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REVIEW PAPER

The Pandemic Effect of Corona Virus (COVID-19)

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ABSTRACT

There is a new world health crisis threatening the public with spread of COVID-19 (Corona virus Disease 2019).Since December 2019,when Covid-19 emerged in seafood market at Wuhan, South China and rapidly spread throughout the world, the virus outbreak has been declared a public health emergency of International concern by World Health Organization (WHO).We have summarize the current clinical characteristics data to guide potential COVID-19 about Prevention, Treatment ,Prevention and further studies of COVID-19.In this review, we extracted data from various Research Report, WHO guidelines and other articles .It is important to caution the readers the new data updating nearly every hour regarding clinical characteristics , diagnosis, treatment strategies, and outcomesCOVID-19. Throughout the world disease has caused varying degrees of illness. Patient show various symptoms usually fever, cough, sore throat, breathlessness, fatigue and malaise among others. The disease is being cured through general treatment, symptomatic treatment, by using antiviral drugs, oxygen therapy and by the immune system. It is necessary to identify the potential cases as soon as possible and isolate the suspected people from the confirmed cases of COVID-19,to prevent the potential transmission of infection to other patients and health care staff.

Keywords: - Corona virus disease 2019, COVID-19, respiratory syndrome, Molecular biology, SARS.

INTRODUCTIO

WHO states that Corona viruses are a large family which may cause illness in animals or humans. In humans, several corona viruses are known to cause respiratory infections ranging from the common cold to move severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).The most recently discovered corona virus causes corona virus disease COVID-19.[1]

Novel corona virus induced pneumonia, which was named as corona virus disease 2019 (COVID-19) by the WHO on the 11th of February 2020, has rapidly increased in epidemic scale since it first appeared in Wuhan, China, in December 2019. On the same day, the international virus classification commission announced that the novel corona virus was named as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). COVID-19 is not the first severe respiratory disease outbreak caused by the corona virus. Just in the past two decades, corona viruses have caused three epidemic diseases, namely, COVID-19, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)[2]. At present, the cases of COVID-19 have been found in many countries around the world. On the 31st of January, 2020, the World Health Organization (WHO) announced that COVID-19 was listed as the Public Health Emergency of International Concern (PHEIC), meaning that it may pose risks to multiple countries and requires a coordinated international response.

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The review tries to explain the molecular immune pathogenesis infection, based on the recent research progress of SARS-CoV-2 and the knowledge from researches on SARS- CoV and MERS- CoV.[2]

On 30th January 2020, the Director – General declared that the outbreak of 2019-nCoV constitutes a Public Health Emergency of International Concern (PHEIC). The WHO Emergency Use Listing (EUL) is open to candidate *in vitro* diagnostics (IVDs) to detect SARS-CoV-2 (originally called 2019-nCoV).

Since 28th February 2020, manufacturers of IVDs for the detection of SARS-CoV-2 nucleic acid are invited to submit an Expression of Interest (EOI) for assessment of candidate IVDs under the EUL procedure, On 17th April, WHO extended the invitation to manufacturers of rapid diagnostic tests (RDTs) intended for antibody detection.

The EUL procedure is developed to expedite the availability of IVDs needed in public health emergency situations. It is intended to assist interested procurement agencies and Member States on the suitability for use of a specific IVD, based on minimum set of available quality safety and performance.

Currently the following IVDs are eligible for EUL submission:

- Assays for the detection of SARS – CoV 2 nucleic acid;
- Rapid diagnostic tests for the detection of IgM/IgG to SARS-CoV-2

Currently, several performance evaluations of SARS-CoV-2 IVDs are being implemented by regulatory authorities reference laboratories and other stakeholders in various regions. Manufacturer are strongly encouraged to participate in initiatives which generate evidence that can be use to support the EUL submission. However, participation external evaluations does not replace the EUL submission nor is participation in such studies mandatory for submission to the WHO EUL.

Replication

Infection begins when the virus enters the host cell, the virus particle is uncoated and the spike protein attaches to its complementary host cell receptor. After attachment, a proteolytic enzyme of the host cell cleaves and activates the receptor-attached spike macromolecule. Depending on the host cell proteolytic enzyme available, cleavage and activation enable cell entry through endocytosis or direct fusion of the viral envelope with the host membrane. (SA 16) The chemical structure of Corona virus RNA consists of 5' methylated head and a 3' polyadenylated tail, through which the RNA attaches to the free ribosomes of the host cell. This lead to the process of translation and formation of a long polypeptide chain. This protein has its enzyme (Proteases) which break the polyprotein into multiple non structure proteins. Corona viruses (CoVs), are the family of viruses that have pricky spikes that project from their surface. They have enveloped RNA viruses, are characterized by club-like spikes that project from their surface, they have a unique replicating process. These viruses are the cause of many types of diseases in mammals and birds leading to enteritis in cows and pigs and upper respiratory infection in humans which may balance.[5]

Symptoms

Maximum of the patients infected with the virus will experience common cold and flu, while few of them remain asymptomatic. 80% of patient

will show mild symptoms of the disease. Adults have the best immunity to fight against the infection but the demerit is that they are more likely to spread the infection A recent study of nearly 140 patients at the Zhongnan Hospital of Wuhan University identified different types of symptom, which lead to a disease known as COVID-19. 99% of the patients developed a fever with extremely high temperature, while more than half experienced fatigue and a dry cough. One-third of the patient developed a dry cough and difficulty in breathing .Research from the Chinese CDC observes that around 80% of corona virus cases are mild, around 15% of patients have infected severe cases, and 5% have become critically ill. A day by day breakdown of corona virus symptoms shows how symptoms progress among typical patients, how the disease, COVID-19, goes from bad to worse.[7]

*Day 1: In the starting day of the symptom, the patient suffers from fever along with fatigue, muscle pain, and a dry cough. Few of them may experience nausea and diarrhoea a few days before the arousal of symptoms.

* Day 5: Patients may suffer from breathing problem especially if they are elderly or have some pre-existing health condition.

* Day 7: According to the Wuhan University study, these are the symptoms of the patient that lead the patient to be admitted in the hospital.

*Day 8: On the 8th day, patients (15%, according to the Chinese CDC) develop acute respiratory distress syndrome (ARDS), a condition where the fluid fills up in the lungs and this is mostly fatal. This usually happens in severe cases.

* Day 10: The progression of the disease leads to worsening of the symptom and at this point the patient is shifted to ICU. Patients with milder symptoms probably have more abdominal pain and loss of appetite. Only a small fraction die. The current mortality rate is around 2%.

* Day 17: On average, after two-and-a-half weeks patients who recover are discharged from the hospital. However, it's difficult to find out the symptoms in the earlier days of the infection. This is usually seen after 5-6 days. [Reported symptoms have ranged from mild to severe illness and death for confirmed corona virus disease 2019 cases. Emergency warning signs of COVID-19 needs medical attention immediately, continuous pain or pressure in the chest, include trouble in breathing, confusion and bluish lips or face. The progressed condition leads to Pneumonia and the incubation period is yet to be determined as the virus is recently identified. As per the new information, symptoms could appear as soon as three days after exposure to as long as 13 days later. Recently published research found that on average, the incubation period is about five days.

Diagnosis of Corona Virus (Covid-19)

Diagnosis allows suspected people to understand that they are infected or not. Diagnosis can help them receive the care they need and it can help them take measures to cut back the probability of infecting others. People who don't know they are infected may not occupy at home and thereby risk infecting others. If the person develops symptoms of corona virus disease 2019 and they have been exposed to the virus, he should consult to doctor. The doctor may decide whether to conduct tests for COVID-19 based on individual signs and symptoms. The doctor may also consider whether an individual had close contact with someone

diagnosed with COVID-19 or travelled to or lived in any areas with ongoing community spread of COVID-19 within last 14 days.[18] Corona virus Disease-2019 tracking and diagnostic testing are critical and also critical to understanding epidemiology, informing case management, and to suppressing transmission. The Corona virus disease outbreak is additionally typical to prevent virus community transmission, including how testing might be rationalized when lack of reagents/ testing kit or testing capacity necessitates prioritization of certain populations group or individuals for testing." (MA 3) To test for COVID-19, doctor or health practitioner may take samples, including a sample of saliva (sputum), a nasal swab and a throat swab, to send to a lab for testing or follow the directions of your local health authority.[9]

Treatment Strategy of Covid 19

We here summarize the current data to guide potential COVID-19 treatment options. It is important to caution readers that new data updating nearly every hour regarding clinical characteristics, diagnose, treatment options, and outcomes for COVID-19. But optimized supportive care remains the backbone of therapy and the clinical efficacy for the subsequent agents is still under investigation or in 121E JMO clinical trials . Most standing clinical and preclinical data on antiviral therapy is taken from other viruses, including SARS-CoV-1, Middle East Respiratory Syndrome, and non-corona viruses (Ebola).

General treatment

A confirmed patient of COVID 19 needs complete bed rest and supportive treatment, ensuring adequate calorie and water intake to reduce the risk of dehydration. Water electrolyte balance and homeostasis need to maintain along with the of monitoring vital signs and oxygen saturation; keeping respiratory tract unobstructed and inhaling oxygen in more severe cases; measuring blood count, C-reactive protein, urine test, and other blood biochemical indexes including liver and kidney function, myocardial enzyme spectrum, and coagulation function according to patient's conditions. Chest imaging should be continuously re-examined and blood gas analysis should be performed when required. [4]

Symptomatic Treatment

Control measures are needed for patients with a high fever. Antipyretic drug treatment should be performed in case the temperature exceeds 38.5 °C. Warm water bath and antipyretic patches are preferred as a preventive measure to lower the temperature. Common drugs include ibuprofen orally, 5–10 mg/kg every time; acetaminophen orally, 10– 15 mg/kg every time. Need to administer sedative arises in case the child suffers from convulsions or seizure.

Oxygen Therapy

The chances of hypoxia are increased as the virus targets the lungs. Nasal catheter, mask oxygen should be immediately provided to the patient. In emergency conditions, Non-invasive or invasive mechanical ventilation should be provided to the patient.

Antiviral Drugs

Group of antiviral drugs including interferon α (IFN-α), lopinavir /ritonavir, chloroquine phosphate, ribavirin , and arbidol are therapeutically useful for the Prevention, Diagnosis, and Treatment of Novel Corona virus-induced Pneumonia by the National Health Commission

(NHC) of the People's Republic of China for tentative treatment of COVID-19 .

IFN-α is administered in the form of vapour inhalation at a dose of 5 million U (and 2 mL of sterile water for injection) for adults, 2 times/day. The dosage of lopinavir/ritonavir is 400 mg/100 mg for adults, 2 times/day. Ribavirin should be administered via intravenous infusion at a dose of 500 mg for adults, 2 to 3 times/day in combination with IFN-α or lopinavir/ritonavir. Chloroquine phosphate is orally administered at a dose of 500 mg (300 mg for chloroquine) for adults, 2 times/day. Arbidol is orally administered at a dose of 200 mg for adults, 3 times/day. The duration of treatment is no more than 10 days.[6]

Favipiravir is a new drug that is under clinical trial for treating COVID-19. On February 15, 2020, China approved it to be a useful drug for treating Novel Influenza. It acts by inhibiting the enzyme RNA dependent RNA Polymerase. Apart from being effective for anti-influenza virus, the drug is capable of blocking the replication of flavi-, alpha-, filo-, bunya-, arena-, noro-, and other RNA viruses. Favipiravir is converted into an active phosphoribosylated form (favipiravir-RTP) in cells and is recoRNA polymerase, thus inhibiting RNA polymerase activity. Therefore, favipiravir may have potential antiviral action on SARS-CoV-2, which is an RNA virus. Remdesivir is another investigational drug under clinical trial for the treatment of COVID-19. Remdesivir is a nucleoside analogue and a broad-spectrum antiviral. Animal experiments indicated that remdesivir can effectively reduce the viral load in lung tissue of mice infected with MERS – CoV , improve lung function, and alleviate pathological damage to lung tissue. A team of researchers from Shanghai Institute of Materia Medical and Shanghai Tech University performed drug screening in silicon and an enzyme activity test, and they reported 30 agents with potential antiviral activity against SARS-CoV-2 on January 2020. These agents are indinavir , saquinavir, lopinavir, carfilzomib, ritonavir, remdesivir, atazanavir, darunavir, tipranavir, fosamprenavir, enzaplatovir, presatovir, abacavir, bortezomib, elvitegravir, maribavir,[12]

raltegravir, montelukast, deoxyrhapontin, polydatin, chalcone, disulfiram, carmofur, shikonin, ebselen, tideglusib, PX-12, TDZD-8, cyclosporin A, and cinanserin. Certain Chinese herbal medicines such as RhizomaPolygoniCuspidati and Radix SophoraeTonkinensis were also found to contain certain active constituents that were effective against SARS-COV-2.

Prevention and Precaution of Covid-19

People should stay aware of the latest information on the COVID-19 outbreak provided by WHO and follow the directions of your local health authority and prevent secondary infections, interrupt human-to-human transmission to your close contacts, health care workers and prevent further international spread most of the people who infected, experience mild illness and recover it, but its infection can be more severe for other individuals. To take care of your health and protect others take the subsequent steps:

Take steps to protect yourself

• Wash your hands regularly and thoroughly with soap and water for at least 20 seconds or with an alcohol based hand rub (hand sanitizer that contains at least 60% alcohol) completely cover your hands and rub them together until they do not dry

especially after you have been visited a public place, or after blowing your nose, sneezing or coughing.

• Hands touch many surfaces and pick up viruses and these contaminated hands, can transfer the virus to your nose, eyes or mouth. So, avoid touching these organs with unwashed hands. Because from there, the virus can enter the body and may cause persons to sick.

• Maintain social distancing (maintain at least 1 meter or 3 feet distance between yourself and anyone) and avoid close contact with people who are sick (who is coughing or sneezing). When infected individuals cough or sneezes, they spray small droplets from their nose or mouth which may contain COVID-19 virus. The person can breathe in these droplets.[17]

• Avoid large events and mass gatherings

Take steps to protect others

• Stay home if you are feeling unwell, unless you're going to get medical care.

• If you have a cough, fever and difficulty breathing, seek medical attention consult online to your doctor.

• If you're sick avoid taking public transportation.

• Whenever you cough or sneeze cover your mouth and nose with a tissue paper.

• Throw used tissues in the trash and wash your hands immediately with antiseptic soap and water.

• If possible, stay isolated in a separate room from family and pets and wear a facemask when you are around Other people (e.g., sharing a room or vehicle). If you are unable to wear a facemask (due to its causes trouble breathing or other reason) then you should cover your coughs and sneezes, and but when the people who are caring for you enter your room they should wear a facemask

. • Stay home for a duration of time and follow your doctor's instructions

. • If you're sick, avoid sharing bedding, dishes, glasses and other household items

• If possible, use a separate bathroom and toilets from the family

• If surfaces are dirty, clean them, and use detergent or antiseptic soap & water before disinfection apply

• Apply disinfectant daily on frequently touched surfaces. This includes desks, phones, keyboards, toilets, faucets, tables, doorknobs, light switches, countertops, handles, and sinks.

• Identify and Isolate Suspected Cases

• Before clinical care is started, Identify the potential cases as soon as possible and isolate the suspected people separately from those who confirmed cases of the virus COVID-19, to prevent the potential transmission of infection to other patients and health care staff.

• Avoid direct physical contact (including physical examination and exposure) to respiratory and other body secretions. For instance, move potentially infectious people to isolation rooms and close the doors. In a working place, make the distance in workers, customers, and other visitors, especially from potentially infectious individuals' location

• In case of need to isolate a patient or patient group, pharmacies should designate and prepare a suitable space

• Most patients presenting in community pharmacies are unlikely to have COVID-19. If they have coughs, colds or flu-like symptoms but not relevant to COVID-19, travel or contact history, pharmacies should proceed in line with their best

practice and routine management of the cross-infection risks to staff and other patients.

• Restrict the number of individuals entering isolation areas, including the room of a patient with suspected and confirmed COVID-19.

• For safe work practice, protect workers to close contact with the infected person by using additional engineering and administrative control.

EPIDEMIOLOGY

As of 15 April 2020, 210 Countries and Territories around the world have reported over 1.998.111 confirmed cases and 126.604 deaths of COVID-19 and show the presence in six continents. According to the medical journal hosted by Johns Hopkins University. Though the proportion of confirmed cases outside China is steadily increasing.Most infected countries data of COVID-19 are summarized in the below chart .

Death Rate Varies by Age, Health and Sex

World Health Organizations Director-General, Tedros Adhanom Ghebreyesus, said that globally, about 3.4% of reported Covid-19 cases have died. Matt Hancock Health Secretary of UK governments said a very best assessment was that the fatality rate was "2% or, likely, lower". However, it varies on a range of factors such as general health, age, sex, and the health system you are living in. In the first huge analysis of more than 44.000 cases from China, the death rate was ten times higher in the very elderly compared to the middle-aged. The death rates were lowest for under the 30s there have been eight deaths in 4.500 cases. And deaths were at least five times more common among individuals with diabetes, high blood pressure or heart or breathing problems. There were even a rather higher number of deaths among men compared to women**.**

COVID-19 death Rate by Age Group: Death Rate = Number of deaths/Number of cases = Probability of dying if infected by the virus (%) Many studies increasingly clear that death rate increases with age Children under 9 years of age seem to be largely unaffected, either with no or mild symptoms or none have died due to COVID-19 infection. While people over the age of Eighty years and those with chronic diseases are the most vulnerable. For those cross 80, approximately 14.80% of those infected die . The fatality rate starts to increase for those over 50 years of age. Those under 50 years who are infected have a death rate of 0.40%, while for those 50-59 years it's 1.3%. For those 60-69 years it's 3.60%, for 70 to 79-year-olds it's 8.00% and for those over 80 years of age, it is 14.8%.[16]

Covid-19 death Rate by Sex Ratio: As the worldwide death toll from the COVID-19 increase, the evidence is growing that more men are becoming seriously ill or dying from the corona virus than women yet its numbers slightly vary country to country it doesn't necessarily reflect differences in biology. Scientists are still not completely sure but maybe on average, men more involve in health-damaging habits such as drinking and smoking than women Show fatality sex difference.

COVID-19 death Rate by Health Conditions: Information made by Centers for Disease Control and Prevention (CDC) and lots of other studies increasingly clear that risk of severe illness and death increases with age. Adults who are both older and not have better medical conditions have a greater risk to become infected. Among adults age

60 or older, more than half also have a serious medical condition rising to nearly two-thirds of people age 80 and older. Older age people and younger adults with serious illness, such as diabetes, heart disease, and lungs disease, have a greater risk of becoming severely ill if they get infected with the corona virus. The death rate for those who not have pre-existing conditions is approximately 1%. Centers for Disease Control and Prevention has issued specific guidance for people who fall into these categories .For those with cardiovascular (heart) disease the death rate is 10.5%, for diabetes death rate is 7.3%, for Chronic respiratory disease (such as asthma and chronic obstructive pulmonary disease) it is 6.3%, for hypertension (high blood pressure) it's 6.0% and the cancer death rate is 5.6% data summarised in.

CLINICAL PATHOLOGY OF SARS-COV-2 (COVID-19)

The disease caused by SARS-CoV-2 is also named as the Severe Specific Contagious Pneumonia (SSCP) and named as Corona virus Disease 2019 by WHO. Compared to SARS-CoV , SARS-CoV-2 has less severe pathogenesis but has superior transmission competence that is evident from the continuously confirmed cases [9]

SARS-CoV-2 in familial clusters was found to be 3-6 days. The mean incubation period of COVID-19 was estimated to be 6.4 days and ranging from 2.1-11.1 days. Among the early affected people of 425 patients, 59 years was the median age group affected, of which more males were affected. Similar to SARS and MERS, the severity of this nCoV is high in age group people above 50 years.

The initial trends suggested that the mortality associated with COVID-19 is comparatively lesser than the previous outbreaks of SARS. The 2019-n-CoV invades the lung parenchyma resulting in severe interstitial inflammation of the lungs. This will be evident on CT images as ground-glass opacity in the lungs lobes. The histolgical examination of lung biopsy samples obtained from COVID-19 infected patient showed diffuse alveolar damage, cellular fibrimyxoid exudates,hyaline membrane formation, and desquamation of pneumonocytes, indicative of acute respiratory distress syndrome. It has also been found that the SARS-CoV-2 infacted patients often have lymphocytopenia along with/ without leukocyte abnormalities. The degree of lumphocytopenia gives an idea about the disease prognosis as it is found positively correlated with the disease severity. Pregnant women are considered to be having ahigher risk of getting infected by COVID-19. The coronaviruses can cause adverse outcomes for the fetus, such as intrauterine growth restriction, spontaneous abortion, preterm delivery, and perinatal death.

Nevertheless, the possibility of intrauterine maternal-fetal transmission (vertical transmission) of CoVs is low, and it is not reported in either SARS or MERS. However, there has been concern regarding the impact of SARS-CoV-2/COVID-19 on the pregnancy.

Researchers have mentioned the probability of in utero transmission of novel SARS-CoV-2 from COVID-19 infected mothers to their neonates in China based upon the rise in IgM,IgG antibody levels and cytokine values in the blood obtained from newly borne infants immediately post-birth; however, reverse transcriptase-polymerase chain

reaction (RT-PCR) did not confirm the presence of SARS-CoV-2 genetic material in the infants.

Vaccines, Therapeutics, and Drugs

The recently emerged viruses such as Zika , Ebola, and Nipah viruses and their high threats to humans, have paved race in exploring of designing and developing advanced vaccines, prophylactics, therapeutics and drugs regimens to counter emergency viruses. Several attempts are being made to design and develop vaccines against corona virus infection, mostly by targeting the Spike glycoprotein . Due to the lack of effective antiviral therapy and vaccines in the present scenario, we have to rely exclusively on enforcing infection control measures to minimize the risk of possible nosocomial transmission. Recently, the receptor for SARS-CoV was confirmed as the human angiotensin-converting enzyme2 (hACE2), and the virus was found to enter the host cell mainly through endocytosis .It was also found that the major components that have critical role in the viral entry include PIKfyve, TPC2, and cathepsin L. These findings are critical since the components described above might act as a potential candidate for vaccines or therapeutics drugs against SARS-CoV-2. [11]

The majority of the therapeutic options and strategies that we are evaluating in SARS-CoV-2 (COVID-19) are taken from our previous experiences in treating SARS-CoV, MERS-CoV , and other emerging viral diseases. Several therapeutic and preventive strategies, including vaccines, immunotherapeutics , and antiviral drugs ,have been explored against the previous corona virus outbreak caused by SARS-CoV and MERS-CoV. These valuable options have already been evaluated for their potency ,efficacy, and safety along with several other ongoing types of research will fuel our search for ideal therapeutic agent against COVID-19. The main reason for the lack of approval and commercially available vaccines or therapeutics agents against the previous corona viruses like SARS-CoV and MERS-CoV might be due to the lack of interest among the pharmaceutical companies. These are outbreak scenario : the demand for drugs or vaccines last for a period until the outbreak lasts. The number of people affected will also be a small proportion of the global drug and vaccine market. So, by the time a new drug or vaccine is developed, there would not be any patient for clinical trials, and also there would not be any market for the newly discovered drugs to be sold. At present, there is no vaccine or therapeutic drugs available for treating COVID-19 infection.

Vaccines

The S protein plays a significant role in the induction of protective immunity against SARS-CoV by mediating T-cell responses and neutralizing-antibody production (168). In the past few decades, we have seen several attempts to develop a vaccine against human corona viruses by using S protein as the target . However, the developed vaccines have minimal application even among closely related strains of the virus due to a lack of cross-protection. That is mainly because of the extensive diversity existing among the different antigenic variants of the virus . The contributions of the structural proteins like a spike (S), matrix (M), small envelope (E), and nucleocapsid (N) proteins of SARS-CoV to induce protective immunity has been evaluated by expressing them in a

recombinant para-influenza virus type 3 vector called BHPIV3. Of the note, the result was conclusive that the expression of M, E, or N proteins without the presence of S protein would not confer any detectable protection with the absence of detectable serum SARS-CoV-neutralizing antibodies . Antigenic determinant sites present over S and N structural proteins of SARS-CoV-2 can be well explored as a suitable vaccine candidate . In the Asian population, S, E, M, and N proteins of novel-SARS-CoV-2 can be tested for developing subunit vaccines against COVID-19 . Identification of the immune-dominant region among the subunits and domains of S protein is critical while developing an effective vaccine against the corona virus. The C-terminal domain of the S1 subunit is considered as the immune-dominant region of the porcine delta corona virus S protein (171). Similarly, further studies are required to determine the immuno-dominant regions of SARS-CoV-2 for facilitating vaccine development. [19,20]

However, our previous attempts to develop a universal vaccine that is effective against both SARS-CoV and MERS-CoV based on T cell epitopes similarity pointed out the possibility of cross-reactivity among corona viruses . That can be made possible by selected potential vaccine targets that are common to both the viruses. The SARS-CoV-2 is found to be closely related to the SARS-CoV understanding of the S protein-based vaccine development in SARS-CoV will help to identify potential S protein vaccine candidates in SARS-CoV-2. Therefore, vaccine strategies based on the whole S protein, S protein subunits, or specific potential epitopes of S protein appear most promising vaccine candidates against corona viruses shortly. The RBD of the S1 subunit of S protein has a superior capacity to induce neutralizing antibodies. This property of RBD can be utilized for developing effective SARS-CoV vaccines either by using RBD containing recombinant proteins or recombinant vectors that encode RBD . Hence, the superior genetic similarity existing between SARS-CoV-2 and SARS-CoV can be utilized to repurpose vaccines that have proven in vitro efficacy against SARS-CoV to be utilized for SARS-CoV-2. The possibility of cross-protection in COVID-19 was evaluated by comparing the S protein sequences of SARS-CoV-2with that of SARS-CoV. The comparative analysis confirmed that the variable residues were found concentrated on the S1 subunit of S protein, an important vaccine target of the virus . Hence, the possibility of SARS-CoV specific neutralizing antibodies providing cross-protection to COVID-19 might be less.

Further genetic analysis is required between COVID-19 and different strains of SARS-CoV and SARS-like (SL) corona viruses to evaluate the possibility of repurposed vaccines against COVID-19. This strategy will be helpful in the scenario of an outbreak since much time can be saved because preliminary evaluation, including in vitro studies, would be already over in such vaccine candidates.

Identifying epitopes that have the potential to become a vaccine candidate is critical to developing an effective vaccine against COVID-19. Immuno-informatics approach has been used for the identification of essential epitopes of cyto-toxic T lymphocyte and B cell from surface glycoprotein of SARS-CoV-2. Recently, a few epitopes have been

recognized from the SARS-CoV-2surface glycoprotein. The selected epitopes explored targeting molecular dynamic simulations evaluating their interaction with corresponding MHC class I molecules. They potentially induce immune responses . The recombinant vaccine can be designed by using rabies virus (RV) as a viral vector. The RV can be made to express MERS-CoV S1 protein on its surface so that an immune response is induced against MERS-CoV. The RV vector-based vaccines against MERS-CoV can induce faster antibody response as well as higher degrees of cellular immunity compared to the Gram-positive enhancer matrix (GEM) particles vector-based vaccine. However, the latter can induce a very higher antibody response at lower doses . Hence, the degree of humoral and cellular immune response produced by such vaccines depends upon the vector used. Dual vaccines are getting more popular recently. Among them, the rabies virus-based vectored vaccine platform is used to develop vaccines against emerging infectious diseases. The dual vaccine developed from inactivated rabies virus particles that express the MERS CoV S1 domain of S protein was found to induce immune responses against both MERS CoV and rabies virus. The vaccinated mice were found to be completely protected from the MERS-CoV challenge . The intranasal administration of the recombinant adeno virus based vaccine in BALB/c mice was found to induce long-lasting neutralizing immunity against MERS spike pseudo typed virus characterized by the induction of systemic IgG, secretory IgA, and lung resident memory T cell responses . Immuno-informatics methods are employed for the genome-wide screening of potential vaccine targets among the different immunogens of MERS-CoV . The N protein, as well as the potential B cell epitopes of the E protein of the MERS-CoV , have been suggested as probable immune protective targets inducing both T-cell and neutralizing antibody responses . The collaborative effort of the scientists of Rocky Mountain Laboratories and Oxford University is on the way for designing a chimpanzee adenovirus-vectored vaccine candidate to counter COVID-19 . The Coalition for Epidemic Preparedness Innovations (CEPI) has initiated three programs to develop SARS-CoV-2 vaccines . CEPI has a collaborative project with Inovio for designing the MERS CoV DNA vaccine that could potentiate effective immunity. CEPI and the University of Queensland are designing the molecular clamp vaccine platform for MERS-CoV and other pathogens, which could assist an easier recognition of antigens by the immune system . CEPI has also funded Moderna to develop a vaccine against COVID-19 in collaboration with Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID), a part of National Institutes of Health (NIH). By employing mRNA vaccine platform technology, a vaccine candidate expressing SARS-CoV-2 spike protein is expected to go through clinical testing in the coming months . On March 16th, Jennifer Haller became the first person outside of China to receive an experimental vaccine that was developed by Moderna against the pandemic virus. Moderna, along with China's CanSino Biologics, became the first research group that launched small clinical trials of vaccines against COVID-19. The study was conducted to

evaluate the vaccine's safety and ability to trigger immune responses . Scientists from all over the world are trying hard to develop working vaccines with robust protective immunity against COVID-19. Vaccine candidates like mRNA-1273 SARSCoV-2 Vaccine, INO-4800 DNA corona virus vaccine and Adenovirus type 5 vector vaccine candidate (Ad5-nCoV) are few examples under Phase-I clinical trials, while Self-amplifying RNA vaccine, Oral recombinant COVID-19 vaccine, BNT162, Plant-based COVID-19 vaccine and Ii-Key peptide COVID-19 vaccine are under preclinical trial mode .

Similarly, the WHO, on its official website, has mentioned a detailed list of COVID-19 vaccine agents that are under consideration. Different phases of trials like live attenuated virus vaccines, formaldehyde alum inactivated vaccine, Adenovirus type 5 vector vaccine, LNP-encapsulated mRNA, DNA plasmid vaccine, S protein, S-trimer, Ii-Key peptide as subunit protein vaccine, among others .

Antiviral drugs

Several classes of routinely used antiviral drugs like oseltamivir (neuraminidase inhibitors), acyclovir, ganciclovir, and ribavirin does not have any effect on COVID-19 and hence not recommended . Oral administration of neuraminidase inhibitors such as oseltamivir has been widely used as an experimental drug for COVID-19 suspected cases in the hospitals of China even though there is no evidence of its efficacy . Recently, the in vitro antiviral efficacy of FAD-approved drugs such as ribavirin, penciclovir, nitazoxanide, nafamostat, and chloroquine were compared with that of the two broad-spectrum antiviral drugs remdesivir and favipiravir against the SARS-CoV-2. Among the evaluated drugs, both remdesivir and chloroquine were found to be highly effective in controlling COVID-19 infection in vitro . The study also pointed out that the three nucleoside analogs such as ribavirin, penciclovir, and favipiravir may not have significant in vivo antiviral effects against SARS-CoV-2 since higher concentrations were required to reduce the viral infection in vitro.[14]

Both remdesivir and chloroquine are currently being used in humans for the treatment of other diseases. They also have a well-defined safety profile in human beings. Hence, such drugs can be used for evaluating their efficacy in patients of novel corona virus infections. Although no antiviral drugs have been approved for the treatment, several therapeutic agents such as lopinavir/ritonavir, chloroquine, and hydroxychloroquine are being proposed for the clinical management of COVID-19 . The molecular docking study conducted in the RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2 using different commercially available anti-polymerase drugs identified that the drugs such as Ribavirin, Remdesivir, Galidesivir, Tenofovir, and Sofosbuvir were found to bind RdRp tightly indicating a great potential to be used as a therapeutic agent against COVID-19 . The broad-spectrum antiviral drug that was developed in the USA, Tilorone dihydrochloride (Tilorone), has been previously found to possess potent antiviral activity against MERS, Marburg, Ebola, and Chikungunya . Even though it had broad-spectrum activity, it was neglected for an extended period. Tilorone is another antiviral drug that might have activity against SARS CoV-2.

Remdesivir, a novel nucleotide analog pro-drug, was developed for the treatment of Ebola virus disease (EVD), and it was also found to inhibit replication of SARS-CoV and MERS-CoV in primary human airway epithelial cell culture system . Recently, in vitro study has proven that remdesivir has superior antiviral activity than lopinavir and ritonavir. Further, in vivo studies conducted in mice also identified that treatment with remdesivir improved pulmonary function and reduced viral loads and lung pathology both in prophylactic and therapeutic regimens compared to lopinavir/ritonavir-IFN-γ treatment in MERS-CoV infection . Remdesivir also inhibits a diverse range of coronaviruses, including circulating human CoV, zoonotic bat CoV, and pre-pandemic zoonotic CoV . Remdesivir is also considered as the only therapeutic drug that significantly reduces pulmonary pathology . All these findings indicate that the drug remdesivir has to be further evaluated for its efficacy in the treatment of COVID-19 infection in humans. The broad-spectrum activity exhibited by remdesivir will help control the spread of disease in the event of a new coronavirus outbreak. Chloroquine is an anti-malarial drug known to possess antiviral activity due to its ability to block virus-cell fusion by raising the endosomal pH necessary for fusion. It also interferes with the virus-receptor binding by interfering with the terminal glycosylation of SARS-CoV cellular receptors, angiotensin-converting enzyme 2 (ACE2) . In a recent multicentre clinical trial that was conducted in China, chloroquine phosphate was found to exhibit both efficacy and safety in the therapeutic management of SARS-CoV-2 associated pneumonia . This drug is already included in the treatment guidelines issued by the National Health Commission of the People's Republic of China.[9]

The preliminary clinical trials using hydroxychloroquine, another aminoquinoline drug, gave promising results. The COVID-19 patients received 600 mg of hydroxychloroquine daily along with azithromycin as a single-arm protocol. This protocol was found to be associated with a significant reduction in the viral load. Finally, it resulted in a complete cure (275) —however, the study comprised a small population and hence the possibility of a misinterpretation. However, in another case study, the authors had raised concerns over the efficacy of hydroxychloroquine-azithromycin in the treatment of COVID-19 patients since no observable effect was seen when they were used. In some cases, the treatment was discontinued due to the prolongation of the QT interval . Hence further randomized clinical trials are required before concluding this matter. Recently, another FDA approved drug ivermectin was found to inhibit the in vitro replication of SARS-CoV-2. The findings from this study indicate that a single treatment of this drug was able to induce a ~5000-fold reduction in the viral RNA at 48h in cell culture . In the coming days, further, in vivo studies will give an insight into the clinical utility of this wonder drug. Nafamostat is a potent inhibitor of MERS-CoV that acts by preventing membrane fusion. Nevertheless, it does not have any sorts of inhibitory action against SARS-CoV2infection . Recently, several newly synthesized halogenated triazole compounds were evaluated using fluorescence resonance energy transfer (FRET) based helicase assays for their

ability to inhibit helicase activity. Among the evaluated compounds, 4-(cyclopent-1-en-3-ylamino)-5-(2-(4iodophenyl)hydrazinyl)-4H-1,2,4-triazole-3-thiol and 4-(cyclopent-1-en-3-ylamino)-5-[2-(4chlorophenyl)hydrazinyl]-4H-1,2,4-triazole-3-thiolwere found to be the most potent. These compounds were used for in silico studies, and molecular docking was accomplished into the active binding site of MERS-CoV helicase nsp13 . Further studies are required for evaluating the therapeutic potential of these newly identified compounds in the management of COVID-19 infection.

Animal models and cell cultures

For studying the pathogenesis and evaluation of vaccines and therapeutics against CoVs, including SARS, MERS-CoVs, and the presently emerging SARS-CoV-2, suitable animal models that could mimic the clinical disease are needed. Various animal models have been assessed for SARS- and MERS-CoVs such as a mouse, guinea pigs, golden Syrian hamsters, ferrets, rabbits, non-human primates like rhesus macaques and marmosets, and cats . The specificity of the virus to human ACE2 (hACE2; receptor of SARS-CoV) was found to be a significant hindrance in developing animal models for SARS-CoV. Consequently, a SARS-CoV transgenic mouse model was developed by inserting the hACE2 gene into the mouse genome . The inability of MERS-CoV to replicate in the respiratory tracts of animals (mice, hamsters, and ferrets) is another limiting factor. However, with genetic engineering, 288-330+/+ MERS-CoV genetically modified mouse model was developed and now is in use for the evaluation of novel drugs and vaccines against MERSCoV . In the past, the small animals (mice or hamsters) have been targeted for closer to humanized structure,. CRISPR-Cas9 gene-editing tool has been used for inserting the genomic alterations in mouse, making them susceptible to MERS-CoV infection . Efforts are on the way to recognize suitable animal models for SARS-CoV2 /COVID-19, identify the receptor affinity of this virus, studying pathology in experimental animal models, exploring virus-specific immune responses and protection studies, which together would give a pace to efforts being made for developing effective vaccines and drugs against this emerging virus. Cell lines such as monkey epithelial cell lines (LLC-MK2 and Vero-B4), goat lung cells, alpaca kidney cells, dromedary umbilical cord cells, advanced ex vivo three-dimensional (3D) tracheobronchial tissue have been explored to study human CoVs (MERS-CoV). Vero and the Huh7 cells (human liver cancer cells) have been used for isolating the SARS-CoV-2. Recently, in an animal model using rhesus monkeys, authors found that neither viral loads in nasopharyngeal and anal swabs along the timeline nor viral replication in all primary tissue compartments at five days post-reinfection was found in re-expose infection.

Impact of COVID 19 on Indian Economy

After the great depression of 1930 in which the global economy has faced the worst recession is now facing the global pandemic of corona virus that has laid the adverse effect on all the economic activates across the world. The sudden decline in economic activities due to the lockdown is unexpected in the history of India. The great economist Keynes has suggested the concept of trade business cycle after the great depression. The

four stage of trade cycle is considered to measure the growth rate and real GDP. [18]

International Monetary Fund (IMF) has projected the GDP growth as 1.9% and this shows the worst growth performance of India after the liberalization policy of 1991 in this fiscal year as the corona virus has disturbed the whole economy . Instead after this the IMF in its latest edition of the World Economy Report has placed India being the fastest growing economy in 2020.

The global economy is projected to contrast sharply by -3%percent in 2020 which is much worse than the financial crises in 2008-09. In India, the impact on real or predictive sectors of the economy is worse than that witnessed in 2008 crises. The country will now face multiple challenges in terms of financial crises, health crises, collapse in commodity prices and much more . The banking system has increased the surplus liquidity because of the demand-side shocks that arises due to uncertainties as well as lock down in the market. There is a huge impact on the financial shock that includes stock market crash, liquidity crises as it began to drain out from global market in banking system and various changes in monetary policies. The US dollar credit crunch has started bothering the world economy due to huge collapse of earnings, dollar denominated debts .

As the most of the companies that depends upon international trade will suffer severe pressure. The global economic production is on decline and expecting a huge recession in the entire economy. The global pandemic has hit the economy which questioned the target to make Indian economy of USD $5 Trillion with 7% of GDP by the year 2024. As per the World Bank latest assessment, India is expected to grow 1.5 percent to 2.8 percent as well as according to IMF, it has projected a GDP growth of 1.9 percent in 2020 and to achieve the object of USD $5 Trillion economy it is expected to grow at 9 percent every year for five years . India's growth trajectory since 2011.[13]

Barriers in Supply chain during COVID-19 in India:

Supply chains are always influenced by some barriers [21]. India is the developing country and Covid-19 has disrupted the supply chain of India. Global supply chains are also disrupted by the Covid-19. Many countries has banned on the import and export of many goods which affected the manufacturing firms across the globe. The barriers for the Indian supply chain caused by the Covid-19 are found out with the academia discussion and supply chain experts. There are total of 18 critical barriers were found out in the study which is discussed in Table 1:

These barriers have the great influence on the Indian supply chain. Although these issues in the supply chain are very generalized which needs further study and prioritization of these barriers will help the industries to overcome from the supply chain issues due to the Covid-19. These barriers can be studied with the MCDMs techniques such as AHP, ANP, TOPSIS, DEMATEL, MAVT, MAUT, VIKOR, Fuzzy set theory based MCDMs and other model validation can be done by data analytics techniques such as: SEM, ANOVA, and ISM.[17]

CONCLUSION

Through this review, we conclude that the disease profile of COVID-19 is dynamic and continues to rapidly evolve. There are still many open questions that are pending about COVID-19. As it is evident

through our literature survey, there are cases where patients confirmed with COVID-19 infection have no chest CT abnormalities, contrasting with subclinical infection presenting with positive imaging findings on CT. It is crucial that the clinical impacts of screening asymptomatic patients with chest CT be determined. A more thorough analysis about the existence of any potential benefit on clinical outcomes needs to be addressed against the known financial costs and exposure to ionizing radiation associated with CT scanning. As more and more suspected cases of COVID 19 infection arises, crisis chance of RT-PCR kits may also be increased. This has led to chest CT being utilized to aid diagnosis in the absence of RT-PCR, as demonstrated in a recent case reported from China and all over world. The progression of the lung changes of COVID-19 on CT imaging is also similar to SARS, with the ground-glass and consolidation getting worse or better over several days. This would be expected, as the two infectious agents are part of the corona virus family. SARS had a mortality rate of 9.5%, whilst the current novel coronavirus appears to have a mortality rate around 2%, based on the number of confirmed cases and deaths. Our study has several limitations, such limitations preclude the possibility of any deep analysis about potential prognostic imaging variables that could aid in the prediction of worse outcomes. Moreover, it does not address the role of imaging in guiding or monitoring medical therapy in the infected individuals.. In conclusion, COVID 19 has a vast effect on society, where proper medication, sanitization and social distancing will help us.

However, advances in designing antiviral drugs and vaccines against several other emerging diseases will help develop suitable therapeutic agents against COVID19 in a short time. Until then, we must rely exclusively on various control and prevention measures to prevent this new disease from becoming a pandemic.

REFERENCES

1. WHO Q&A on coronaviruses (COVID-19) March 2020, https://www.who.int/news-room/q-a-detail/q-a-coronaviruses.
2. Murphy A, and Bell D.J, et al. COVID-19, Radiopedia. https:// radiopaedia.org/articles/covid-19-2?lang=us.
3. Singhal, T. A Review of Coronavirus Disease-2019 (COVID-19). Indian J Pediatr (2020). https://doi.org/10.1007/s12098-02003263-6.
4. Center for disease controle and prevention, coronavirus disease 2019 (COVID-19). https://www.cdc.gov/ coronavirus/2019-ncov/symptoms-testing/symptoms.html.
5. Velavan TP, Meyer CG. The COVID-19 epidemic. Trop Med Int Health. 2020;25(3):278–280. doi:10.1111/tmi.13383 https:// pubmed.ncbi.nlm.nih.gov/32052514/.
6. Countries where COVID-19 has spread, World ometers, 26March 2020. https://www.worldometers.info/coronavirus/ countries-where-coronavirus-has-spread/.
7. Shereen M.A, Khan S, COVID-19 infection: origin, transmission, and characteristics of human coronavirusesJournal of Advanced Research, 16 March 2020. https://www.sciencedirect.com/science/article/pii/S2090123220300540.
8. Age, Sex, Existing Conditions of COVID-19 Cases and Deaths.
9. WHO Coron avirus disease (COVID-19) technical guidance: Laboratory testing for 2019-nCoV in humans. https://www. who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance.
10. Erin K. McCreary E.K, and Pogue J.M, COVID-19 Treatment: A Review of Early and Emerging Options, on behalf of the Society of Infectious Diseases Pharmacists. https://watermark. silverchair.com
11. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020. doi:10.1056/NEJMoa2001316.
12. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients

with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020. doi: 10.1001/jama.2020.1585.
13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: A descriptive study. Lancet 2020; 395: 507-13.
14. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. Int J Infect Dis 2020; 92: 214-7.
15. mai N, Cori A, Dorigatti I, Baguelin M, Donnelly CA, Riley S, et al. Report 3: Transmissibility of 2019-nCoV. Available from: https://www.imperial.ac.uk/media/imperial-college/medicine/sph/ide/gida-fellowships/Imperial-College-COVID19-transmissibility-25-01-2020.pdf, accessed on February 28, 2020.
16. Ghani AC, Donnelly CA, Cox DR, Griffin JT, Fraser C, Lam TH, et al. Methods for estimating the case fatality ratio for a novel, emerging infectious disease. Am J Epidemiol 2005;162 : 479-86.
17. Read JM, Bridgen JR, Cummings DAT, Ho A, Jewell CP. Novel coronavirus 2019-nCoV: Early estimation of epidemiological parameters and epidemic predictions. medRxiv 2020. doi: https://doi.org/10.1101/2020.01.23.20018549.
18. Centers for Disease Control and Prevention. MERS clinical features. Atlanta, USA; CDC; 2019. Available from: https://www.cdc.gov/coronavirus/mers/clinical-features.html, accessed on February 16, 2020. .
19. Kim JY, Choe PG, Oh Y, Oh KJ, Kim J, Park SJ, et al. The first case of 2019 novel coronavirus pneumonia imported into Korea from Wuhan, China: Implication for infection prevention and control measures. J Korean Med Sci 2020; 35 : e61.
20. Pandey A, Kaur R, Kumar S, Lakhawat SS, Kumar V. Coronavirus Disease 2019 (COVID-19) Outbreak: A Pandemic and Public Health Emergency. International Journal of Advanced Science and Technology. 2020; 29(5): 12442-12449.
21. Battegay M, Kuehl R, Tschudin-Sutter S, Hirsch HH, Widmer AF, Neher RA. 2019-novel Coronavirus (2019-nCoV): Estimating the case fatality rate – A word of caution. Swiss Med Wkly 2020; 150 : w20203

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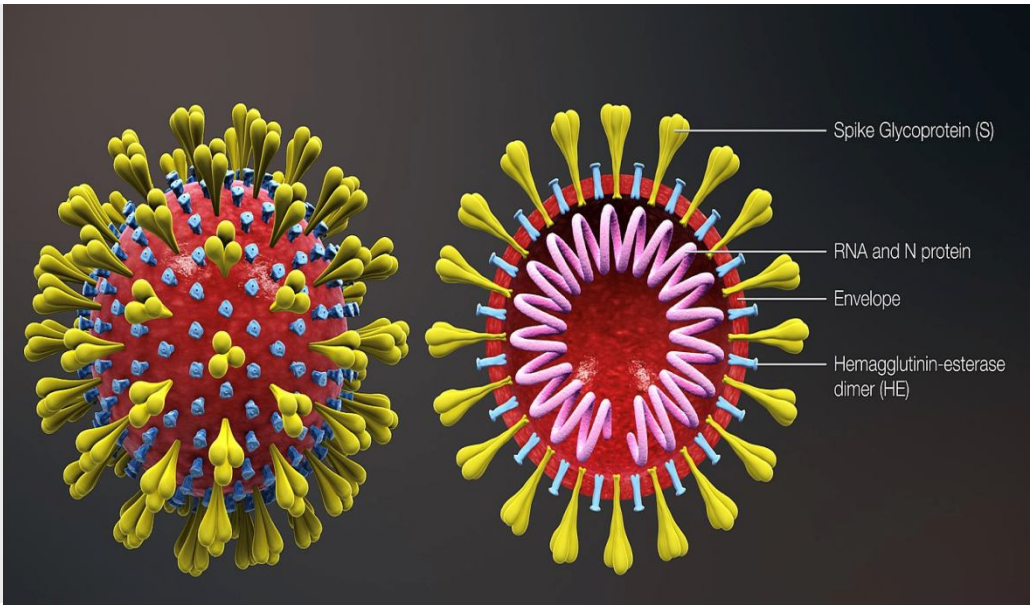

Figure1: Corona virus proteins

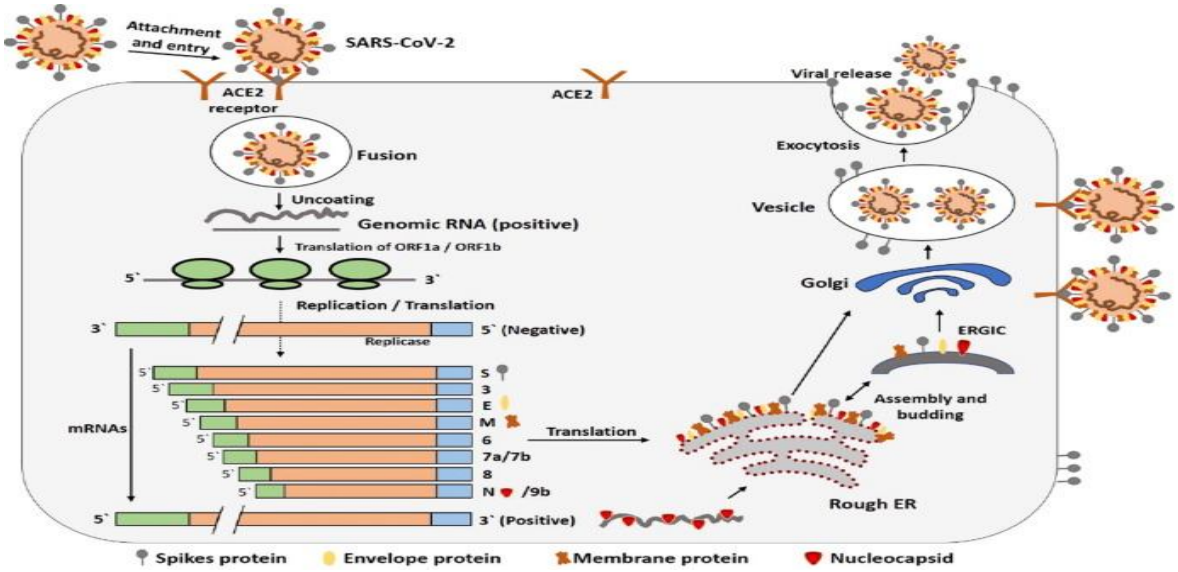

Figure2: Replication process of Corona virus

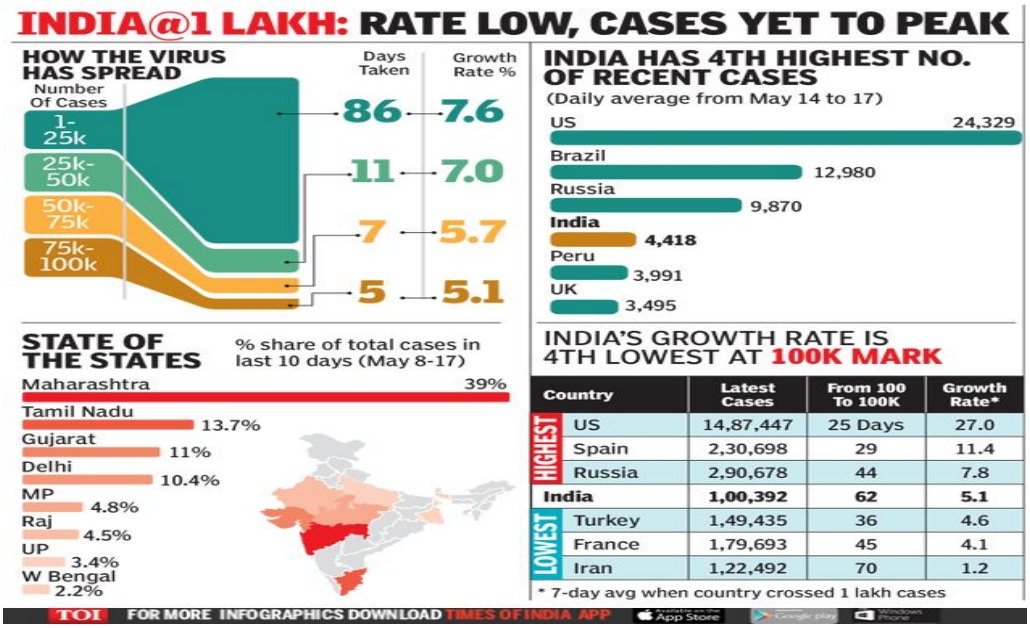

Figure3: Death rate in India

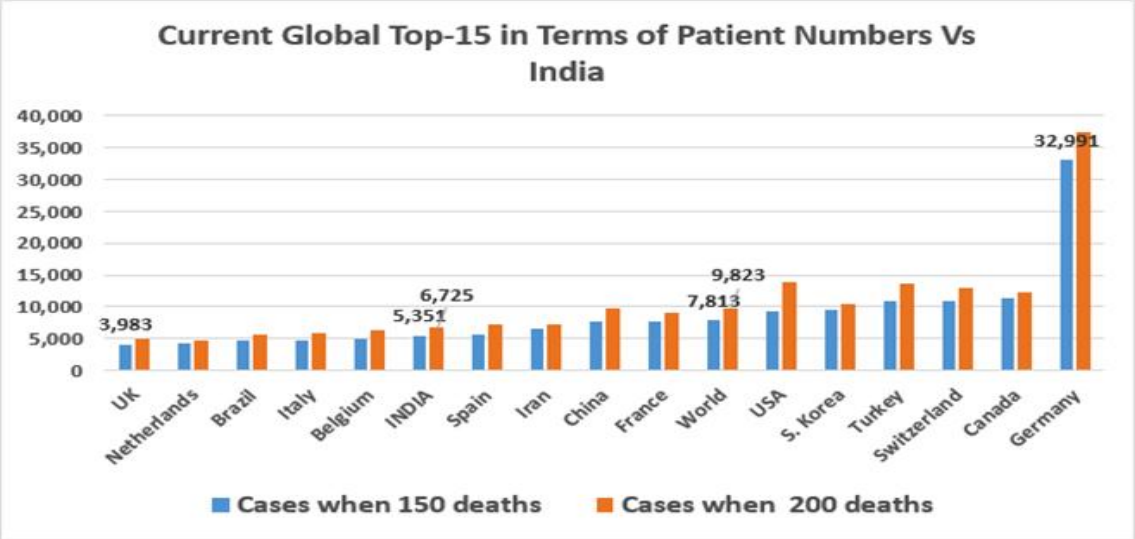

Figure4: Current Global Top-15 in Terms of Patient Numbers Vs India