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7. Novel Coronavirus (SARS-CoV-2): A Pandemic Era

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Abstract:

SARS-CoV-2 belongs to the betacoronavirus genus. Betacoronaviruses infect mammals, are zoonotic pathogens, and can cause severe respiratory disease in human being. Till date there are no drugs or vaccine to control the infection of this pandemic disease. Alternatively few drugs like anti-viral, anti-malarial and antibiotic, plasma therapy and other traditional system of medicine (Ayurveda and Homeopathy) are used against pandemic COVID-19 disease. The success of herd immunity depends on the higher proportion of the population that must be immune in order to stop an epidemic. An epidemic dies out when an average infection can no longer reproduce it. This occurs when large fraction of an infected hosts contacts is immune this threshold between where an infection can and cannot reproduce itself defines the fraction of the population required for heard immunity.

Keyword:

Virus, Covid-19, SARS-CoV-2, herd Immunity, RT-PCR, Rapid Antigen Testing.

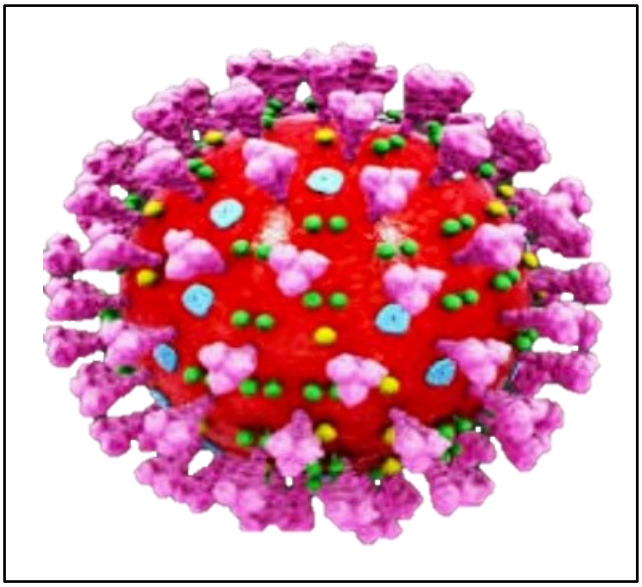
Introduction:

A Pandemic Era of 21st century- Human beings has been affected with several bacterial and viral outbreaks, epidemics and pandemics since time immemorial. Three deadly epidemics/pandemics have occurred during 18th-20th century: the great plague of Marseille, 1720; the Asian cholera, 1817-1824; and the Spanish Flu, 1918-20. Three deadly virus diseases have plagued humankind in the 21st century- Severe Acute Respiratory Syndrome (SARS, 2002), Middle East Respiratory Syndrome (MERS, 2012) and the nCoronavirus disease (COVID-19, December 2019-to till date). The COVID-19 pandemic is the heart-breaking global health crisis of our time. Emerging from late last year in Asia, the virus has

spread to every continent except Antarctica. Though it's not as deadly as SARS or MERS, it's much more contagious. This Virus has affected many lives from locality to global.

Current Scenario - As on 3rd September 2020, reported number of confirmed cases was 26.1M with 864K deaths globally. Same day India has reported 3.85M confirmed cases with 67K deaths. Considering the low testing capacity and restricted testing strategy in many countries, number of confirmed cases and deaths is likely underreported.

On February 11, 2020 the International committee on Taxonomy of viruses named the virus 'severe acute respiratory syndrome ncoronavirus (SARS-CoV-2). Picking up a formal name for the novel coronavirus and the disease it caused is conductive to communication in clinical and scientific research.The virus belongs to the β- coronavirus family, a large class of viruses that are frequent in nature. Like other viruses, SARS-CoV-2 has many potential natural hosts, intermediate hosts and final hosts. These cause major challenges for the prevention and treatment of viral infection (Wang L. et al. 2020).



Compared with severe acute Respiratory Syndrome and Middle East Respiratory Syndrome Coronavirus (SARS-CoV and MERS-CoV, respectively), SARS-CoV-2 has highly transmissibility and infectivity, and a low mortality rate (Liu et al., 2020).

Travel Genome analysis of SARS-CoV and bat SARS coronavirus (SARSr-CoV-RaTG13) were 79.5% and 96%, respectively (Chen et al., 2020). This implies that SARS-CoV-2 might originate from bats.

1. Genetic structure and pathogenic mechanism of SARS CoV-2:

nCoronavirus are enveloped, non-segmented, positive- sense single-stranded RNA viruses (ssRNA virus) with a diameter of 80-120nm.They have the largest genome among all RNA viruses (Wang L. et al., 2020). There are four types of viruses namely α-coronavirus, β-coronavirus, δ-coronavirus and γ- coronavirus. Prior to SARS-CoV-2, six coronavirus were now known to cause disease in human beings, including SARS-CoV and MERS-CoV. SARS-CoV-2, like SARS-Cov and MERS-CoV, belongs to the family of β-coronavirus.The genome is packed inside a helical capsid formed by the nucleocapsid protein and later surrounded by an envelope. The genome sequence homology of SARS-CoV-2 and SARS is approximately 79%; SARS-CoV-2 is closer to the SARS- like bat coronavirus (MG772933) than SARS-Cov (Wu et al., 2020), which descended from SARS-like bat coronavirus. Interestingly, several analyses have shown that SARS-CoV-2 uses angiotension- converting enzyme 2(ACE2) as its receptor, in common with SARS-Cov (Hoffmann et al., 2020).

Very recently, we published a review on nCoronavirus and mentioned that Covid-19 belongs to the Category- Coronaviruses; Order- Nidovirales; Family-Coronaviridae; Genus-Betacoronavirus; Species- SARS-CoV2. Betacoronaviruses can infect mammals, are zoonotic pathogens, and can cause severe respiratory disease in humans (Kaushik & Singh, 2020). Other viruses in this family are SARS coronavirus and MERS coronavirus. Covid-19 (SARS-CoV-2) has approximately 79% sequence identity to SARS-CoV and 50% to MERS-CoV. Fehr et al., (2015) published a research paper on Coronaviruses: an overview of their replication and pathogenesis in Methods Mol Biol. They report that Covid-19 (SARS-CoV-2) virus consists: a spike (S) protein, dimer (HE) hemagglutinin-esterase, a membrane (M) glycoprotein, an envelope (E) protein, a nucleocapsid (N) protein and ssRNA- Single standard ribonucleic acid (Figure-1).

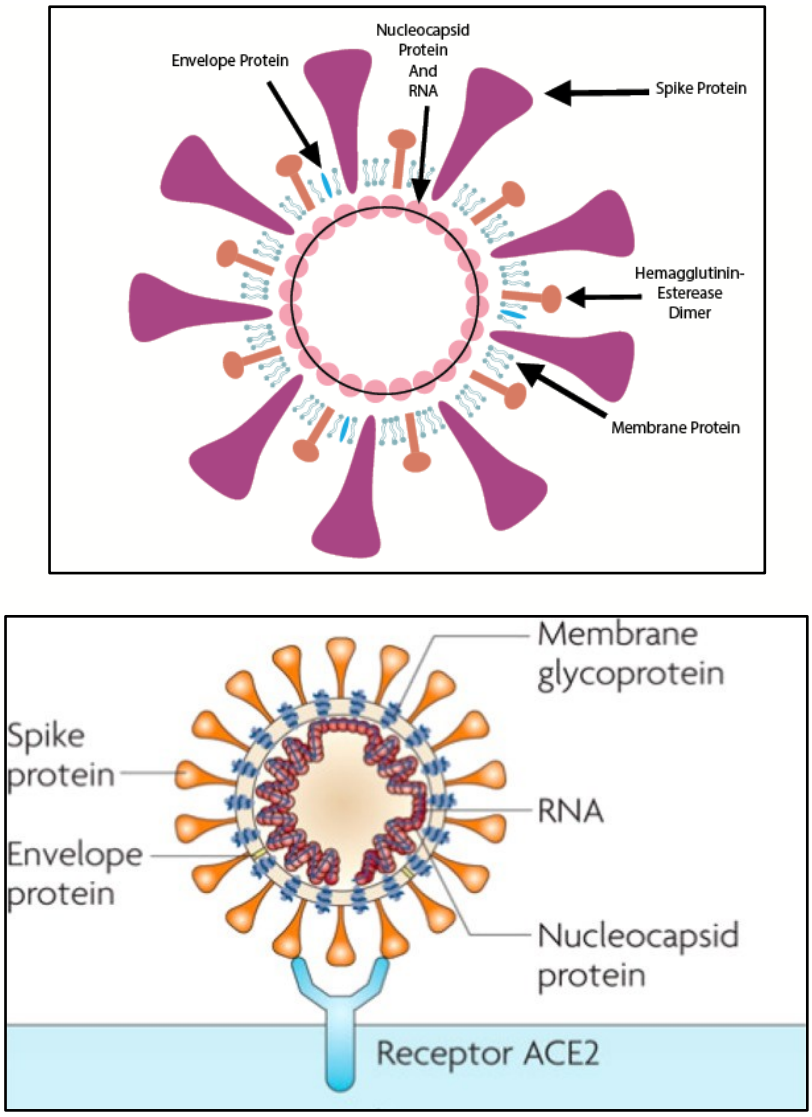


Figure-1-nCoronavirus structure with receptor ACE2

Spike protein (S) - The surface of the spikes is homotrimers are mainly glycosylated. Trans membrane protease serin type 2 (TMPRSS2) [6] composed of two separate polypeptides S1 and S2, respectively. The subunit S1 form head of the spike has a receptor binding domain which ultimately binds to nCoronavirus host receptor ACE2. Subunit S1 triggers a conformational change in (S) protein and promotes membrane fusion with the help of Subunit S2.

ssRNA are largest of all RNA virus genome (single standard RNA genome) about ~27-32 Kb in size.

Nucleocapsid protein (N protein) is abundant phosphoprotein. N proteins contribute only protein with N-terminal and C-terminal. It binds the ssRNA genome in beads on a string type conformation.

Envelope protein (E) is the smallest (max. 109 amino acid) structural protein. It involves in various ways such as assembly, budding and formation of envelop etc. Envelop proteins E may oligomerize and form ion channel. This virion goes for pathogenesis.

Membrane protein (M) is the most abundant transmembrane (III) glycoprotein. It contains approximately 230 amino acids. It does not contain signal sequence and exists as a dimer in the virion. Glycoprotein M maintains the bioactive and antigenic character. It may have two conformations (long & compact) to onset and promote membrane curvature to bind with nucleocapsid.

Hemagglutinin-esterase dimer protein (HE) is present in N-coronaviruses. The HE protein attached with sialic acids receptor present on surface host cell surface. The protein activities are enhanced through S protein-mediated cell entry and virus spread by mucosa of the host (Kaushik and Singh, 2020; Lu et al., 2020).

nCoronavirus strongly recognize its corresponding receptors on target cells through S-proteins on their surface; entry to the cells finally results in infection. Phylogenetics analyses undertaken with available full genome sequences suggest that bats appear to be the reservoir of COVID-19 virus, but the intermediate hosts has not yet been recognized.(World Health Organisation,2020). A structure model analysis shows that SARS-CoV-2 binds to ACE2 with more than 10-fold stronger affinity than SARS-CoV, at a level above the threshold required for virus infection (Wrapp et al., 2020).

The mechanism by which SARS-CoV-2infects humans beings via binding S-protein to ACE2, the strength of the interaction for risk of human transmission, rate of infection, and how SARS-CoV-2 causes different body organ damage still remain unfold, more research, data and studies are needed. On the basis of several results it comes to know that faster transmission capability of SARS-CoV-2 in humans compared with SARS-CoV, and higher number of confirmed cases worldwide of COVID-19 compared with SARS-CoV infection. Considering the higher affinity of SARS-CoV-2 binding to ACE2 may be a potential candidate for the treatment of COVID-19 (Wang L., et.al. 2020).

2. Transimission of SARS-CoV-2:

On the basis of previous epidemiological results it revealed that there are three factors involved in rapid spreading of viral: source of infection, route of transmission and susceptibility (Barreto et al., 2006). The case for SARS-CoV-2 described briefly below-

2.1. Source of infection:

Bats are considered to be the natural hosts of SARS-CoV-2, and pangolins and snakes are thought to be intermediate hosts, however some of the studies deny that snakes are host. A study from Wuhan Institute of Virology showed 96.2% similarity in the gene sequence between SARS-CoV-2 and bat coronavirus with the help of sequencing technology. This subsequently implies that bats are the potential source of SARS-CoV-2 (Zhou et al., 2020). By macrogenomic sequencing, molecular biological detection and electron microscope analysis, found 99% similarity between SARS-CoV-2 isolated from pangolins and the virus strains currently infecting humans beings (Xu et al., 2020).

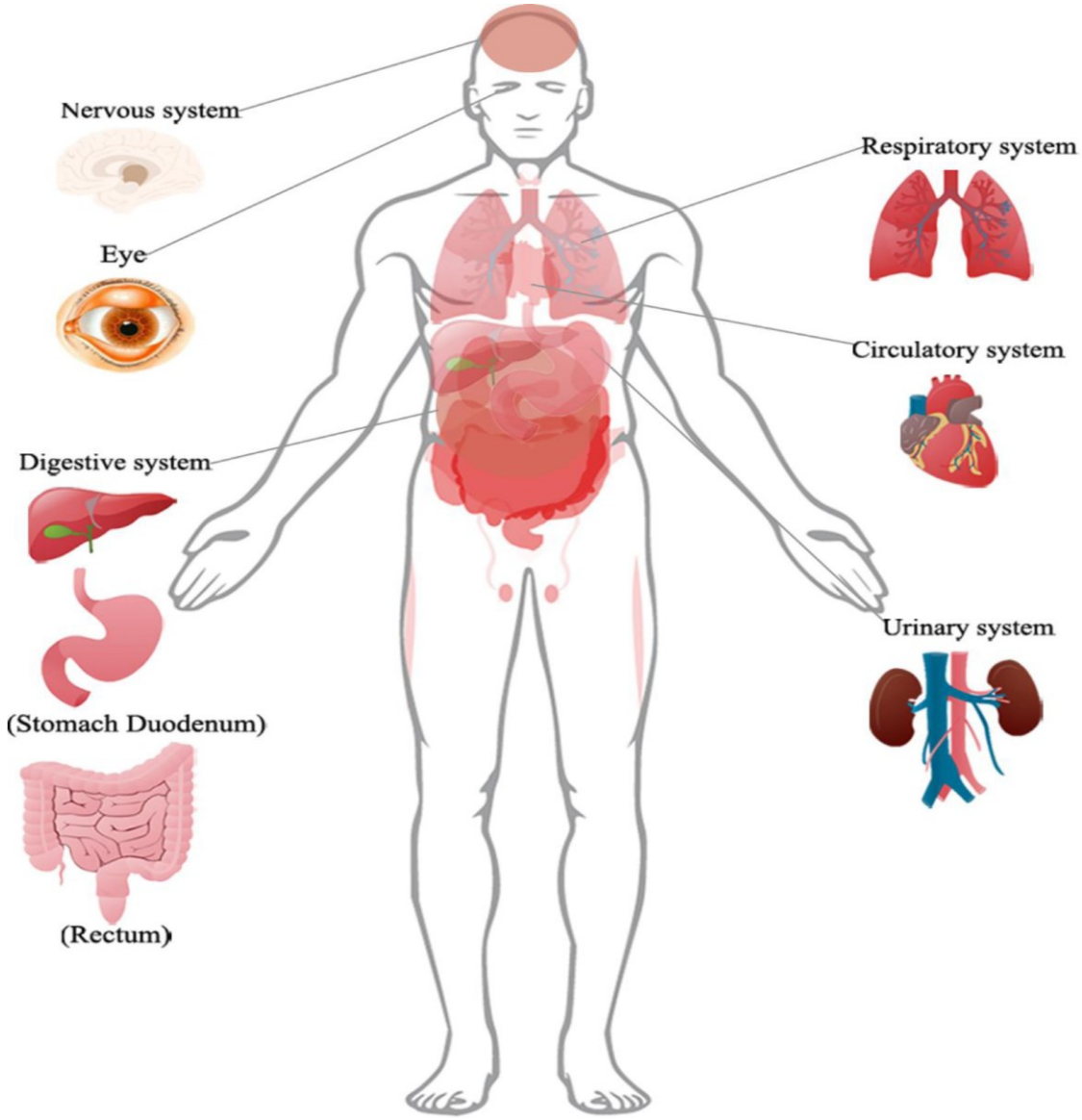


Fig. 2. Organ involvement confirmed by clinical features or biopsy in patients with COVID-19. Source - https://doi.org/10.1016/j.ijantimicag.2020.105948

Bats are the potential natural reservoir and pangolins as the possible intermediate host of the virus. Although no studies to date have fully elucidated the potential natural host and intermediate host of SARS-CoV-2, evidence shows that the virus might be sourced from wild animals (Wang L., et al., 2020). On the basis of data and result at present, it is considered that the main source of infection of SARS-CoV-2 is patients with COVID-19. However, question remains unanswered whether these patients are infectious during the incubation period.The median time from exposure to onset of symptoms suggests that the 14-Day quarantine period recommended by the WHO and other organisations are reasonable.

2.2 Route of transmission:

Droplets and close contact from person to person (about 6 feet/1.8 metres) are the most common routes of transmission of SARS-CoV-2, person-to-person spread mainly occur via respiratory droplets when an infected person coughs or sneezes, and aerosol transmission may be another route. Researchers have also investigated SARS-CoV-2 in samples of stool, gastrointestinal tract, saliva and urine. Based on bioinformatics, evidence has indicated that the digestive tract may be a route of SARS-CoV-2 infection (Wang J. et al, 2020). SARS-CoV-2 RNA has been detected consistently in gastrointestinal tissue from patients with COVID-19. Also in research, SARS-COV-2 was detected in the tears and conjunctival secretions of patients with COVID-19. In a study of nine pregnant women with COVID-19 indicated that the possibility of intrauterine vertical transmission between mothers and infants during late pregnancy was temporarily excluded. However, available data on pregnant women infected with SARS-CoV-2 are inadequate; further studies are required to verify the possibility of vertical transmission in women (Wang L. et al., 2020). Also, there is rare expectation when breastfeeding or feeding expressed breast milk is not recommended. Given low rates of transmission of respiratory viruses through breast milk, the World Health Organisation currently states that mothers with COVID-19 can breastfeed.

2.3 Susceptible Population And Viral Latenc:

An epidemiological investigation report stated that old aged people are most susceptible to SARS-CoV-2 (median age at death 75 years), and most of the patients who died had severe medical problems or a history of surgery before admission (Wang, W. et al., 2020). During research according to data collected it was found that, median incubation period was 3 days (range0-24days), and the median time from symptom onset to death was 14 days. For SARS-CoV infection, the median latency was 4 days, the average interval from symptom to hospital admission was 3.8 days, and the average interval from hospital admission to death was 17.4 days (Lessler et al., 2009). The incubation period for COVID-19 is quit shorter than that for SARS. However, the maximum latency of SARS-CoV-2 currently observed is as high as 24 days, which may increase the higher risk of virus transmission and more and more people will be susceptible to this. Further, people aged≥70 years had a shorter median interval(11.5 days) from symptom to death compared with patients aged <70 years (20 days), revealing, that disease progression is more rapid in elderly people as compared to younger ones. So definitely, our focus should be on elderly people who might be more vulnerable to

SARS-CoV-2. Also, people of any age are at increased risk of severe illness from COVID-19: Cancer, Chronic Kidney disease, COPD (chronic obstructive pulmonary disease).

3. Clinical Characteristics Of SARS-Cov-2 Infection:

SARS-CoV-2 produces an acute viral infection in humans with a median incubation period of 3 days (Guan et al., 2020); this is similar to SARS-CoV with an incubation period of 2-10 days. The most common symptoms of COVID-19 are fever (87.9%), cough (67.7%), and fatigue (38.1%), diarrhoea (3.7%), and vomiting (5.0%) are rare, loss of smell, similar to other coronavirus infections. The disease may also occur with mild symptoms only, including low fever, cough, sore throat, being tasteless (In India some of the reported cases it was found that a person infected to COVID-19 lost its taste without any other symptoms) shortness of breath or difficulty in breathing. Risk factors for illness are yet not clear. Disease in children appears to be rare and mild with 2.4% of the total reported cases among individuals aged less than 19 years. A small number of populations of those aged fewer than 19 years have developed severe (2.5%) or critical disease (0.2%) (World Health Organization, 2020). In a research there is evidence that COVID-19 can cause damage to not only lungs but also tissues and organs. Also, there is an evidence of ocular surface infection in patients with COVID-19, and SARS-CoV-2 RNA was detected in eye secretions of patients (Ai et al., 2020). Tissues samples of stomach rectal mucosa and duodenum have also been tested positive for SARS-CoV-2 RNA (Xio et al., 2020). In addition, the radiographic features of coronaviruses are similar to those which are found in community-acquired pneumonia caused by some other organisms (Wong et al., 2003). The most important tool to diagnose this pneumonia is computed tomography (CT) scan. A recent study observed that most of the patients about (90%) had bilateral chest CT findings, and the sensitivity of chest CT to suggest COVID-19 was 97%. Having chest CT imaging features with clinical symptoms could facilitate early diagnosis of COVID-19 pneumonia. If we compare with bacterial pneumonia, patients with COVID-19 had a lower oxygenation index. Laboratory observations states that 82.1% of patients were lymphopenia and 36.2% of patients were thrombocytopenic (Wang L. 2020).

4. Diagnosis Of SARS-Cov-2:

The detection of viral nuclei acid is the standard for non-invasive diagnosis of COVID-19. Also, the detection of SARS-CoV-2 nuclei acid has high specificity and low sensitivity, so it may be possible false- negative results and the testing time may be relatively long (Wang L.

2020). Experts to understand the two main kinds of tests for COVID-19 diagnosis and their reliability, according to experts, all the tests available in the market for testing COVID-19 have their own pros and cons but RT-PCR remains the best standard for testing.

4.1 RT-PCR (Reverse Transcription- Polymerase Chain Reaction):

This test has high specificity rate; gives less false positives, which is considered as the gold standard for testing. This test is performed by taking swabs from nasal and oral tracts both which are then put in viral transport medium and brought to the lab. It is then processed under the bio-safety level-2 plus facilities; then RNA extraction is done to detect the presence of the virus. RT-PCR test has a specificity (ability to identify those without the disease) of approximately 100 percent whereas, the sensitivity rate (ability to identify those with disease) of about 67 percent; subsequently, it means that RT-PCR test will not give false positives but there may be a chance of about 30-35 percent of getting false-negatives; there are mainly three reasons, first one is the technology itself which one cannot consider as limitations. Secondly, if the samples are not taken in a proper manner then the result can be a false-negative. This is the only reason why both nasal and oral swabs are taken. Thirdly, people are now seeing it as a preventive test means they are getting the test done without having any symptoms of COVID -19.

4.2 Rat (Rapid Antigen Testing):

It has a moderate sensitivity (around 50%) and high specificity which simply means if a test is done on 100 patients of COVID-19, it will give positive results for only 50 of them. According to ICMR, if RAT gives negative result but one has a symptom of influenza like illness, then one should undergo RT-PCR test. However, RAT has its own advantages that it can be done on a mass level. Now the number of tests being performed is about thousands.

4.3 Race For The Vaccine:

Scientists around the world are working on vaccines and medicines for COVID-19, More than 100 projects are on the way for development of vaccines. Russia reported its first vaccine on 11th August, 2020 named Sputnik-V. Strategies include attenuated strain vaccine, genetically modified and synthetic peptides vaccine, Nano particle based vaccine, self-amplifying RNA molecules etc. The vaccine, ChAdOx1 nCoV-19, is based on an adenovirus

vaccine vector and the SARS-CoV-2 spike protein. Its aim is to make body recognise and develop immune response to S protein thus preventing SARS-CoV-2 virus from entering human cells and therefore prevent infection. In India, Serum Institute of India, Pune has tied up with an American biotech company to develop a live attenuated vaccine. Hyderabad based Bharat Biotech has teamed up with university of Wisconsin Madison and a US based firm. If these trials are successful, a vaccine is expected by end of 2020 after the completion of protocols.

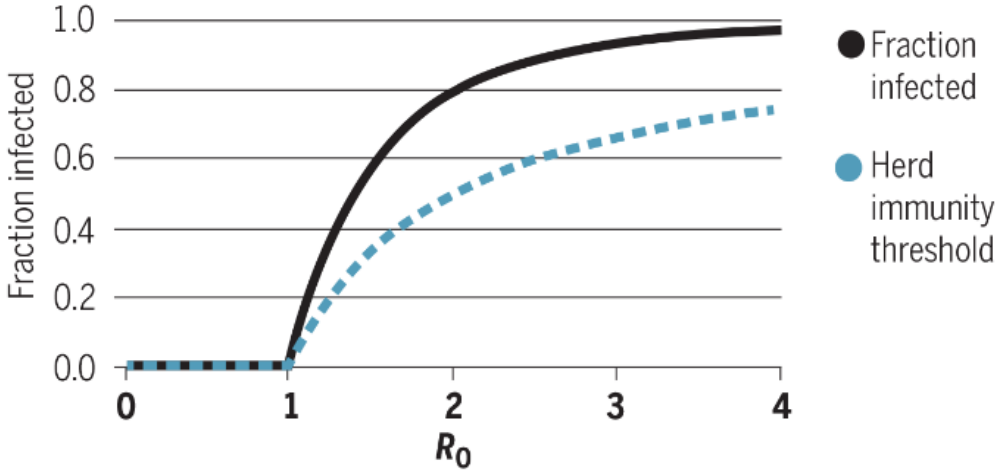
5. Herd Immunity Mathematics:

The early spread of Covid-19 has divulged critical information about potential size of the pandemic, if it were allowed to grow unchecked. This information can be mathematically studied with the help of mathematical modelling of infectious diseases. The total number of people infected in a population is determined by the intrinsic reproductive number, R_0. This number is the expected number of secondary cases caused by an index case in another susceptible population. Also, R_0 can be expressed as the transmission rate/ divided by the rate at which people recover or mortal. For accuracy describe R_0 in reference to a pathogen and host population, because the number is partially under host control. It also helps in determining the average long-term generality in the population, assuming new susceptible persons prevent the disease from dying out. As an epidemic increases and few of the population become immune, the average number of secondary cases caused by an infected person is called the effective reproductive number R_t. In India a decline trend in Covid-19 cases or a small spring to summer epidemic might be taken as evidence that interventions have been especially effective or that herd immunity has been achieved (Kaushik and Singh, 2020) (Figure -3).

An epidemic dies out when an average infection can no longer reproduce it. This occurs when large fraction of an infected hosts contacts is immune this threshold between where an infection can and cannot reproduce itself defines the fraction of the population required for herd immunity. It can be calculated precisely if the epidemiology of the pathogen is well known and is used to guide vaccination strategies. Herd immunity is constantly eroded by the births of new susceptible hosts and sometimes by the waning of immunity in previously infected host (Cobey, 2020).

Figure-3: Pandemic size and herd immunity

The fraction of the population that becomes infected with a transmissible disease in a simple epidemic model increases non-linearly with the intrinsic reproductive number R_0, and will exceed the threshold for herd immunity. R_0 is the expected number of cases caused an indexed case. Interventions can reduce R_0, the total fraction of the population infected, and the threshold for herd immunity.



Source: Cobey S. Modeling infectious disease dynamics. Science 24 April 2020, 10.1125/science.abb5659.

The durability of immunity to Covid-19 is not yet known till date, but births will promote virus survival. Thus like other transmissible pathogens, Covid-19 is likely to circulate in humans for many years to come. Steps taken by Indian Government are appreciable against pandemic Covid-19. The infection rate in India remains low relative with respect to large population size. Credit goes to fast action like Lockdown, physical distancing and susceptible people will be quarantine (Cobey, 2020).

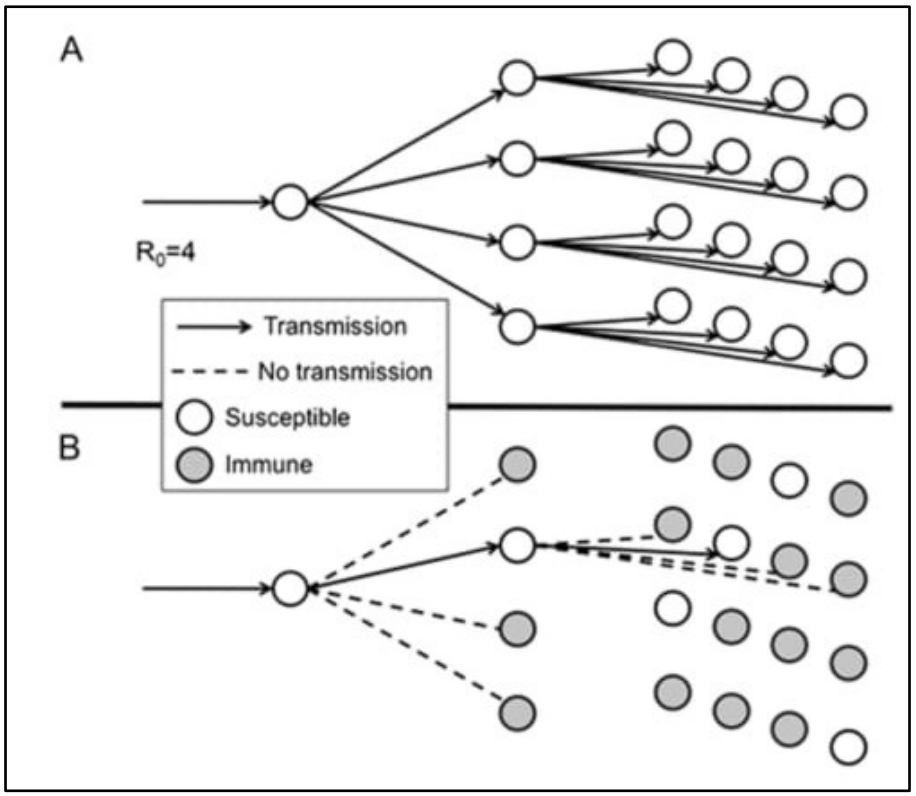


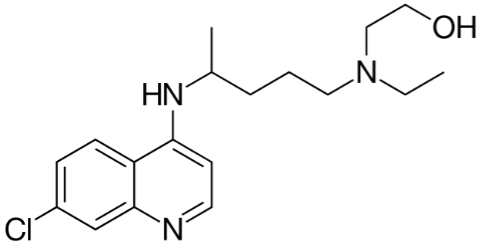
Fig.4- A- Transmission of disease with an R0 of 4 in a susceptible population.

B- Transmission of disease with an R0 of 4 in a population in which three of every four people is immune i.e. Rt in this latter scenario is equal to 1.

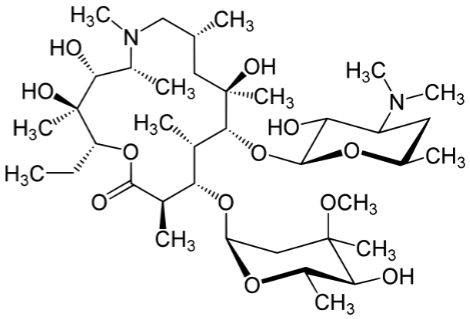
6. Drugs used in COVID-19:

Currently, there is no specific medicine or vaccine for the treatment of coronavirus. The US FDA has approved the antiviral compound, remdesivir, as an experimental drug for COVID-19. Remdesivir is supposed to accelerate the recovery of patients suffering from the disease, but the effectiveness of the drug is yet to be peer-reviewed. Favipiravir is the first approved nCoronavirus drug in China.

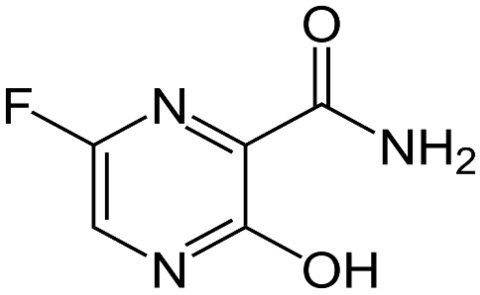
Azithromycin (AZ) is antibiotic unlike antiviral drug hydrochloroquine (HCQ) and used for the treatment of a number of bacterial infections. Chloroquine is also an effective anti-malarial drug and is included in World Health Organisation's list of essential medicines.



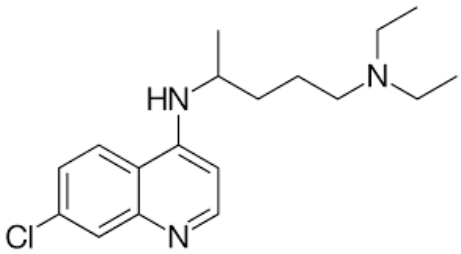
Hydroxychloroquine (HCQ)



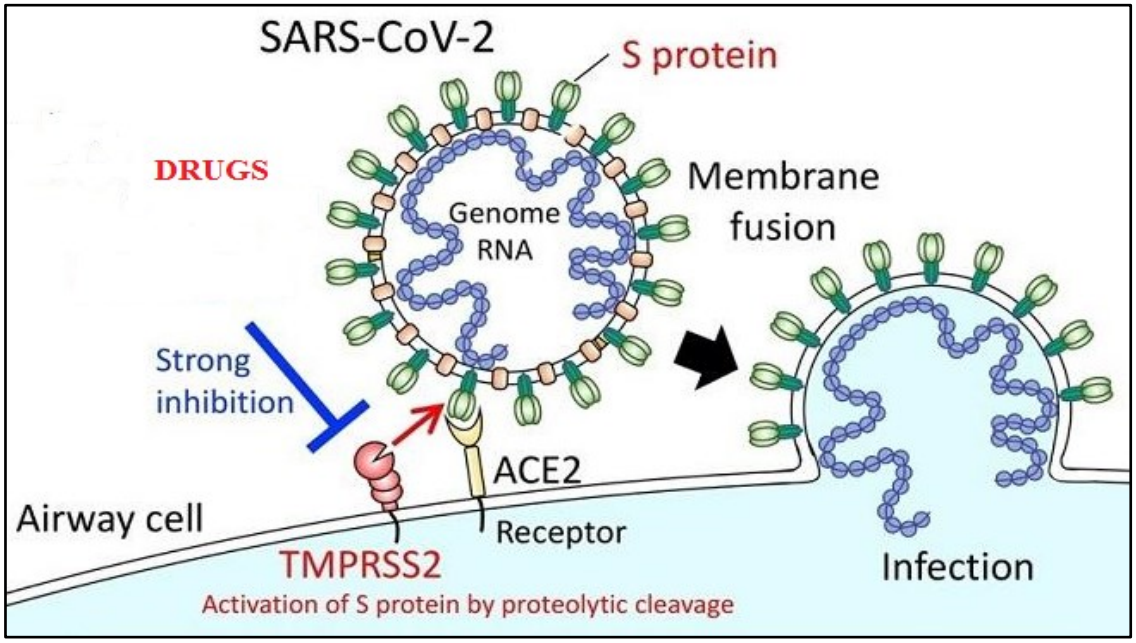
Azithromycin (AZ)



Favipiravir



Chloroquine



Drugs May Inhibits Entry Of SARS-Cov-2

7. Preventive Measures:

WHO (2020) reported that the corona viruses can mutate effectively, which makes them so contagious. To prevent transmission, people should stay at home and rest while symptoms are active. Prevention is, so far, the best practice in order to reduce the impact of COVID-19 considering the lack of effective treatment (Kumar, 2020). Ginnaro et al. (2020) suggested that at the moment, there is no vaccine available and the best prevention is to avoid exposure to the virus. In order to achieve this goal, the main measures are the following:

1. to use face masks;
2. to cover coughs and sneezes with tissues;
3. to wash hands regularly with soap or disinfection with hand sanitizer containing at least 60% alcohol;
4. to avoid contact with infected people;
5. to maintain an appropriate distance from people; and
6. to refrain from touching eyes, nose and mouth with unwashed hands.
7. Maintain at least 1 m (3.28 feet) distance between yourself and anyone who is coughing or sneezing.

8. Immune Booster Ayush Kadha:

Drink herbal tea/decoction (Kadha) made from Tulsi (*Ocimum sanctum*), Dalchini (*Cinnamomum tamala*), Kalimirch (*Black pepper*), Shunthi (*Gingiber officinale*) and Munakka (*Vitis vinifera*)- once or twice a day. Add jaggery (natural sugar) and/or fresh lemon (*Citrus limon*) juice to your taste, if needed.

Beside this Ministry of AYUSH also recommends the following self-care guidelines for preventive health measures. These are as follows-

1. Drink Cow Milk- Half tea spoon Haldi (*Curcuma longa*) powder in 150 ml hot cow milk- once or twice a day.
2. Drink warm water throughout the day.
3. Daily practice of Yogasana, Pranayama and meditation for at least 30 min.
4. Spices like Haldi (*Curcuma longa*), Jeera (*Cuminum cyminum*), Dhaniya (*Coriandrum sativum*) and Lahsun (*Allium sativum*) garlic are recommended in cooking.

5. Take Chyavanprash 10g in the morning. Diabetics should take sugar free.

9. Plasma Therapy:

Rojas et al. (2020) reported that the clinical administration of the blood plasma from recovered covid-19 patients to those severely affected by the disease could be a safe option without adverse effects, according to a study which may lead to better treatment protocols against novel corona virus infection. Salaza et al. (2020) reported in his research article that on March 28, researchers from the Houston Methodist Hospital in the US, began clinical trials to transfuse plasma from recovered covid-19 patients into critically ill patients and they noted that 19 out of 25 patients improving with the treatment and 11 discharged from the hospital.

The Economics Times (2020) reported in his news that physician scientists around the world scrambled to test new drugs and treatments against the COVID-19 virus, convalescent serum therapy emerged as potentially one of the most promising strategies. Salaza et al. (2020) also reported that the scientists in the century-old therapeutic approach dates back to at least as early as 1918 to fight the Spanish Flu by using convalescent serum therapy.

Casadevall and Pirofski (2020) reported that convalescent plasma therapy was used with some success during the 2003 SARS pandemic, the 2009 influenza H1N1 pandemic and the 2015 Ebola outbreak in Africa. They said early on in the Covid-19 pandemic, there were a handful of critically ill patients in China who showed improvement from plasma therapy, following which their team at Houston Methodist hospital targeted the Covid-19 virus with the procedure. Altair Data Analytics Summit (2020) clearly reported in his news that, it is not clear if the 25 patients given convalescent plasma would have improved without the treatment, adding that all patients were treated with multiple other medications, including antiviral and anti-inflammatory agents. “We cannot conclude that the patient outcomes were due solely to administration of convalescent plasma”. They said a randomized clinical trial would help address some questions, including whether patients would have better outcomes if plasma transfusions were administered sooner after the onset of symptoms.

10. Heating, Ventilation And Air Conditioning (HVAC) Systems:

Heating, ventilation and air conditioning (HVAC) systems and managing indoor air during the COVID-19 pandemic measures to improve indoor air quality focus on two processes: Air cleaning and ventilation. Air cleaning refers to the use of filters or air purifiers to catch indoor containments, including virus- containing particles. Most of the homes and buildings have filters as part of their HVAC systems.

Ventilation refers to the introduction of fresh outdoor air into an indoor environment. Through dilution, ventilation can lower the indoor concentration of containments, which also includes virus particles. At homes, ventilation can be improved by opening windows or doors so long as there is no safety risk to those inside the home. In kitchen and bathroom exhaust fans can also aid in improving in-home ventilation by adding to air exchange and directly removing air containments from a room.

11. Ecological Lessons and Conclusions:

The pandemic COVID-19 transmits a number of ecological and economic lessons for the future survivability of human beings. We must learn to live in harmony with nature. We need to possible implement for ecological conservation and restoration of nature. We need to revise urban planning; instead of invaded growing city areas and also we need to plan human habitation systematically in town. We need to setup a new model of economy beyond the model of globalised economy. Studies in this domain are urgently needed to minimize the impact of the outbreak. Over the last five decades the emergence of many different corona viruses that cause a wide variety of human diseases has occurred. It is likely that these viruses will continue to emerge and to evolve and cause human health outbreaks owing to their ability to recombine, mutate, and infect multiple species and cell types. Future research on corona viruses will continue to investigate many aspects of its replication and pathogenesis.

References:

1. Ai, T., Yang, Z., Hou, H., Zhan, C., Chen, C., Lv, W., *et al.* (2020). Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology, Article 200642, 10.1148/radiol.2020200642.

2. Altair Data Analytics Summit (2020) Covid-19 plasma therapy safe, without adverse side effects: Study. The Indian Express 3 June 2020.

3. Barreto, M.L., Teixeira, M. G. and Carmo E.H. (2006). Infectious diseases epidemiology. J Epidemiol Community Health, 60: 192-195.

4. Casadevall, A. and Pirofski, L. (2020). The convalescent sera option for containing COVID-19. J Clin Invest 130: 1545-1548.

5. Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F. and Han, Y. et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 nCoronavirus pneumonia in Wuhan, China: a descriptive study. Lancet, 395 (10223): 507-513.

6. Cobey S. Modeling infectious disease dynamics. Science 24 April 2020, 10.1125/science.abb5659.

7. Fehr A.R. and Perlman S. (2015). Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 2015; 1282:1–23. doi.org/10.1007/978-1-4939-2438-7_1.

8. Gennaro F.D., Pezzoli D., Marotta C., Antunes M., Racalbuto V., et al. (2020) Coronavirus Diseases (COVID-19) current status and future perspectives: A narrative review. Int J Environ Res Public Health, 17: 2690.

9. Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W.H., Ou, C.Q., He, J.X. *et al.* (2020). Clinical characteristics of 2019 novel coronavirus infection in China. N Engl J Med (2020), 10.1056/NEJMoa2002032.

10. Hoffmann, M., Kleine-Weber, H., Kruger, N., Muller, M., Drosten, C. and Pohlmann S. (2020). The nCoronavirus 2019 (2019-nCoV) uses the SARS-coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. bioRxiv2020.01.31.929042.

11. Kaushik, H. and Singh V. K. (2020). Mathematics of Covid-19 in India and their possible control by *Allium sativum* (L.). Asian J of Advances in Medical Sciences, **2(1):** 21-27.

12. Kumar P. (2020). Overview on coronavirus (COVID-19). Asian J Adv Med Sci 2: 15-20.

13. Lessler, J., Reich, N.G., Brookmeyer, R., Perl, T.M., Nelson, K.E. and Cummings D.A. (2009). Incubation periods of acute respiratory viral infections: a systematic review. Lancet Infect Disease, 9:291-300.

14. Liu, Y., Gayle, A.A, Wilder-Smith, A. and Rocklov J. (2020). The reproductive number of Covid-19 is higher compared to SARS coronavirus. J Med 27(2). taaa021, 10.1093/jtm/taaa021.

15. Lu, R., Zhao, X., Li, J., et al. (2020). Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The Lancet. Published online January 29, doi.org/10.1016/S0140-6736(20)30251-8.

16. Rojas, M., Rodrguez, Y., Monsalve, D.M., Ampudia, Y.A., Camacho, B., *et al.* (2020). Convalescent plasma in Covid-19: Possible mechanisms of action. Autoimmun Rev 19: 102554.

17. Salazar, E., Perez, K.K., Ashraf, M., Chen, J., Castillo, B., *et al.* (2020). Treatment of coronavirus disease 2019 (COVID-19) patients with convalescent plasma. Am J Pathol. 190(8): 1680–1690.

18. The Economics Times (2020). Covid-19 plasma therapy safe, without adverse side effects: Study.

19. Wang, J., Zhao, S., Liu, M., Zhao, Z., Xu, Y., Wang, P. *et al.* (2020) ACE2 expression by colonic epithelial cells is associated with viral infection, immunity and energy metabolism. MedRxiv, (2020)2020.02.05.20020545.

20. Wang, L., Wang, Y., Ye, D. and Liu, Q. (2020) A review of the 2019 novel coronavirus (SARS-COV-2) based on current evidence. International J of Antimicrobial Agents, 55(6): 105948. doi.org/10.1016 /j.ijantimicag.2020.105948.

21. Wang, W., Tang, J., and Wei F. (2020). Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China J Med Virol, 92 : 441-447.

22. WHO (2020). Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations. Scientific Brief, 29 March, 2020.

23. Wong, K.T., Antonio, G.E., Hui, D.S., Lee, N., Yuen, E.H., Wu, A. *et al.* (2003). Severe acute respiratory syndrome: radiographic appearances and pattern of progression in 138 patients. Radiology, 228: 401-406.

24. World Health Organization (2020). Report of the WHO-China Joint Mission on Coronavirus disease 2019 (Covid-19). 16-24 February, 2020.

25. Wrapp, D., Wang, N., Corbett, K.S., Goldsmith, J.A., Hsieh, C.L., and Abiona, O. *et al.* (2020). Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science, 367 (6483): 1260-1263.

26. Wu, A., Peng, Y., Huang, B., Ding, X., Wang, X., and Niu, P., et al. (2020). Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe, 27(3):325-328.

27. Xiao F., Tang M., Zheng X., Li C., He J., Hong Z., *et al.* (2020). Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology, doi:10.1053/j.gastro. 2020.02.055.

28. Xu, X., Chen, P., Wang, J., Feng, J., Zhou, H., Li, X. *et al.* (2020). Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modelling of its spike protein for risk of human transmission. Sci China Life Sci, 63(3):457-460.

29. Zhou, P., Yang, X.L., Wang, X.G., Hu, B., Zhang, L., Zhang, W. *et al.* (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature, 579 (7798):270-273.