolonged prothrombin time, elevated liver

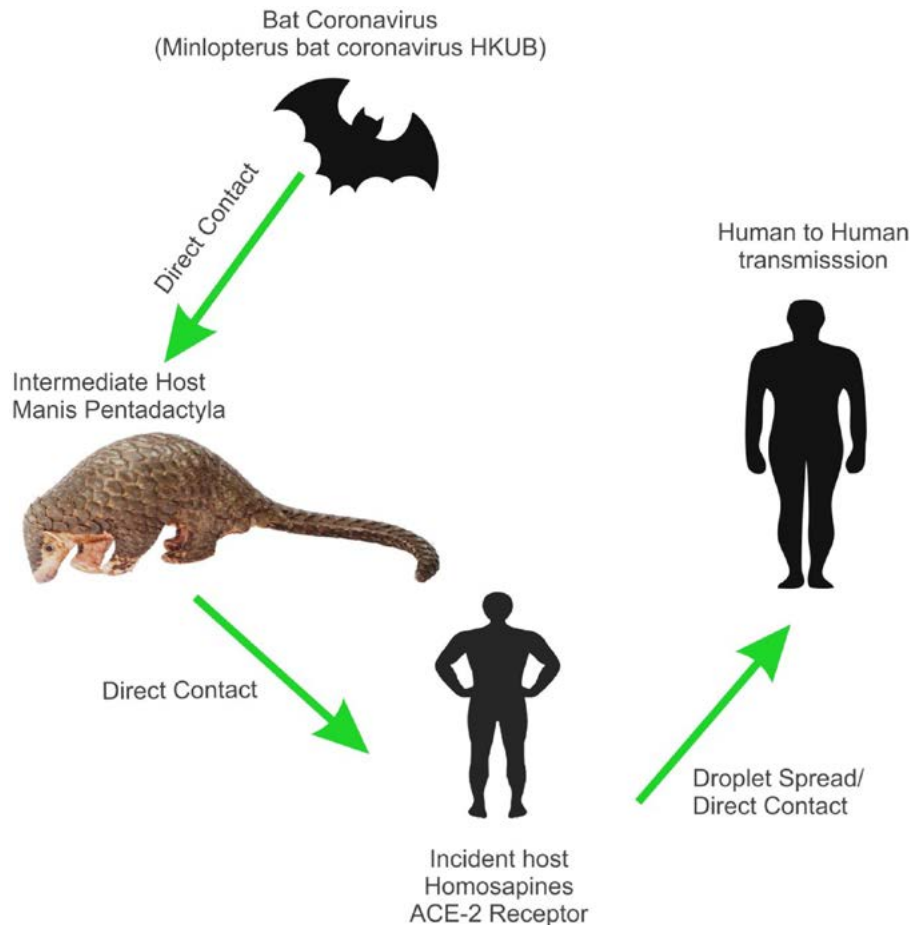


Fig. 4. Transmission Cycle of Novel Coronavirus in Bat to Human
The image is modified from source [5]

enzymes, Interleukin 6 and procalcitonin might increase in severe cases²⁷⁻²⁹. On imaging the findings associated are ground glass opacities with consolidation³⁰.

The confirmed diagnosis is made by detection of SARS-CoV-2 by means of polymerase chain reaction(PCR).Sensitivity of the result depends upon the type of sample, the quality of sample collected, the day on which sample was collected. The overall sensitivity of PCR within first week of appearance of symptoms is 67%. Bronchoalveolar lavage has the highest sensitivity of 90%³¹.

Recently few companies have developed ready to use kits for detection of novel SARS- CoV-2 which have been evaluated and approved by ICMR. These gave 100% positive and negative results^{32, 33}. Closed systems which have recently confirmed by the US FDA for emergency testing, are Xpert Xpress SARS-CoV-2 by Gene Expert (Cepheid, USA) , Abbott Laboratories (USA) 5-min point-of-care tests (Abbott ID NOW COVID-19) with a portable thermocycler and Biofire (Biomereieux, US FDA approved).These all require biosafety level 2 for processing of samples.

Another test which is recently approved by ICMR is Probe free COVID-19 testing detection assay with 100% sensitivity and specificity developed at Indian Institute of Technology, Delhi³⁴. An additional test which is being evaluated and awaiting ICMR approval is magnetic nanoparticle based- RNA extraction kit for PCR and LAMP test³⁵. Besides the molecular tests, many serological tests are also approved by ICMR³⁶. The antigen detection kits which are not available in India but some are approved that detects proteins of the COVID-19 virus in samples like sputum, throat swab. The sensitivity varies from 30% to 80%³⁷.

Besides antigen detection, there is another type of diagnostic test for COVID-19; it is rapid and detects the antibodies in patients infected with COVID-19.

It is proved by several studies that antibodies appear in the second week after onset of symptoms. Again the sensitivity of these kits varies with days of symptoms and kind of kits used³⁶⁻³⁸. For antibody detection a repeat testing is advised after 8-10 days for every individual³⁹. On 22nd of April it was requested by ICMR not to use those kits till further advisory is laid down and

till the kits are fully evaluated by NIV, Pune.

Enzyme Linked ImmunoSorbant Assay: These tests qualitatively assess the presence of IgG/IgM antibody in sera of the COVID-19 cases. These tests are relatively safer to perform but find little use in routine diagnostics⁴⁰. The quantitative antibody testing will be a boon for plasma therapy. Studies are still required to find out the antibody titres to be produced after infection/ exposure which can prevent re infection from same type of SARS-CoV-2 Viruses.

Limitation of Testing

Molecular Testing

Setting up molecular virology laboratory itself is a big challenge which requires specific designing for unidirectional workflow. The processing of samples needs well trained and experienced technicians along with microbiologist.

Serological Testing

It is not applicable for routine clinical use. It is only approved for surveillance purpose in hotspot areas, for epidemiological purpose and it must be accompanied always by a PCR testing. There is wide variation in the sensitivity and specificity of these kits.

Pool Testing

This kind of testing is approved by ICMR to speed up the surveillance screening. In these strategy five samples are mixed and run in one go instead of testing them individually basically to increase COVID-19 screening.⁴¹

Treatment of COVID-19^{42,43}

Self-care is Mandatory to Prevent COVID-19 Infection

This includes maintenance of healthy life style at home by taking healthy diet, complete sleep, social distancing and cleaning and disinfecting frequently touched surfaces at home. Good respiratory etiquettes, waste management also forms an integral part in abating infection at community level.

According to WHO ,trials are done on drugs that directly blocks the Replication of SARS-CoV-2 inside human lungs The trials done on some of the drugs are as follows:

Remdesivir

This is an intravenous antiviral drug that could block infection of coronaviruses. In Vitro experiments showed that Remdesivir can work against SARS-CoV-2 in cells of mice. It targets

key viral proteins called Proteases that helps in viral multiplication thus working of the virus is stopped but still trials are needed. Remdesivir are successfully used in US in treatment of some patients.

Lopinavir/Ritonavir

These drugs are used against viruses like HIV. It also blocks the main viral proteins called "proteases". Experiments showed that it works against SARS-CoV-2 in vitro cells and in mice. It can increase the natural defences of the body's cells against COVID-19.

Chloroquine and Hydroxychloroquine

These drugs are frequently used in the treatment of malaria, lupus and rheumatoid arthritis since long time and the U.S. Food and Drug Administration has already given the approval but few researches in human and primate cells showed that this can be given as a treatment to COVID-19 patients. Chloroquine could stop the spread of SARS-CoV, that was proved by the study done in 2005, in human cell culture. Entry and Replication of SARS-CoV virus in human cells is inhibited by this drug. It also works on SARS-CoV-2 in same way.

Antiviral EIDD-2801⁴⁴

It is an oral drug called EIDD-2801. The experiment was done in test-tube containing human lung and airway cells and was published in journal of Science Translational Medicine on April 6. The viruses RNA gets mutated by this drug and such mutated RNA makes its numerous copies, thus blocking the capacity of the infectivity of Viruses and thus viruses are unable to infect cells.

Plasma Therapy

For COVID-19^{45,46} It is basically a passive immunisation in which antibodies are transferred from infected person who has been recovered from the disease COVID-19 to person who is suffering from a SARS-CoV-2 infection. In administering plasma other treatment protocols should be followed. It basically decreases the duration of infection thus enhancing recovery. It is given in the patient having severe disease or any life-threatening problems. The therapy is effective in a patient as it cures breathlessness thus oxygen requirement is decreased. It is effective when it is used within the first 14 days of symptoms. This therapy has not been approved by ministry of Health and family welfare. Trials and researches are still in process.

Tetracyclines

Mohit Sodhi, at the University of British Columbia, Canada supported the usage of tetracyclines for treating COVID-19 patients. In a letter to the Editor Pharmacotherapy that was published online on April 8, 2020. The rationale for using tetracyclines is that it has the lipophilic nature of the tetracyclines along with its ability to inhibit matrix metalloproteinases (MMPs), anti-inflammatory properties and possible antiviral activity⁴⁷.

Other standard treatments such as antibiotics azithromycin, invasive or non-invasive ventilation and extracorporeal membrane oxygenation (ECMO) and vasopressor were also used.

Vaccine trials for COVID-19 proposals of more than 120 vaccines are being given globally and WHO is tracking details of their validity and feasibility of safety and efficacy on those vaccine candidates. Recently 6 vaccines are in clinical evaluation and about 70 in pre-clinical evaluation. To name a few Serum Institute, Zydus Cadilla, KGMU in partnership with NBRI etc. It is also to remember that it will take another one and half years for a vaccine to develop and experts say that besides herd immunity it is vaccine which can save life. WHO is encouraging regular direct discussion between researchers at lab level and vaccine developers to accelerate the conversation of scientific results. It also encourages discussion alarms and proposes rapid and strong methods for vaccine evaluation⁴⁸.

Herd Immunity

It is said that herd immunity strategy can help in overcoming this COVID-19 infection. This will happen only when virus infects 60% of population get infection and are asymptomatic⁴⁹. A diagrammatic representation is shown in Fig. 5. Reinfection: On April 25, 2020 The WHO said that there is no evidence that people who have recovered from COVID-19 cannot be re-infected. It was also said that already infected people should not be considered immune as cases are there where reinfection has been reported⁵⁰.

Immunoinformatics Aided Identification of nCovid 2019

Thousands of deaths and confirmed cases (Lakhs) have occurred worldwide due to this Coronavirus 2019 outbreak. Because of this

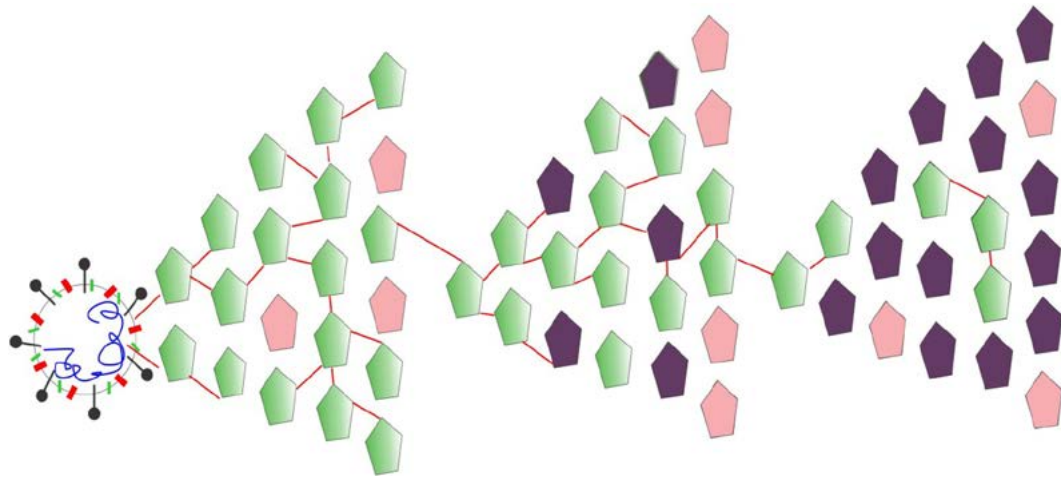


Fig. 5. Journey of the Herd Immunity (The image modified from source [49])

pandemic it is necessary to identify immune epitopes that is identification of T cell and B cell epitopes in the surface glycoprotein of novel Coronavirus 2019.

A study was done by Baruah, V et al to identify significant cytotoxic T lymphocyte (CTL) and B cell epitopes in the COVID-19 surface glycoprotein. They identified five CTL epitopes, three B cell epitopes in the viral surface glycoprotein. These five epitopes binds to their corresponding MHC class I molecules with continuous hydrogen bonds, thus initiating Immune response. This was Published in Journal of Medical Virology in March 2020 they also proved that the surface glycoprotein of COVID-19 having 76.3% identity and 87.3% similarity with the spike glycoprotein of SARS-CoV⁵¹.

Impact of Quarantine and Resilience for COVID-19

Thousands of deaths and confirmed cases in Lakhs have occurred worldwide due to the novel Coronavirus 2019 outbreak. In order to stop spread every country is doing Quarantine, Isolation, and Lockdown.

What is Quarantine and Isolation?

When people who have been exposed to the infecting disease are kept separated from others for observing the development of symptoms till incubation period is Quarantine. If the people are infected with the contagious disease, are separated from healthy ones is Isolation. Both cause significant, usually negative Psychological impact on such people due to certain factors like financial loss, fear of spreading infection and

their own health, social stigma etc. It also causes increase in domestic violence, divorce, and suicide rates. Psychological symptoms like post-traumatic stress symptoms, frustration, confusion, irritation, insomnia, poor concentration, anxiety, and depression may occur. So in order to avoid such mental health problems certain resilience factors is to be followed. The individuals to be quarantined or isolated, should be informed clearly about the situation, clear government protocol of such action, general and medical helps to be provided, duration of quarantine or isolation and its benefits should be explained ⁵².

Risk Assessment of COVID-19: Enhanced Surveillance^{53,54}

COVID-19 was declared a pandemic by WHO on 11th March, 2020. Though the infection started in China but later it spread globally. WHO suggested that the government of all countries to take actions on a society level to prevent the spread of this disease. In India numerous cases have appeared in many States, like Kerala, Karnataka, Telangana, Maharashtra, Uttar Pradesh, Rajasthan, Delhi, Punjab, and Ladakh.

India has reported travel related cases but large outbreaks, wide-spread community transmission are still the major risk in India. The following strategy is being implemented: Extensive contact tracing, searching of cases, doing tests of all suspected cases and high risk contacts, all suspected and confirmed cases to be isolated with proper medical facility, quarantining all contacts and social distancing.

Active surveillance is to be done in the areas where cases and contacts are more in number. There is a need to increase number of laboratories with testing facility of COVID-19 cases, hygienic isolation wards and spaces especially designated as COVID-19 hospitals/COVID-19 blocks with proper medical facilities need to be created and control measures like lockdown and social distancing to be taken. Prophylactic measures like Hydroxy-chloroquine to be administered to the healthcare workers and asymptomatic household contacts of confirmed cases. Awareness programmes, explaining of benefit and loss of ongoing situation to be done through audio, social and visual media.

Big Data Driven COVID-19 Health Risk Identification^{55,56}

In order to track, monitor and control the spread of COVID-19 all over world, big data driven model is needed that require certain tools like Artificial intelligence, Supercomputer, helps of research organizations and Government sectors for Coronavirus updates and to understand the nature of the virus. Researchers are creating some websites so that one can track all the open data and documents regarding Coronavirus.

Lots of information are required mainly Hospital Data and other information like availability of Hospital Resources, impact of the virus in different human, travel restrictions, stay at home orders is needed to create Big Data Driven model. Even experts in data and public health are needed to help combat COVID-19. Big data components like biological and biomedical research, social media, big organizations like Amazon Web Services, Google Cloud helps the scientists to open datasets and analytics tools for controlling Coronavirus spread. "This is, in essence, a big data problem.

"We're trying to track the spread of a disease around the world," It was said by James Hendler, who is a Professor of Computer, Web, and Cognitive Science at Rensselaer Polytechnic Institute (RPI).

Economic Impact of COVID-19 Outbreak

The more recent Coronavirus pandemic has brought forth many unprecedented economic fluctuations affecting almost every part of the world. For an example, when the virus came to light the investors were not even aware of how it

could affect financial markets.

Many major events all around the world have been cancelled- Professional sports leagues and the summer Olympics (Tokyo 2020) have been suspended. Major technical conferences and other events have been scrapped around the world. All these causes serious blow to the world economy. Earlier in March, economic loss has surpassed 1.1 billion dollars and it has progressed geometrically. As of the impact on India-Unemployment rose from 6% in mid-March to 26% in mid April, 14 crores of people lost employment. Indian economy is estimated to lose over 4.5 billion dollars every day since the 21 day lockdown. Major companies have suspended their operations. Stock markets had their worst losses in history on 23rd March 2020. India's GDP has been estimated to fall from 5.3 % to 2.5% Global economists have predicted a more brutal blow to the economy than the Great Financial Crisis of 2008 and even the Great Depression. New startups all over the world are severely affected. According to the United Nations global economy could be reduced by almost 1% in 2020 because of this pandemic. Economists said that China's economy could contract for the first time since 1970. In China, Cars sales have dropped by 68% and in the US by 48%. United Nations Development Program (UNDP) has predicted \$220 billion reduction in revenue in developing countries.

For the solution, we would have to remind ourselves of the basics of the working of an economy to come out of this major recession. Reduction in spending, debt restructuring (lowering debts), wealth redistribution from the rich to the poor, all three methods are deflationary and lastly the Central Bank prints new money which is inflationary. This is a very risky time. Economists need to frame the policies in such a way that all the four ways are balanced, i.e. the deflationary ways balances with the inflationary ways and there is a beautiful deleveraging⁵⁷.

Manage The Risk of Future Outbreaks

Many strategies can be laid down for managing future outbreaks this can be as follows:

Before Any Outbreak Surveillance of wildlife for high-risk pathogens in the high risk areas. It also includes antimicrobials given to animals for their growth which is also responsible for increase in Antibiotic resistance in the world

Surveillance and risk reduction in people with high chances of contact with wildlife and people with unnatural eating habits. Surveillance of improve biosecurity of the wildlife trade and animal markets. Surveillance of labs performing research on these microorganisms must be conducted. In countries like India one very important step to manage future outbreak is to have a robust medical infrastructure right from Primary health centres at lowest level to investing in capacity building and medical research in order that we produce high quality, all sort of medical equipment, diagnostic amenities, therapeutic interventions at national level. At hospital level now it becomes very important to have an infection control team with knowledge of infection control. Trained Infection control Doctors (preferably Medical Microbiologist) and nurses are the need of the hour. These people are responsible for laying down policies along with administrative support in medical set up and implementation of these policies and discussion of the problem at daily basis. So that during outbreak one knows the basic principle of Infection control and prevention that is "standard precaution". At community level it becomes important that organization with knowledge in IPC to come forward for community teachings, trainings and lectures so that maximum public is reached out and has a basic idea of infection control practices.

During Outbreak Once all the facilities are available then during outbreak it becomes important to contain infection with various measures. It becomes very important to identify source with testing strategies. The principle to be used can be "testing maximum, identifying case, isolation, treatment and contact tracing". Infection prevention measures at community level play a very important role in containing infection. Advocating social distancing, use of protective equipments, respiratory etiquettes as is required in present scenario. It also depends on the type of disease and mode of infection for that particular outbreak.

After outbreak the most important step to be taken is to revive economy of all the victims. Specific plan to manage post outbreak economy loss especially for the daily wagers should be made⁵⁸.

CONCLUSION

There is a need to know about the dynamics and immune kinetics of SARS CoV2. The various transmission routes of infection must be kept in mind. Infection control and preventive measures must be followed at community and hospital level. These measures are key to control the spread of virus. At the same time a surveillance of the wildlife and lab doing researches on microorganisms must be done. A strong dedication and commitment from all the individuals (like social distancing, hand hygiene, use of mask, cough etiquettes) along with strengthening of medical infrastructure and production of quality medical equipment is the need of the hour. Many studies regarding treatment including plasma therapy and vaccine development is in process. The mere detection of SARS-CoV-2 in various samples run on PCR is not the end. Researchers should come up with quantitative detection of viruses in the given sample and simultaneously a viral culture to be performed to find out the viability of virus in those samples (cases). Studies can be performed in context to viral load and its relation to infectivity or viral culture and its relation to infectivity which could help in finding out the nature of the virus regarding transmission to other individuals. This can further aid us in identifying those individuals (having live virus) to go for isolation. Studies related to antibody titre present after recovery of COVID-19 cases and re-infection among those can also be performed by the researchers to find out the nature of this novel virus.

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CONFLICT OF INTEREST

The authors declares that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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ETHIC STATEMENTS

This article does not contain any studies with human participants or animals performed by any of the authors.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript and/or the Supplementary Files

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