CORONA VIRUS

A Project Report Submitted In Partial Fulfilment of the Requirements

For The Degree Of

BACHELOR OF PHARMACY

BY

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B. Pharm Final Year

(Enroll. No - 2016/2112)

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DECLARATION

I, Raja Ram (Enrol. No -2016/2112) student of B Pharm final year, **MAHATMA GANDHI COLLEGE OF PHARMACEUTICAL SCIENDES, JAIPUR,** hereby declare that the project entitled **"CORONA VIRUS"** Submitted to **MGCPS** during the academic year 2016-2020 is a record of original work done by me under the guidance of **MR. ASHOK KUMAR SHARMA** Asst. Professor. The results embodied in this thesis have not been submitted to any other University or Institute for the award of any Degree.

Place: JAIPUR

Date: 25/02/2020

Student Signature

RAJA RAM

ENDORSEMENT BY THE GUIDE

This is to be certify that **RAJA RAM** (Enrol. No 2016-2112) has carried out the project work presented entitled **" CORONA VIRUS"** for the award of Bachelor of pharmacy from MGCPS, Jaipur affiliated to RUSH Jaipur under my own supervision. This report is a bonafide record of the review work carried out by the candidate and the project work has not form the basis of award of any other degree or diploma etc. of this or any other university

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ACKNOWLEDFMENT

Every work started and carried out with systematic approach turns out to be successful. Any accomplished requires the effort of many people and this work is no different. This project difficult due to numerous reasons some of error correction was beyond my control. Sometime, I was like rudderless boat without knowing what to do next. It was then the timely guidance of that has seen us through all these odds. I would be very grateful to them for their inspiration, encouragement and guidance in all phase of the endeavour.

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1. INTRODUCTION

According to the World Health Organization (WHO), viral diseases continue to emerge and represent a serious issue to public health. In the last twenty years, several viral epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) from 2002 to 2003, and H1N1 influenza in 2009, have been recorded. Most recently, the Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in Saudi Arabia in 2012.

In a timeline that reaches the present day, an epidemic of cases with unexplained low respiratory infections detected in Wuhan, the largest metropolitan area in China's Hubei province, was first reported to the WHO Country Office in China, on December 31, 2019. Published literature can trace the beginning of symptomatic individuals back to the beginning of December 2019. As they were unable to identify the causative agent, these first cases (n=29) were classified as "pneumonia of unknown etiology." The Chinese Center for Disease Control and Prevention (CDC) and local CDCs organized an intensive outbreak investigation program. The etiology of this illness was attributed to a novel virus belonging to the coronavirus (CoV) family.

On February 11, 2020, the WHO Director-General, Dr. Tedros Adhanom Ghebreyesus, announced that the disease curaused by this new CoV was a "COVID-19," which is the acronym of "coronavirus disease 2019". In the past twenty years, two additional CoVs epidemics have occurred. SARS-CoV provoked a large-scale epidemic beginning in China and involving two dozen countries with approximately 8000 cases and 800 deaths (fatality rate of 9,6%), and the MERS-CoV that began in Saudi Arabia and has approximately 2,500 cases and 800 deaths (fatality rate of 35%) and still causes as sporadic cases.

This new virus is very contagious and has quickly spread globally. In a meeting on January 30, 2020, per the International Health Regulations (IHR, 2005), the outbreak was declared by the WHO a Public Health Emergency of International Concern (PHEIC) as it had spread to 18 countries with four countries reporting human-to-human transmission. An additional landmark occurred on February 26, 2020, as the first case of the disease, not imported from China, was recorded in the United States (US).

Initially, the new virus was called 2019-nCoV. Subsequently, the task of experts of the International Committee on Taxonomy of Viruses (ICTV) termed it the SARS-CoV-2 virus as it is very similar to the one that caused the SARS outbreak (SARS-CoVs).

The CoVs have become the major pathogens of emerging respiratory disease outbreaks. They are a large family of single-stranded RNA viruses (+ssRNA) that can be isolated in different animal species. For reasons yet to be explained, these viruses can cross species barriers and can cause, in humans, illness ranging from the common cold to more severe diseases such as MERS and SARS. Interestingly, these latter viruses have probably originated from bats and then moving into other mammalian hosts — the Himalayan palm civet for SARS-CoV, and the dromedary camel for MERS-CoV — before jumping to humans. The dynamics of SARS-Cov-2 are currently unknown, but there is speculation that it also has an animal origin.

The potential for these viruses to grow to become a pandemic worldwide represents a serious public health risk. Concerning COVID-19, the WHO raised the threat to the CoV epidemic to the "very high" level, on February 28, 2020. On March 11, as the number of COVID-19 cases outside China has increased 13 times and the number of countries involved has tripled with more than 118,000 cases in 114 countries and over 4,000 deaths, WHO declared the COVID-19 a pandemic.

1.1 HISTORY

The history of human coronaviruses began in 1965 when Tyrrell and Bynoe[1] found that they could passage a virus named B814. It was found in human embryonic tracheal organ cultures obtained from the respiratory tract of an adult with a common cold. The presence of an infectious agent was demonstrated by inoculating the medium from these cultures intranasally in human volunteers; colds were produced in a significant proportion of subjects, but Tyrrell and Bynoe were unable to grow the agent in tissue culture at that time. At about the same time, Hamre and Procknow were able to grow a virus with unusual properties in tissue culture from samples obtained from medical students with colds. Both B814 and Hamre's virus, which she called 229E, were ether-sensitive and therefore presumably required a lipid-containing coat for infectivity, but these 2 viruses were not related to any known myxo- or paramyxoviruses. While working in the laboratory of Robert Chanock at the National Institutes of Health, McIntosh et al[3] reported the recovery of multiple strains of ether-sensitive agents from the human respiratory tract by using a technique similar to that of Tyrrell and Bynoe. These viruses were termed "OC" to designate tha t they were grown in organ cultures.

Within the same time frame, Almeida and Tyrrel performed electron microscopy on fluids from organ cultures infected with B814 and found particles that resembled the infectious bronchitis virus of chickens. The particles were medium sized (80–150 nm), pleomorphic, membrane-coated, and covered with widely spaced club-shaped surface projections. The 229E agent identified by Hamre and Procknow and the previous OC viruses identified by McIntosh et al had a similar morphology

In the late 1960s, Tyrrell was leading a group of virologists working with the human strains and a number of animal viruses. These included infectious bronchitis virus, mouse hepatitis virus and transmissible gastroenteritis virus of swine, all of which had been demonstrated to be morphologically the same as seen through electron microscopy. This new group of viruses was named coronavirus (*corona* denoting the crown-like appearance of the surface projections) and was later officially accepted as a new genus of viruses.

Ongoing research using serologic techniques has resulted in a considerable amount of information regarding the epidemiology of the human respiratory coronaviruses. It was found that in temperate climates, respiratory coronavirus infections occur more often in the winter and spring than in the summer and fall. Data revealed that coronavirus infections contribute as much as 35% of the total respiratory viral activity during epidemics. Overall, his proportion of adult colds produced by coronaviruses was estimated at 15%.

In the 3 decades after discovery, human strains OC43 and 229E were studied exclusively, largely because they were the easiest ones to work with. OC43, adapted to growth in suckling mouse brain and subsequently to tissue culture, was found to be closely related to mouse hepatitis virus. Strain 229E was grown in tissue culture directly from clinical samples. The 2 viruses demonstrated periodicity, with large epidemics occurring at 2- to 3-year intervals. Strain 229E tended to be epidemic throughout the United States, whereas strain OC43 was more predisposed to localized outbreaks. As with many other respiratory viruses, reinfection was common.[10] Infection could occur at any age, but it was most common in children.

Despite the extensive focus placed exclusively on strains 229E and OC43, it was clear that there were other coronavirus strains as well. As shown by Bradburne, coronavirus strain B814 was not serologically identical with either OC43 or 229E. Contributing to the various strain differences in the family of coronaviruses, McIntosh et al found that 3 of the 6 strains previously identified were only distantly related to OC43 or 229E.

Epidemiologic and volunteer inoculation studies found that respiratory coronaviruses were associated with a variety of respiratory illnesses; however, their pathogenicity was considered to be low. The predominant illness associated with infections was an upper respiratory infection with occasional cases of pneumonia in infants and young adults. These viruses were also shown to be able to produce asthma exacerbations in children as well as chronic bronchitis in adults and the elderly.

While research was proceeding to explore the pathogenicity and epidemiology of the human coronaviruses, the number and importance of animal coronaviruses were growing rapidly. Coronaviruses were described that caused disease in multiple animal species, including rats, mice, chickens, turkeys, calves, dogs, cats, rabbits and pigs. Animal studies included, but were not limited to, research that focused on respiratory disorders. Study focus included disorders such as gastroenteritis, hepatitis and encephalitis in mice; pneumonitis and sialodacryoadenitis in rats; and infectious peritonitis in cats. Interest peaked particularly regarding areas of encephalitis produced by mouse hepatitis virus and peritonitis produced by infectious peritonitis virus in cats. Pathogenesis of these disease states was various and complex, demonstrating that the genus as a whole was capable of a wide variety of disease mechanismsHuman and animal coronaviruses were segregated into 3 broad groups based on their antigenic and genetic makeup. Group I contained virus 229E and other viruses, group II contained virus OC43 and group III was made up of avian infectious bronchitis virus and a number of related avian viruses

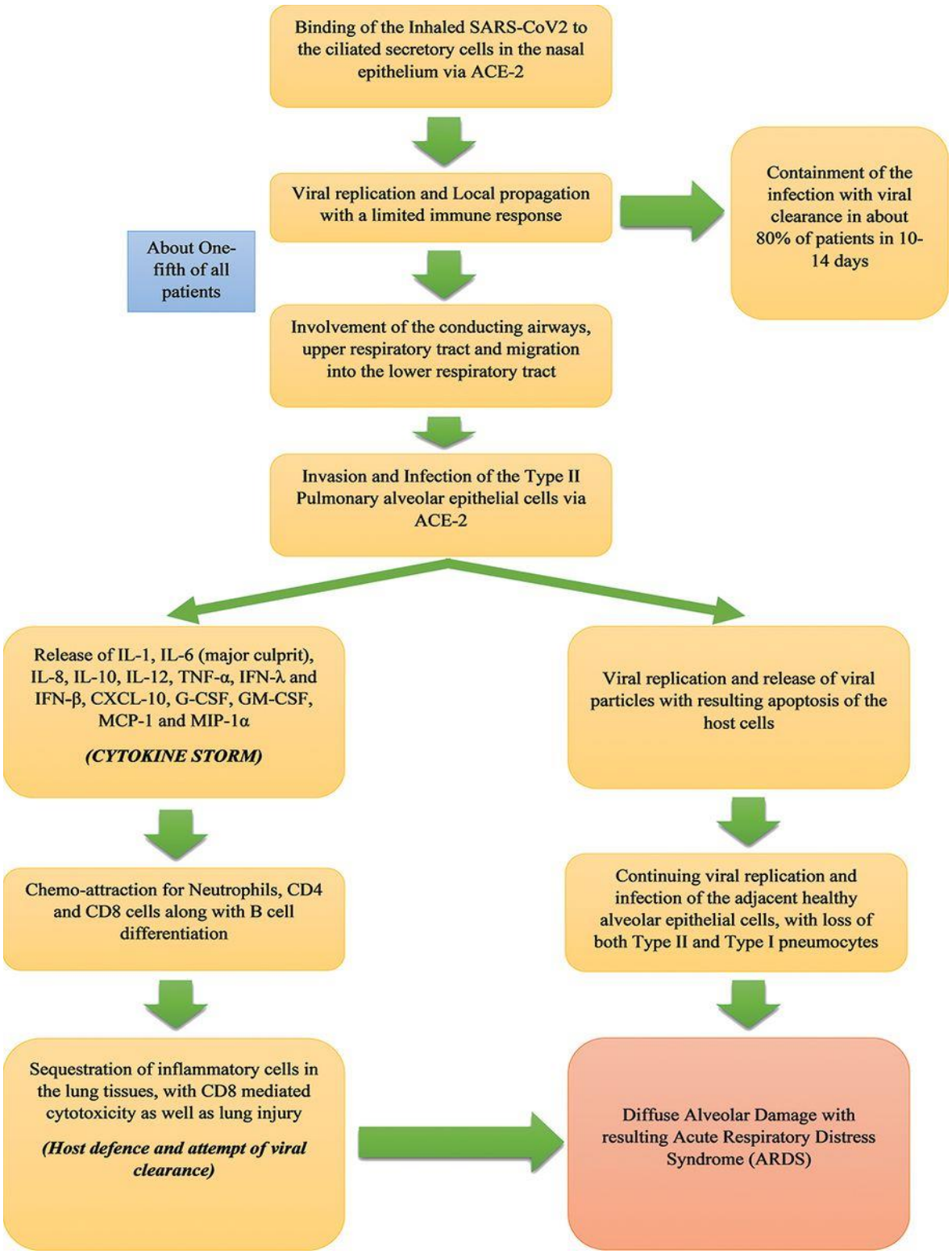
1.2 PATHOPHYSIOLOGY OF CORONA

The cause of kidney involvement in COVID-19 is likely to be multifactorial, with cardiovascular comorbidity and predisposing factors (eg, sepsis, hypovolaemia, and nephrotoxins) as important contributors.

Cardio renal syndrome, particularly right ventricular failure secondary to COVID-19 pneumonia, might lead to kidney congestion and subsequent AKI. Similarly, left ventricular dysfunction might lead to low cardiac output, arterial under filling, and kidney hypoperfusion.

Autopsy data indicate that the endothelium is affected in the lung and in the kidney, where it is probably responsible for proteinuria. Furthermore, virus particles were reported to be present in renal endothelial cells, indicating viraemia as a possible cause of endothelial damage in the kidney and a probable contributor to AKI.

Additionally, SARS-CoV-2 can directly infect the renal tubular epithelium and podocytes through an angiotensin-converting enzyme 2(ACE2)-dependent pathway and cause mitochondrial dysfunction, acute tubular necrosis, the formation of protein reabsorption vacuoles, collapsing glomerulopathy, and protein leakage in Bowman's capsule.

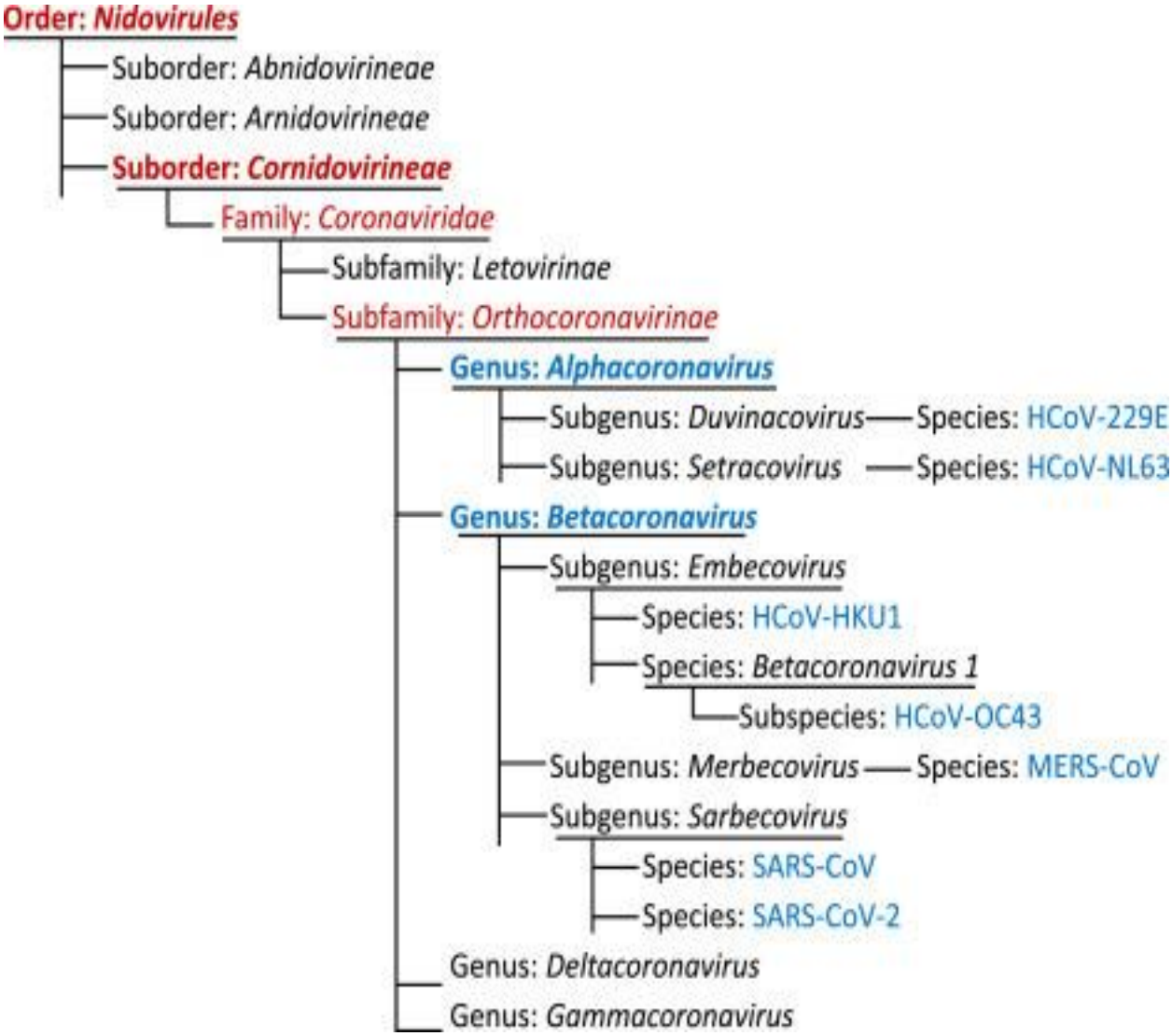


Figure; 1 Pathophysiology of COVID-19. CXCL-10, C-X-C motif chemokine ligand 10; IFN, interferon; IL, interleukin; MCP-1, monocyte chemoattractant protein-1; MIP-1α, macrophage inflammatory protein-1α; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; TNF-α, tumour necrosis factor-α; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony-stimulating factor.

1.3 CORONA

The COVID-19 pandemic, also known as the coronavirus pandemic, is an ongoing pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The outbreak was first identified in Wuhan, China, in December 2019.

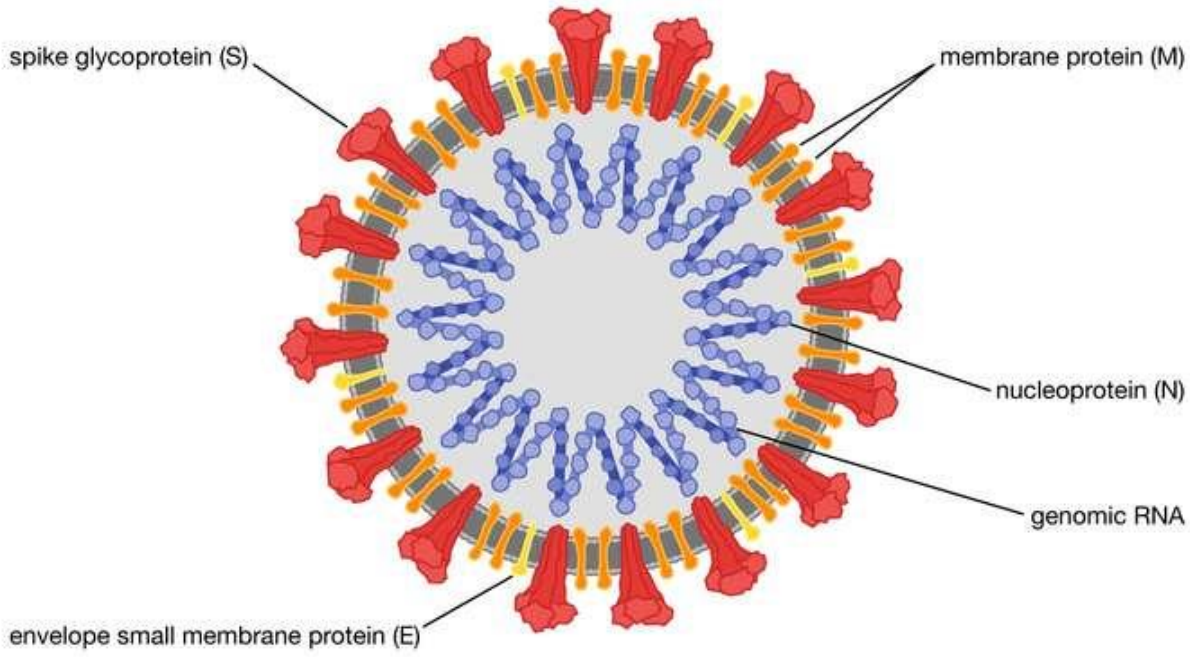
The World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January, and a pandemic on 11 March. A global coordinated effort is needed to stop the further spread of the virus. A pandemic is defined as "occurring over a wide geographic area and affecting an exceptionally high proportion of the population." The last pandemic reported in the world was the H1N1 flu pandemic in 2009.



Figure; 2 Corona virus family and species

Coronaviruses are important human and animal pathogens. At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in the Hubei Province of China. It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world. On 30th January 2020 India recorded its first COVID-19 case in state of Kerala. It was a student who had travel history to china. And till the start of June India has over 200 thousand confirmed cases.

1. Coronaviruses are everywhere. They are the second leading cause of the common cold (after rhinoviruses) and until recent decades, rarely caused any disease more serious than a common cold in humans. The first coronavirus was isolated in 1937. Some cause illness in people and others circulate among other animals, including camels, cats and bats. Since its discovery, related coronaviruses have been found to infect cattle, pigs, horses, turkeys, cats, dogs, rats and mice. The first human coronavirus was cultured in the 1960s from
2. nasal cavities of people with the common cold. The 4 major categories of coronavirus are known by



Figure; 3 Consequences for Creative Europe programme and related activities.

The Greek letters alpha, beta, delta and gamma. Only alpha and beta coronaviruses are known to infect humans. These viruses spread through the air and are responsible for about 10-30% of colds worldwide. Long known to cause upper respiratory infections, coronaviruses were not felt to

significantly cause pneumonia until relatively recently. Seven human corona virus (HCoVs) have now been identified: HCoV-229E, HCoV-OC43, HCoV-NL63, HCoV-HKU1, SARS-CoV (which causes severe acute respiratory syndrome), MERS-CoV (Middle East respiratory syndrome) and now SARS-CoV-All but SARS-CoV-2 appear to be established human pathogens with worldwide distribution, causing upper and lower respiratory tract infections, especially in children. Typically, HCoV infection follows a seasonal pattern similar to that of influenza, although Hong Kong researchers found that HCoV-NL63 infections mainly occurred in early summer and autumn.

While there aren't many coronaviruses that cause lower respiratory disease in humans, they can have serious consequences for those they infect. Coronaviruses are zoonotic, meaning they can be transmitted between animals and people, but most infect only their specific animal host. Rarely, animal coronaviruses can evolve to infect and spread among people.

This was the case with Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV). SARS killed nearly 10% of the 8,096 people who fell ill in 29 countries. A total of 774 people died, according to the World Health Organization. MERS is even more deadly, claiming more than 30% of people it infects.

Unlike SARS, outbreaks of MERS are still occurring, since 2012, MERS has caused 2,494 confirmed cases in 27 countries and killed 858 people. SARS-CoV and MERS-CoV generally spread between people who are in close contact, which resulted in many fatalities of healthcare workers.

These viruses spread similar to the flu virus, and past MERS-CoV and SARS-CoV outbreaks have been complex, requiring comprehensive public health responses.

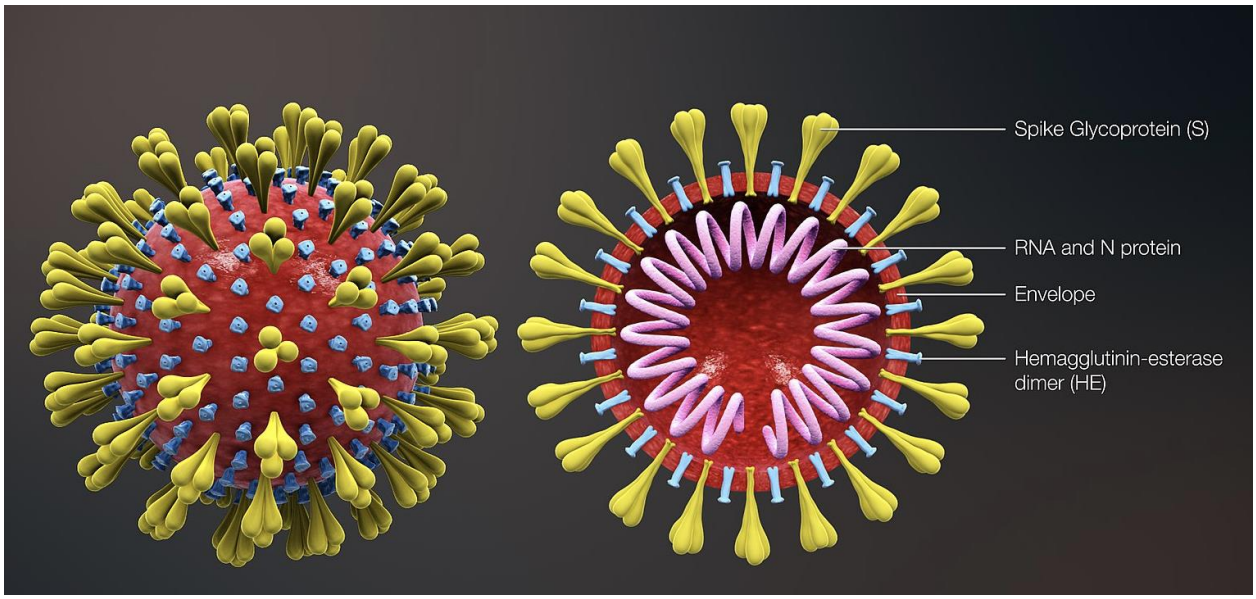
The rapid public health responses to these outbreaks were able to quickly determine that the SARS-CoV genome sequence is different from all other known coronaviruses and that it was first transmitted from civet cats to humans, though bats were determined to be the reservoir. Scientists also quickly found that MERS-CoV spread from dromedary camels to humans. Therefore, it's important to briefly discuss coronavirus genetics

Coronaviruses, so named because they look like halos (known as coronas) when viewed under the electron microscope, are a large family of RNA viruses. The typical generic coronavirus genome is a single strand of RNA, 32 kilobases long, and is the largest known RNA virus genome.

Coronaviruses have the highest known frequency of recombination of any positive-strand RNA virus, promiscuously combining genetic information from different sources when a host is infected with

multiple coronaviruses. In other words, these viruses mutate and change at a high rate, which can create havoc for both diagnostic detection, as well As therapy (and vaccine) regimens.

Coronaviruses have an unusual replication process, which involves a 2-step replication mechanism. Many RNA virus genomes contain a single open reading frame (ORF), which is then translated as a single polyprotein that is catalytically cleaved into smaller functional viral proteins, but coronaviruses can contain up to 10 separate ORFs. Most ribosomes translate the biggest one of these ORFs, called replicase, which alone is twice the size of many other RNA viral genomes. The replicase gene encodes a series of enzymes that use the rest of the genome as a template to produce a set of smaller, overlapping messenger RNA molecules, which are then translated into structural proteins — the building blocks of new viral particles. For a detailed, complete description of coronavirus replication and pathogenesis,



Figure; 4 Structural view of a coronavirus

1.4 TYPES OF CORONA VIRUS

Scientists have divided coronaviruses into four sub-groupings, called alpha, beta, gamma, and delta. Seven of these viruses can infect people:

- 229E (alpha)
- NL63 (alpha)
- OC43 (beta)

- HKU1 (beta)
- MERS-CoV, a beta virus that causes Middle East respiratory syndrome (MERS)
- SARS-CoV, a beta virus that causes severe acute respiratory syndrome (SARS)
- SARS-CoV-2, which causes COVID-19

229E Alpha Coronavirus

The initially described coronavirus strain 229E has been previously identified as the second most frequent cause of common cold after rhinoviruses in healthy adults. Predominant symptoms were acute rhinorrhea, nasal congestion, and/or sore throat. Nasal discharge was the hallmark of all symptoms after inoculation of HuCoV-229E to healthy volunteers, and further observed symptoms were malaise, headache, chills, and cough.

HCoV-229E has been associated with bronchitis, acute exacerbations of COPD, and pneumonia in infants, children, and elderly persons with underlying illnesses. Life-threatening infections have only been described in immunocompromised patients, but the correlation of HCoV-229E with LRTI in healthy adult individuals is uncertain. An adult patient with pneumonia tested positive for HCoV-229E has been described in a study conducted in rural Thailand, but it is not made clear if other comorbidities were present.

Nine Italian patients hospitalized with LRTI have also been tested positive for HCoV-229E; however, their age is not specified. Although numerous studies have tentatively linked 229E infections to severe respiratory tract illness over many years, no study controlling for age and underlying illness has demonstrated an epidemiologic association between infection with HcoV-229E in healthy adults and any illness other than the common cold. Furthermore, no case of HCoV-229E-associated ARDS has been reported in immunocompetent adults. Only a few cases of pulmonary infection and ARDS have been described in a 76-year-old woman infected with the closely related alpha coronavirus HCoV-NL63 [16] and in a 39-year-old woman with poorly controlled DM and infected with the beta coronavirus HCoV-OC43.

NL 63 Alpha coronavirus

In this study, we show that NL63 is temporally associated with lower respiratory tract symptoms in infants. The presence of coronavirus NL63 was concomitant to an acute episode of cough or wheeze and rhinitis, as well as disturbances in life activities, and led to a clinical picture similar to that induced by other members of this family. Symptoms were limited to 2 weeks in most cases. As 2 of 6 NL63-positive infants had never experienced any previous respiratory symptoms, and as the upper respiratory

symptoms in the other 4 NL63-positive infants immediately preceded the studied period, the recovery of NL63 in the respiratory samples of these infants was not a remnant of a previous upper respiratory infection. In addition, the viral shedding was documented only at the peak of the symptoms and, in half of the cases; the virus was cleared concomitant to symptom resolution. Taken together, these observations support our conclusion that NL63 should be considered as a cause of lower respiratory illness in early life. Adding this agent to the list of respiratory viruses will decrease the proportion of respiratory diseases of unknown etiology.

Our findings are consistent with recent reports in which coronavirus NL63 has been recovered in 2–3.6% of respiratory specimens in mixed populations of children, adults and elderly persons suffering from acute respiratory tract infection. A recent report in children with respiratory diseases in Connecticut showed that this virus may account for a significant proportion (up to 8%) of respiratory diseases in infants. Given the known ability of coronaviruses to cause pneumonia, our results also suggest that NL63 might be considered as a potential cause of complications in immunocompromised children or children with chronic pulmonary diseases. Cases of severe lower respiratory diseases, including bronchiolitis, have been described in hospitalized children. At this time, NL63 seems to be an infrequent cause of severe lower respiratory tract complications in adults, suggesting that most adults have been exposed at a young age to the virus.

MERS-CoV

Middle East respiratory syndrome (MERS) is a viral respiratory disease caused by a novel coronavirus (Middle East respiratory syndrome coronavirus, or MERS-CoV) that was first identified in Saudi Arabia in 2012.

Typical MERS symptoms include fever, cough and shortness of breath. Pneumonia is common, but not always present. Gastrointestinal symptoms, including diarrhoea, have also been reported. Some laboratory-confirmed cases of MERS-CoV infection are reported as asymptomatic, meaning that they do not have any clinical symptoms, yet they are positive for MERS-CoV infection following a laboratory test. Most of these asymptomatic cases have been detected following aggressive contact tracing of a laboratory-confirmed case.

Approximately 35% of reported patients with MERS-CoV infection have died.

Although most of human cases of MERS-CoV infections have been attributed to human-to-human infections in health care settings, current scientific evidence suggests that dromedary camels are a major reservoir host for MERS-CoV and an animal source of MERS infection in humans. However,

the exact role of dromedaries in transmission of the virus and the exact route(s) of transmission are unknown.

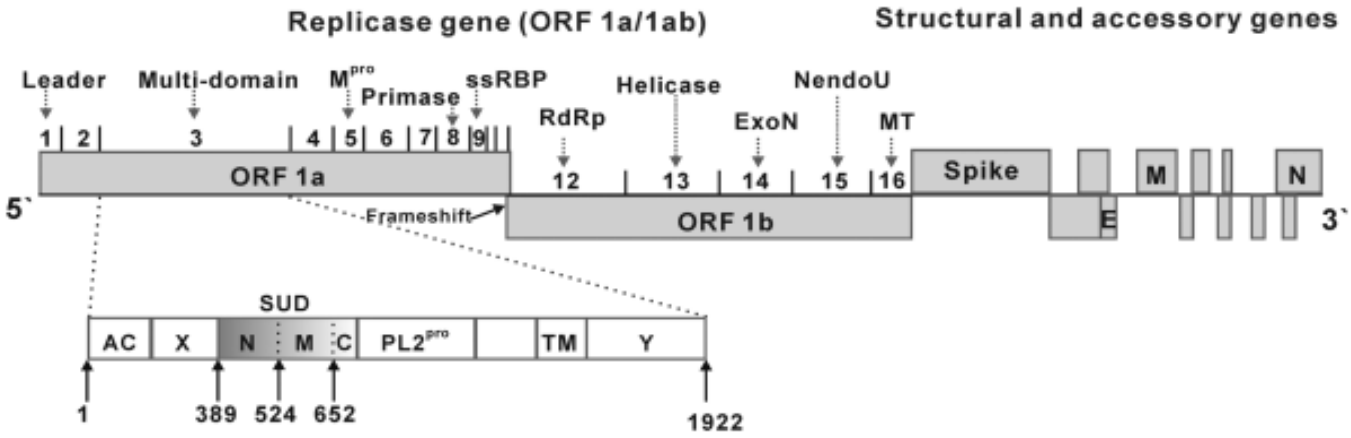
(SARS) Severe Acute Respiratory Syndrome;

Severe acute respiratory syndrome (SARS) is a viral respiratory illness caused by a coronavirus, called SARS-associated coronavirus (SARS-CoV). SARS was first reported in Asia in February 2003. The illness spread to more than two dozen countries in North America, South America, Europe, and Asia before the SARS global outbreak of 2003 was contained.

Currently, there is no known SARS transmission anywhere in the world. The most recent human cases of SARS-CoV infection were reported in China in April 2004 in an outbreak resulting from laboratory-acquired infections. CDC and its partners, including the World Health Organization, continue to monitor the SARS situation globally. Any new updates on disease transmission and SARS preparedness activities will be posted at this site.

SARS-CoV-2, which causes COVID-19

Viruses enter cells and initiate infection by binding to their cognate cell surface receptors. The expression and distribution of viral entry receptors therefore regulates their tropism, determining the tissues that are infected and thus disease pathogenesis. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the third human coronavirus known to co-opt the peptidase angiotensin-converting enzyme 2 (ACE2) for cell entry. The interaction between SARS-CoV-2 and ACE2 is critical to determining both tissue tropism and progression from early SARS-CoV-2 infection to severe coronavirus disease 2019 (COVID-19).



Figure; 5 SARS-CoV genome and proteins

As with all coronaviruses, SARS-CoV-2 cell entry is dependent on its 180-kDa spike (S) protein, which mediates two essential events: binding to ACE2 by the amino-terminal region, and fusion of viral and cellular membranes through the carboxyl-terminal region. Infection of lung cells requires host proteolytic activation of spike at a polybasic furin cleavage site. To date, this cleavage site is found in all spike proteins from clinical SARS-CoV-2 isolates, as well as some other highly pathogenic viruses (e.g., avian influenza A), but it is absent from SARS-CoV and is likely to have been acquired by recombination between coronaviruses in bats. Cleavage by the furin protease therefore expands SARS-CoV-2 cell tropism and may have facilitated transmission from bats to humans. Membrane fusion also requires cleavage by additional proteases, particularly transmembrane protease serine 2 (TMPRSS2), a host cell surface protease that cleaves spike shortly after binding ACE2. SARS-CoV-2 tropism is therefore dependent on expression of cellular proteases, as well as ACE2.

Other proteins that enable SARS-CoV-2 cell entry are also emerging, including neuropilin 1 (NRP1), a receptor that binds the carboxyl-terminal RXXR motif in spike that is exposed after furin cleavage. How NRP1 promotes cell entry is unclear, but it may further increase the cell types infected.

1.5 CAUSE OF CORONA

Virology and pathogenesis Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms. Other than SARS-CoV-2, there are six known coronaviruses in humans: HCoV-229E, HCoV-OC43, SARS-CoV, HCoVNL63, HCoV-HKU1, and MERS-CoV. Coronavirus has caused two large-scale pandemics in the last two decades: SARS and MERS.

To detect the infection source of COVID-19, China CDC researchers collected 585 environmental samples from the Huanan Seafood Market in Wuhan, Hubei Province, China on 1 January and 12 January 2020. They detected 33 samples containing SARS-CoV-2 and indicated that it originated from wild animals sold in the market. Then, researchers used the lung fluid, blood, and throat swab samples of 15 patients to conduct laboratory tests. These laboratory tests found that the virus-specific nucleic acid sequences in the sample are different from those of known human coronavirus species. Laboratory results also indicated that SARSCoV-2 is similar to some of the beta (β) coronaviruses genera identified in bats, which is situated in a group of SARS/SARS-like CoV.

Coronaviruses are a group of viruses that can cause disease in both animals and humans. The severe acute respiratory syndrome (SARS) virus strain known as SARS-CoV is an example of a coronavirus. SARS spread rapidly in 2002–2003.

The new strain of coronavirus is called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 the virus causes coronavirus disease 19 (COVID-19).

Around 80% of people with COVID-19 recover without specialist treatment. These people may experience mild, flu-like symptoms. However, 1 in 6 people may experience severe symptoms, such as trouble breathing.

The new coronavirus has spread rapidly in many parts of the world. On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a pandemic. A pandemic occurs when a disease that people are not immune to spreads across large regions.

1.6 Spread

COVID-19 is caused by the SARS-CoV-2 virus, which spreads between people, mainly when an infected person is in close contact with another person.

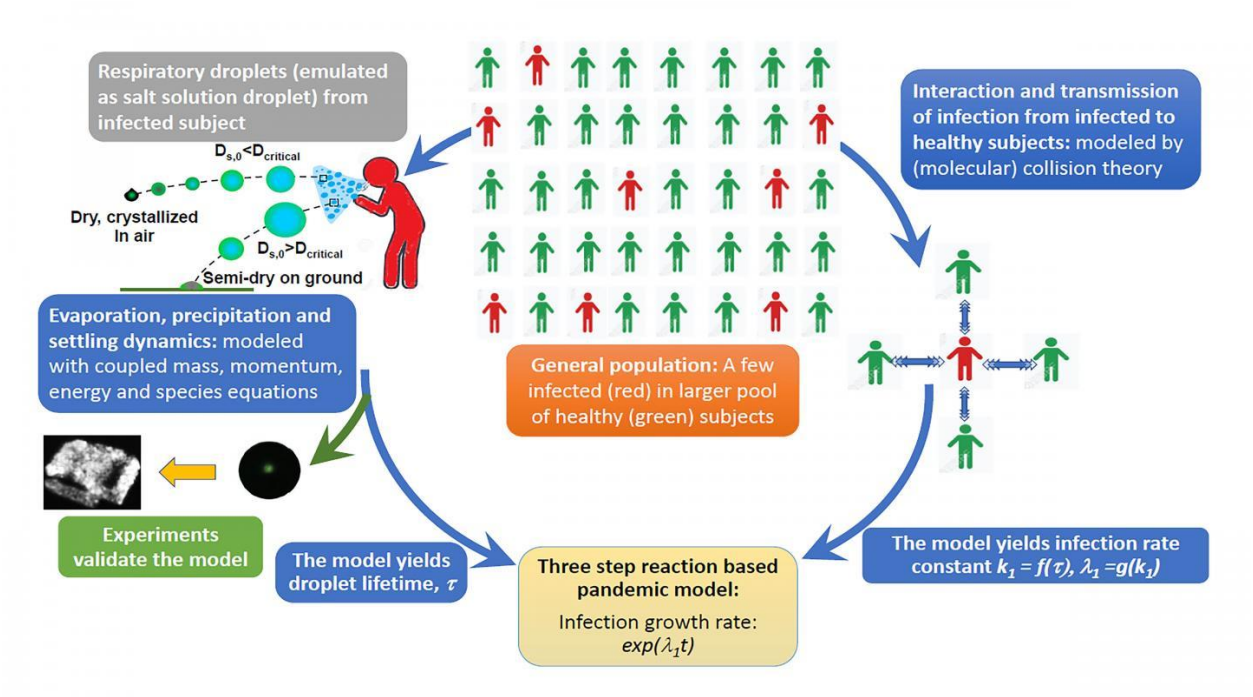
The virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe heavily. These liquid particles are different sizes, ranging from larger 'respiratory droplets' to smaller 'aerosols'.

Other people can catch COVID-19 when the virus gets into their mouth, nose or eyes, which is more likely to happen when people are in direct or close contact (less than 1 metre apart) with an infected person.

Current evidence suggests that the main way the virus spreads is by respiratory droplets among people who are in close contact with each other.

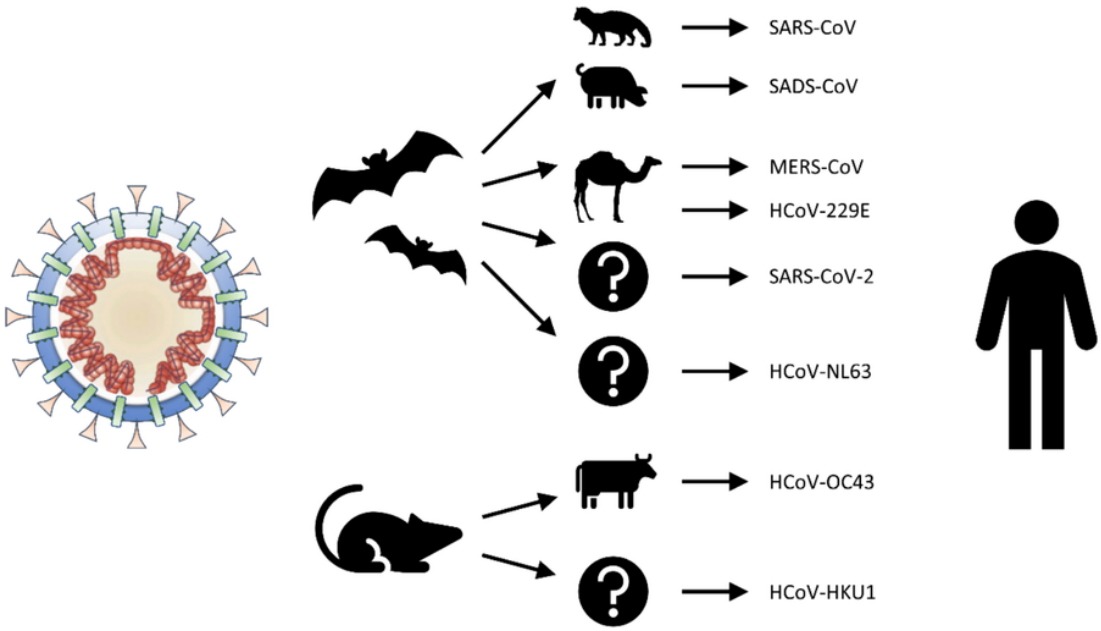
Aerosol transmission can occur in specific settings, particularly in indoor, crowded and inadequately ventilated spaces, where infected person(s) spend long periods of time with others, such as restaurants, choir practices, fitness classes, nightclubs, offices and/or places of worship. More studies are underway to better understand the conditions in which aerosol transmission is occurring outside of medical facilities where specific medical procedures, called aerosol generating procedures, are conducted.

The virus can also spread after infected people sneeze, cough on, or touch surfaces, or objects, such as tables, doorknobs and handrails. Other people may become infected by touching these contaminated surfaces, then touching their eyes, noses or mouths without having cleaned their hands first.



Figure; 6 flow diagrams outlining the interconnections of the model developed

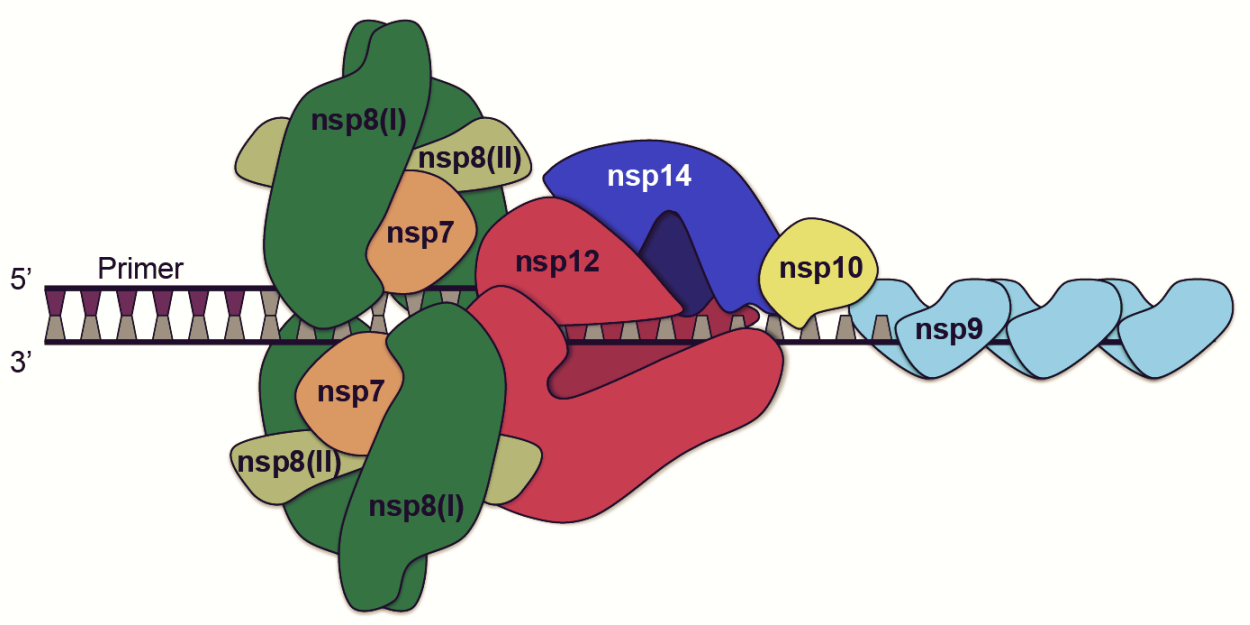
To conduct next-generation sequencing from bronchoalveolar lavage fluid and cultured isolates, researchers enrolled nine inpatients in Wuhan with viral pneumonia and negative in common respiratory pathogens. The results of this next-generation sequencing indicated that SARS-CoV-2 was more distant from SARS-CoV.



Figure; 7 Origins of human coronaviruses with possible intermediate hosts

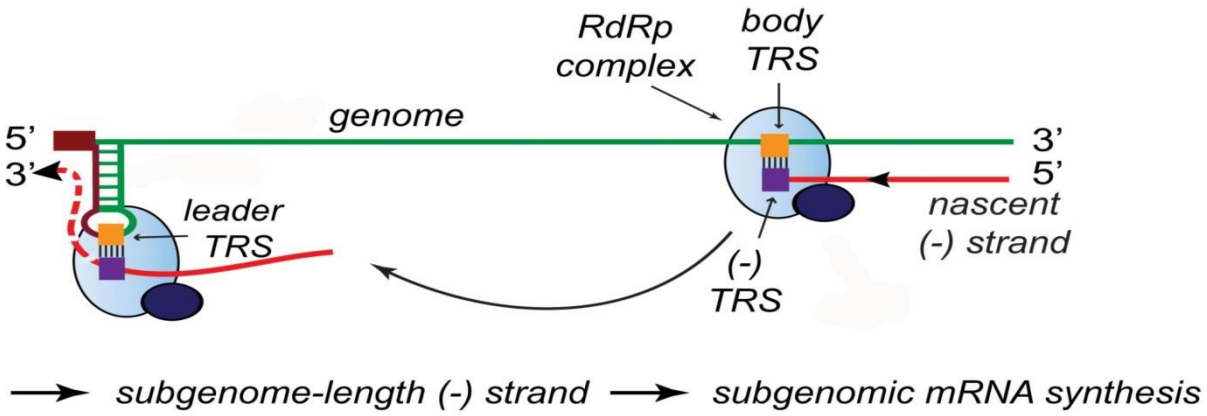
1.7 Transmission Of Corona The current pandemic of coronavirus disease 2019 (COVID-19) cases demands greater infection control precautions. Nebulizers generate aerosol particles in the size of 1–5 μm, which can carry bacteria and viruses into the deep lung. The risk of infection transmission via droplet nuclei and aerosols may increase during nebulizer treatments because of the potential to generate a high volume of respiratory aerosols that may be propelled over a longer distance than is involved in a natural dispersion pattern.

Model of the replicase-transcriptase complex of a coronavirus. Illustration shows how the RNA sliding clamp for processivity and primase domain for priming (nsp7 and nsp8 – green/orange) could assemble on viral dsRNA and interact with the putative multi-subunit coronavirus polymerase complex consisting of RdRp for replication (nsp12 – red), ExoN for proofreading (nsp14 – dark blue), and ExoN cofactor (nsp10 – yellow). To initiate replication-transcription there is a short (~6 N.T.) primer generated by the non-canonical RdRp activity of nsp8 (I and II). Binding of ssRNA by RNA binding proteins (nsp9 – light blue) to avoid secondary structure is also shown. A helicase to unwind RNA (nsp13) is not shown downstream.

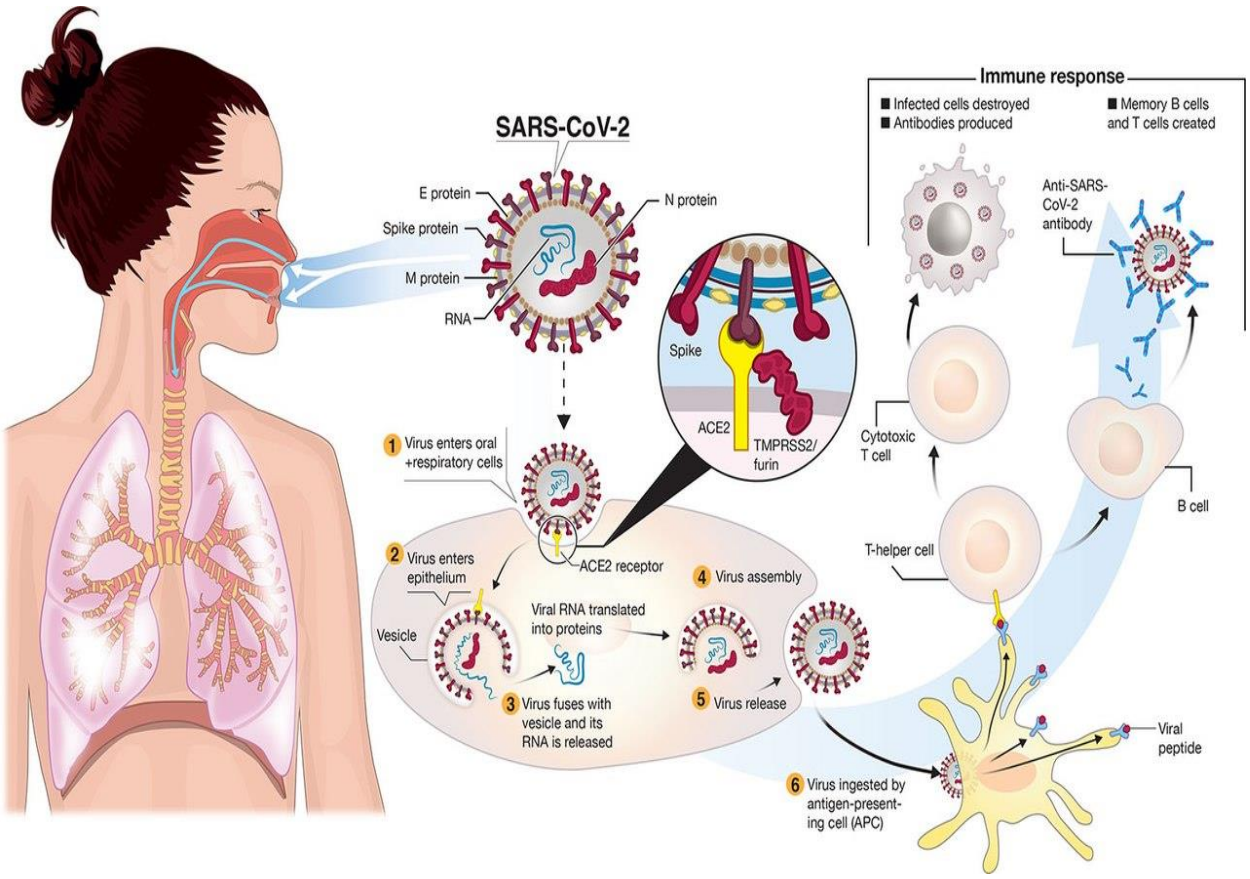


Figure; 8 Nested set of subgenomic mRNAs

Model of the replicase-transcriptase complex of a coronavirus. Illustration shows how the RNA sliding clamp for processivity and primase domain for priming (nsp7 and nsp8 – green/orange) could assemble on viral dsRNA and interact with the putative multi-subunit coronavirus polymerase complex consisting of RdRp for replication (nsp12 – red), ExoN for proofreading (nsp14 – dark blue), and ExoN cofactor (nsp10 – yellow). To initiate replication-transcription there is a short (~6 N.T.) primer generated by the non-canonical RdRp activity of nsp8 (I and II). Binding of ssRNA by RNA binding proteins (nsp9 – light blue) to avoid secondary structure is also shown. A helicase to unwind RNA (nsp13) is not shown downstream.



Figure; 9 Transcription of nested mRNAs



Figure; 9 Transmission and life-cycle of SARS-CoV-2 causing COVID-19

Transmission and life-cycle of SARS-CoV-2 causing COVID-19. SARS-CoV-2 is transmitted via respiratory droplets of infected cases to oral and respiratory mucosal cells. The virus, possessing a single-stranded RNA genome wrapped in nucleocapsid (N) protein and three major surface proteins: membrane (M), envelope (E) and Spike, replicates and passes to the lower airways potentially leading to severe pneumonia. The gateway to host cell entry (magnified view) is via Spike-converting enzyme 2 (ACE2) interactions with cleavage of Spike in the prefusion state by proteases TMPRSS-2/furin. A simplified depiction of the life cycle of the virus is shown along with potential immune responses elicited.

2 Furthermore, the larger particles may stimulate both patients' and bystanders' cough and thus increase the risk of spreading the disease.

3 There is a possibility that nebulizer therapy in patients with COVID-19 infection can transmit potentially viable coronavirus to susceptible bystander hosts. In recent years there has been a welcome shift, in some centres, from the use of nebulizers to metered-dose inhalers with valved holding chambers. For example, in Alberta, Canada, any order for nebulizer is now restricted and a nebulizer is to be used only in the following situations:

• Patients with severe, life-threatening respiratory disease (e.g., those with severe or impending respiratory arrest, or those with hypoventilation or ventilation compromise, continuous nebulization, end-stage chronic obstructive pulmonary disease, cystic fibrosis)

• Patients who are uncooperative or are unable to follow the directions required for using a metered-dose inhaler with spacer;

• Patients with a history of poor response to metered-dose inhaler with spacer. However, despite a large body of evidence suggesting their lack of superiority or inferiority compared with metereddose inhalers with valved holding chambers,

4 nebulizers are still widely used in many health care facilities (especially in the United States). Given the current outbreak of COVID19, Alberta Health Services in Canada has now requested that any plan or order for nebulizer therapy be reconsidered. To reduce the risk of transmission of all infectious respiratory illnesses in health care facilities, we would encourage all caregivers in all other provinces to align with the above restrictions and seriously consider avoiding the use of nebulizers. Keeping our patients and staff safe should be our priority.

Whether or not they have symptoms, infected people can be contagious and the virus can spread from them to other people.

Laboratory data suggests that infected people appear to be most infectious just before they develop symptoms (namely 2 days before they develop symptoms) and early in their illness. People who develop severe disease can be infectious for longer.

While someone who never develops symptoms can pass the virus to others, it is still not clear how frequently this occurs and more research is needed in this area.

2. Literature Review

Pranab Chatterjee, Nazia Nagi et al (2020) A novel coronavirus (nCoV) spillover event, with its epicenter in Wuhan, People's Republic of China, has emerged as a public health emergency of international concern. This began as an outbreak in December 2019, and till February 28, 2020, there have been 83,704 confirmed cases of novel coronavirus disease 2019 (COVID-19) globally, with 2,859 deaths, resulting in an overall case fatality rate of 3.41 per cent (95% confidence interval 3.29-3.54%). By this time (February 28, 2020) 58 countries or territories and one international conveyance (Diamond Princess Cruise Ship) were affected. As a part of the global response to manage and contain the pandemic, major emphasis was placed on generating research intelligence to guide evidence-based responses to contain the virus, which was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), owing to its genetic similarities with the SARS virus. This review summarizes the emerging evidence which can help guide the public health response, particularly in India. Key areas have been identified in which research needs to be conducted to generate critical intelligence for advising prevention and control efforts. The emergence of SARS-CoV-2 has once again exposed the weaknesses of global health systems preparedness, ability to respond to an infectious threat, the rapidity of transmission of infections across international borders and the ineffectiveness of knee-jerk policy responses to emerging/re-emerging infectious disease threats. The review concludes with the key learning points from the ongoing efforts to prevent and contain COVID-19 and identifies the need to invest in health systems, community-led response mechanisms and the need for preparedness and global health security.(8)

Vincenzo Galasso, Vincent Pons (2020) Using original data from two waves of a survey conducted in March and April 2020 in eight OECD countries (N = 21,649), we show that women are more likely to see COVID-19 as a very serious health problem, to agree with restraining public policy measures adopted in response to it, and to comply with them. Gender differences in attitudes and behavior are substantial in all countries, robust to controlling for a large set of sociodemographic, employment, psychological, and behavioral factors, and only partially mitigated for individuals who cohabit or have direct exposure to COVID-19. The results are not driven by differential social desirability bias. They carry important implications for the spread of the pandemic and may contribute to explain gender differences in vulnerability(9)

Rahi Abouk, Babak Heydari (2020) Anecdotal evidence points to the effectiveness of COVID-19 social distancing policies, however, their effectiveness vis-a-vis what is driven by public awareness and voluntary actions have not been studied. Policy variations across US states create a natural experiment to study the causal impact of each policy. Using a difference-in-differences methodology,

location-based mobility, and daily state-level data on COVID-19 tests and confirmed cases, we rank policies based on their effectiveness. We show that statewide stay-at-home orders had the strongest causal impact on reducing social interactions. In contrast, most of the expected impact of more lenient policies were already reaped from non-policy mechanisms. Moreover, stay-at-home policy results in a steady decline in confirmed cases, starting from ten days after implementation and reaching a 37% decrease after fifteen days, consistent with the testing practices and incubation period of the disease.(10)

Steven Riley , Christophe Fraser, (2003) We present an analysis of the first 10 weeks of the severe acute respiratory syndrome (SARS) epidemic in Hong Kong. The epidemic to date has been characterized by two large clusters-initiated by two separate "super-spread" events (SSEs)-and by ongoing community transmission. By fitting a stochastic model to data on 1512 cases, including these clusters, we show that the etiological agent of SARS is moderately transmissible. Excluding SSEs, we estimate that 2.7 secondary infections were generated per case on average at the start of the epidemic, with a substantial contribution from hospital transmission. Transmission rates fell during the epidemic, primarily as a result of reductions in population contact rates and improved hospital infection control, but also because of more rapid hospital attendance by symptomatic individuals. As a result, the epidemic is now in decline, although continued vigilance is necessary for this to be maintained. Restrictions on longer range population movement are shown to be a potentially useful additional control measure in some contexts. We estimate that most currently infected persons are now hospitalized, which highlights the importance of control of nosocomial transmission.(11)

Tanu Singhal (2019) There is a new public health crises threatening the world with the emergence and spread of 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province, China in December 2019. There have been around 96,000 reported cases of coronavirus disease 2019 (COVID-2019) and 3300 reported deaths to date (05/03/2020). The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. The disease is mild in most people; in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction.(12)

Matteo Di Nardo, Grace van Leeuwen, (2019) At the time of writing, there are already millions of documented infections worldwide by the novel coronavirus 2019 (2019-nCoV or severe acute

respiratory syndrome coronavirus 2 (SARS-CoV2)), with hundreds of thousands of deaths. The great majority of fatal events have been recorded in adults older than 70 years; of them, a large proportion had comorbidities. Since data regarding the epidemiologic and clinical characteristics in neonates and children developing coronavirus disease 2019 (COVID-19) are scarce and originate mainly from one country (China), we reviewed all the current literature from 1 December 2019 to 7 May 2020 to provide useful information about SARS-CoV2 viral biology, epidemiology, diagnosis, clinical features, treatment, prevention, and hospital organization for clinicians dealing with this selected population.(13)

Piyush P Mehta, Vividha S Dhapte-Pawar (2021) Coronaviruses disease 2019 (COVID-19) is the most crucial threat, the world has ever witnessed. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of this disease pandemic. The World Health Organization has confirmed the continuing epidemic as a worldwide public health crisis. Presently, the research on COVID-19 is even in the primitive stage. Studies on unveiling the natural route of COVID-19 infection and related pathophysiology, the biology of pulmonary airways pose a more rational restorative approach in the management of COVID-19. Thus, based on the existing facts, we methodically reviewed the efforts put forth by various research institutes, pharmaceutical companies and biotechnology firms in pulmonary delivery to prevent and control the COVID-19. This article would be valuable for the healthcare community, which is efficiently dealing with the SARS-CoV-2 crisis.(14)

Na Zhu, Dingyu Zhang, (2020) In December 2019, a cluster of patients with pneumonia of unknown cause was linked to a seafood wholesale market in Wuhan, China. A previously unknown beta coronavirus was discovered through the use of unbiased sequencing in samples from patients with pneumonia. Human airway epithelial cells were used to isolate a novel coronavirus, named 2019-nCoV, which formed a clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily. Different from both MERS-CoV and SARS-CoV, 2019-nCoV is the seventh member of the family of coronaviruses that infect humans. Enhanced surveillance and further investigation are ongoing. (Funded by the National Key Research and Development Program of China and the National Major Project for Control and Prevention of Infectious Disease in China.(14)

Harapan Harapan, (2019) n early December 2019, an outbreak of coronavirus disease 2019 (COVID-19), caused by a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), occurred in Wuhan City, Hubei Province, China. On January 30, 2020 the World Health Organization

declared the outbreak as a Public Health Emergency of International Concern. As of February 14, 2020, 49,053 laboratory-confirmed and 1,381 deaths have been reported globally. Perceived risk of acquiring disease has led many governments to institute a variety of control measures. We conducted a literature review of publicly available information to summarize knowledge about the pathogen and the current epidemic. In this literature review, the causative agent, pathogenesis and immune responses, epidemiology, diagnosis, treatment and management of the disease, control and preventions strategies are all reviewed.(15)

Dinesh Kumar Rajendran Varthini Rajagopal, (2019) Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the seventh-generation coronavirus family causing viral pandemic coronavirus disease (COVID-19) across globe affecting millions of people. The objectives of this study are to (1) identify the major research themes in COVID-19 literature, (2) determine the origin, symptoms and modes of transmission of COVID, (3) recommend the intervention and mitigation strategies adopted by the Governments globally against the spread of COVID-19 and the traumatization among the public? and study the possible drugs/treatment plans against COVID-19. A systematic literature review and comprehensive analysis of 38 research articles on COVID-19 are conducted. An integrated Research focus parallel-ship network and keyword co-occurrence analysis are carried out to visualize the three research concepts in COVID-19 literature. Some of our observations include: as SARS-CoV-2's RNA matches ~ 96% to SARS-CoV, it is assumed to be transmitted from the bats.The common symptoms are high fever, dry cough, fatigue, sputum production, shortness of breath, diarrhoea etc. A lockdown across 180 affected counties for more than a month with social-distancing and the precautions taken in SARS and MERS are recommended by the Governments.

Researchers' claim that nutrition and immunity enhancers and treatment plans such as arbidol, lopinavir/ritonavir, convalescent plasma and mesenchymal stem cells and drugs including remdesivir, hydroxychloroquine, azithromycin and favipiravir are effective against COVID-19. This complied report serves as guide to help the administrators, researchers and the medical officers to adopt recommended intervention strategies and the optimal treatment/drug against COVID-19.(16)

Tanu Singhal, (2019) There is a new public health crises threatening the world with the emergence and spread of 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus originated in bats and was transmitted to humans through yet unknown intermediary animals in Wuhan, Hubei province, China in December 2019. There have been around

96,000 reported cases of coronavirus disease 2019 (COVID-2019) and 3300 reported deaths to date (05/03/2020). The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. The disease is mild in most people; in some (usually the elderly and those with comorbidities), it may progress to pneumonia, acute respiratory distress syndrome (ARDS) and multi organ dysfunction. Many people are asymptomatic. The case fatality rate is estimated to range from 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein (CRP). The computerized tomographic chest scan is usually abnormal even in those with no symptoms or mild disease. Treatment is essentially supportive; role of antiviral agents is yet to be established. Prevention entails home isolation of suspected cases and those with mild illnesses and strict infection control measures at hospitals that include contact and droplet precautions. The virus spreads faster than its two ancestors the SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), but has lower fatality. The global impact of this new epidemic is yet uncertain.(17)

Abdiaziz Harun Mohamed et al (2019) pandemic has brought difficult situations for citizens of nations across the world. The impact however, may be more severe for others in the Third World Countries, who are in desperate situations and whose conditions may well further deteriorate if not put into considerations. While this pandemic affects different dimensions of life and society in general, this paper examines the impact of the outbreak COVID-19 pandemic on Somaliland Economy and analyzes the need for mitigation measures of this pandemic. The research methodology of this paper reviews secondary data which were collected through various magazines, articles, newspapers and published journals. The study focuses on descriptive research design and the sample design selected for this study which was illustrative. This study observed that COVID-19 is affecting the Somaliland economy through loss of jobs and other incomes, gradual recession and deterioration of public financial and private business sectors of the nation. The study discovers that for the recovery of the economy, certain mitigation measures and policy interventions must be administered, which includes health and social protection, fiscal policy and financial, industrial and trade policies. Therefore, the expected outcomes from administration of the policy instruments would be reduction in human suffering and the enhancement of the recovery of the economy from bankruptcy and recession.(18)

Kamleshun Ramphul, Stephanie G. Mejias (2019) In December 2019, several patients from Wuhan,

China were admitted to hospitals with symptoms of pneumonia. As the number of patients presenting with similar symptoms started to rise, the causative agent was eventually isolated from samples. It was initially called the 2019 novel coronavirus (2019-nCoV) and has been recently relabelled as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); the disease it causes has been named coronavirus disease 2019 (COVID-19). Over the next few weeks, the virus spread from Wuhan to affect different provinces in China and, after a few months, it is now present in 109 countries. As of March 10, 2020, there have been 113,702 confirmed cases globally, and 4,012 deaths have been registered. The World Health Organization (WHO) called COVID-19 a pandemic on March 11, 2020. There are multiple drug trials going on with some positive results. However, since no vaccine is available, the best way to combat the virus is by preventive methods.(19)

See all articles Search Google Scholar (2020) Smoking history and its potential association with COVID-19 has attracted many researchers and the lay public alike. However, the studies published to date have several methodological limitations and are mainly from China. We set out to synthesize evidence on smoking and COVID-19 relationship drawn on cohort studies only which are published in non-Chinese population settings.(20)

George Santangelo (2020) In the past few months, the scientific community has ramped up research in response to the SARS-CoV-2 pandemic; dozens of peer-reviewed articles and preprints on this topic are being added to the literature every day (Figure 1). This rapidly expanding effort has created challenges for scientists and the medical community who need to analyze thousands of scholarly articles for insights on the virus. Recently, the National Library of Medicine at NIH joined the White House and key industry and university leaders to release the COVID-19 Research Dataset (CORD-19) and call on the AI community to develop text mining tools that help analyze and summarize the over 45,000 coronavirus articles. The CORD-19 dataset represents the most comprehensive, freely available library of machine readable coronavirus scholarly literature to date, with hundreds of AI tools and technologies already created. (21)

Ishan Poudel Ankur Sah Swarnakar (2020) Coronavirus Disease 2019 (COVID-19) is a respiratory illness caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). It is considered to be first reported from Wuhan, Hubei Province, China in December 2019. As of present, there are over 3.7 million identified cases worldwide and more than 259,000 deaths have been reported. This disease, its incubation period, course, complications, and the basis of spread remains a potential question due to variation in the pattern of spread around the globe and relatively fewer number of

large-scale studies at present. This literature review aims to study the available data on its spread and incubation period. A literature search using PubMed with regular keywords 'coronavirus' and 'COVID-19', and Medical Subject Headings (MeSH) search for their etiology and pathogenicity was done with the search builder. The literature search revealed 26,689 studies among which 14 studies were selected for review. Studies were selected after the application of inclusion criteria and exclusion criteria with the removal of duplicates, and careful review for the outcome of interest 'incubation period'. Among the 14 studies selected for review, there were eight review articles, five case reports, and one comparative study. The current literature review concludes that the mean incubation period for most of the literature falls between five days to 12 days with minimum reported time from known exposure to the onset of a symptom being one day and the maximum reported time from exposure to the onset of a symptom being 18 days.(22)

Ancy Ochieng, Priya Chidambaram (2021) The COVID-19 pandemic has disproportionately affected residents and staff in nursing homes and other long-term care facilities (LTCFs). While this group is in the top priority group for vaccine distribution in all states, some may remain at risk as the pandemic continues to spread across the country, particularly LTCF staff for whom vaccination rates have been low. In addition, the pandemic may have exposed vulnerabilities in LTCFs that can inform future efforts to address infectious disease outbreaks. This brief summarizes the findings of 30 studies between April 2020 and January 2021 that examined potential factors associated with COVID-19 cases and/or deaths in LTCFs. Key takeaways include: The prevalence of COVID-19 cases in the community is consistently associated with COVID-19 cases and/or deaths in long-term care facilities. Staff infections appear to be a link between cases in the community and long-term care facilities, although it is unclear if the staff infections were the result of community spread or pre-existing cases in LTCFs. Long-term care facilities that are for-profit or have higher shares of residents who are people of color (or are located in communities with a large share of people from communities of color) were more likely to have COVID-19 cases and deaths. Urban location and large bed size are also associated with cases and deaths, which may reflect other factors such as community spread or association between bed side and case count. Among studies that examine the association between CMS overall quality ratings and infection control deficiencies in nursing facilities, most find no clear association with COVID-19 cases or deaths, but a small number of studies do. Nursing homes with higher staffing levels, including those with higher CMS 5-star quality ratings for staffing are associated with fewer cases or deaths in the facility. It should be noted that many of these studies were conducted in real time, as the pandemic was gaining force and shifting geographically; it is possible

that results from studies conducted in the earlier months may not reflect changes that have occurred over the course of the year. Further, we did not identify research that examines the role of PPE shortages, staff shortages, or state or facility policy on cases or deaths in LTCFs. While a successful vaccination effort should mitigate the future risk of serious illness and deaths due to COVID-19, this analysis identifies factors that may make residents and staff of nursing homes and other LTCFs vulnerable if sufficient numbers are not vaccinated,(23)

3. Sings & Symptoms

Signs and symptoms of coronavirus disease 2019 (COVID-19) may appear two to 14 days after exposure. This time after exposure and before having symptoms is called the incubation period. Common signs and symptoms can include:

- Fever
- Cough
- Tiredness

Early symptoms of COVID-19 may include a loss of taste or smell.

Other symptoms can include:

- Shortness of breath or difficulty breathing
- Muscle aches
- Chills
- Sore throat
- Runny nose
- Headache
- Chest pain
- Pink eye (conjunctivitis)
- Nausea

- Vomiting
- Diarrhea
- Rash

This list is not all inclusive. Children have similar symptoms to adults and generally have mild illness.The severity of COVID-19 symptoms can range from very mild to severe. Some people may have only a few symptoms, and some people may have no symptoms at all. Some people may experience worsened symptoms, such as worsened shortness of breath and pneumonia, about a week after symptoms start. People who are older have a higher risk of serious illness from COVID-19, and the risk increases with age. People who have existing medical conditions also may have a higher risk of serious illness. Certain medical conditions that increase the risk of serious illness from COVID-19 include:

- Serious heart diseases, such as heart failure, coronary artery disease or cardiomyopathy
- Cancer
- Chronic obstructive pulmonary disease (COPD)
- Type 2 diabetes
- Obesity or severe obesity
- Smoking
- Chronic kidney disease
- Sickle cell disease
- Weakened immune system from solid organ transplants
- Pregnancy

Other conditions may increase the risk of serious illness, such as:

- Asthma
- Liver disease

- Overweight
- Chronic lung diseases such as cystic fibrosis or pulmonary fibrosis
- Brain and nervous system conditions
- Weakened immune system from bone marrow transplant, HIV or some medications
- Type 1 diabetes
- High blood pressure

4. Diagnosis

If you develop symptoms of coronavirus disease 2019 (COVID-19) or you've been exposed to the COVID-19 virus, contact your doctor. Also let your doctor know if you've had close contact with anyone who has been diagnosed with COVID-19.

Factors used to decide whether to test you for the virus that causes COVID-19 may differ depending on where you live. Depending on your location, you may need to be screened by your clinic to determine if testing is appropriate and available.

In the U.S., your doctor will determine whether to conduct tests for the virus that causes COVID-19 based on your signs and symptoms, as well as whether you have had close contact with someone diagnosed with COVID-19. Your doctor may also consider testing if you are at higher risk of serious illness or you are going to have a medical procedure.

To test for the COVID-19 virus, a health care provider takes a sample from the nose (nasopharyngeal swab) or throat (throat swab). The samples are then sent to a lab for testing. If you're coughing up sputum, that may be sent for testing. The FDA has authorized at-home tests for the COVID-19 virus. These are available only with a doctor's prescription.

Nucleic Acid Amplification Testing (NAAT) ; At present confirmation of cases of COVID-19 is based on the detection of viral RNA by nucleic acid amplification tests (NAAT) such as real-time reverse transcriptase polymerase chain reactions (RT-PCR) with confirmation by nucleic acid sequencing when necessary (WHO 2020e). The viral genes targeted so far include the N, E, S, ORF and RdRp genes (Fig. 9.5) according to SARS-Co GenBank Different protocols followed by various countries.

Figure; 10 Requirements for specimen collection, packaging and transport

One of the following conditions should be met to consider a case as laboratory confirmed by NAAT in areas with no SARS-CoV-2 circulation:

- A positive NAAT result for at least two different targets on the SARS-CoV-2 virus genome, of which at least one target is preferably specific for SARS-CoV-2 virus using a validated assay;
- One positive NAAT result for the presence of betacoronavirus, and SARS-CoV-2 virus further identified by sequencing partial or whole genome of the virus as long as the sequence target is larger or different from the amplicon probed in the NAAT assay used.

Relative positions of amplicon targets on SARS-CoV-2 genome. ORF open reading frame, RdRp RNA-dependent RNA polymerase, E envelop proteingene, N nucleocapsid protein gene, M membrane protein gene, S spike protein gene

When there is ambiguity in results, sample should once again be collected from the patient and, if appropriate, sequencing of the virus from the original specimen or of an amplicon generated from an appropriate NAAT assay, different from the NAAT assay initially used, should be obtained to provide a reliable test result.

Areas where SARS-CoV-2 virus is widely circulating a simpler logarithm might suffice; for example screening of a single differential target is sufficient. One or more negative results do not rule out the possibility of SARS-CoV-2 virus infection. A number of factors could lead to a negative result in an infected individual, including:

- Poor quality of the specimen, containing little patient material (as a control, consider determining whether there is adequate human DNA in the sample by including a human target in the PCR testing).
- The specimen was collected late or very early in the infection.
- The specimen was not handled and shipped appropriately (non-maintenance of cold chain).
- Technical reasons inherent in the test, e.g. virus mutation or PCR inhibition.

If a negative result is obtained from a patient with a high index of suspicion for SARS-CoV-2 virus

infection, particularly when only upper respiratory tract specimens were collected, additional specimens, including from the lower respiratory tract if possible, should be collected and tested.

Viral Sequencing

Sequencing does not have a role in the initial laboratory diagnosis of SARS-CoV-2 but can be helpful in the following circumstances:

- Providing confirmation of the presence of the virus.
- Monitor for viral genome mutations that might affect the performance of medical countermeasures, including diagnostic tests.
- Virus whole genome sequencing can also inform molecular epidemiology studies.

Viral Culture

Viral culture is not recommended for the laboratory diagnosis of SARS-CoV-2. But viral culture can be used for research purposes like isolation of the virus, studying the properties of the virus and development of vaccine. Human airway epithelial cell lines were used for the initial isolation of the virus.

Challenges for Diagnosis

Early diagnosis of COVID-19 is essential for the timely management as well as isolation of confirmed cases to prevent further transmission of patients. However, sample collection, transport and kit validation are major bottlenecks in the diagnosis of COVID-19. A study found that the total positivity of cases by initial RT-PCR were around 30–60% (Ai et al. 2020). This largely depends on the time at which sample has been collected as PCR positivity will be seen during the early days of symptoms. Furthermore, the sensitivity of the testing kits is a matter of debate and thereby a sizeable number of patients may not be identified, which may ultimately be detrimental in the early diagnosis and treatment of COVID-19 cases. Also in low- and middle-income countries (LMIC) (Hopman et al. 2020), the healthcare system is not robust enough as a result of which the testing laboratories often face difficulties in the performance of molecular testing.

5. Prevention

1. Wash your hands frequently and carefully Use warm water and soap and rub your hands for at least 20 seconds. Work the lather to your wrists, between your fingers, and under your fingernails. You can

also use an antibacterial and antiviral soap.

Use hand sanitizer when you cannot wash your hands properly. Rewash your hands several times a day, especially after touching anything, including your phone or laptop.

2. Avoid touching your face **SARS-CoV-2 can live on some surfaces for up to 72 hours. You can get the virus on your hands if you touch a surface like:**

- gas pump handle

Figure; 11 How to Get Kids to Stop Touching Their Faces

- your cell phone
- a doorknob

Avoid touching any part of your face or head, including your mouth, nose, and eyes. Also avoid biting your fingernails. This can give SARS-CoV-2 a chance to go from your hands into your body.

3. Stop shaking hands and hugging people — for now

Similarly, avoid touching other people. Skin-to-skin contact can transmit SARS-CoV-2 from one person to another.

4. Don’t share personal items

Do not share personal items like:

- phones

- makeup
- combs

It's also important not to share eating utensils and straws. Teach children to recognize their reusable cup, straw, and other dishes for their own use only.

5. Cover your mouth and nose when you cough and sneeze

SARS-CoV-2 is found in high amounts in the nose and mouth. This means it can be carried by air droplets to other people when you cough, sneeze, or talk. It can also land on hard surfaces and stay there for up to 3 days.

Use a tissue or sneeze into your elbow to keep your hands as clean as possible. Wash your hands carefully after you sneeze or cough, regardless.

6. Clean and disinfect surfaces

Use alcohol-based disinfectants to clean hard surfaces in your home like:

- countertops
- door handles
- furniture
- toys

Also, clean your phone, laptop, and anything else you use regularly several times a day.

Disinfect areas after you bring groceries or packages into your home.

Use white vinegar or hydrogen peroxide solutions for general cleaning in between disinfecting surfaces.

7. Take physical (social) distancing seriously

If you're carrying the SARS-CoV-2 virus, it'll be found in high amounts in your spit (sputum). This can happen even if you don't have symptoms.

Physical (social) distancing also means staying home and working remotely when possible.If you must go out for necessities, keep a distance of 6 feet (2 m) from other people. You can transmit the virus by speaking to someone in close contact to you.

8. Do not gather in groups

Being in a group or gathering makes it more likely that you'll be in close contact with someone.

This includes avoiding all religious places of worship, as you may have to sit or stand too close to another congregant. It also includes not congregating at parks or beaches.

9. Avoid eating or drinking in public places

Now is not the time to go out to eat. This means avoiding restaurants, coffee shops, bars, and other eateries. The virus can be transmitted through food, utensils, dishes, and cups. It may also be temporarily airborne from other people in the venue. You can still get delivery or takeaway food. Choose foods that are thoroughly cooked and can be reheated. High heat (at least 132°F/56°C, according to one recent, not-yet-peer-reviewed lab study) helps to kill coronaviruses. This means it may be best to avoid cold foods from restaurants and all food from buffets and open salad bars.

10. Wash fresh groceries

Wash all produce under running water before eating or preparing.

The CDC Trusted Source and the FDA Trusted Source do not recommend using soap, detergent, or commercial produce wash on things like fruits and vegetables. Be sure to wash hands before and after handling these items.

11. Wear a (homemade) mask

The Centers for Disease Control and Prevention (CDC) recommends Trusted Source that almost everyone wears a cloth face mask in public settings where physical distancing may be difficult, such as grocery stores.

When used correctly, these masks can help prevent people who are asymptomatic or undiagnosed from transmitting SARS-CoV-2 when they breathe, talk, sneeze, or cough. This, in turn, slows the transmission of the virus.

Figure; 12 Face masks during the COVID-19 pandemic

The CDC's website provides instructions Trusted Source for making your own mask at home, using basic materials such as a T-shirt and scissors.Some pointers to keep in mind:

Wearing a mask alone will not prevent you from getting a SARS-CoV-2 infection. Careful handwashing and physical distancing must also be followed.

- Cloth masks aren't as effective as other types of masks, such as surgical masks or N95 respirators. However, these other masks should be reserved for healthcare workers and first responders.
- Wash your hands before you put on your mask.
- Wash your mask after each use.
- You can transfer the virus from your hands to the mask. If you're wearing a mask, avoid touching the front of it.
- You can also transfer the virus from the mask to your hands. Wash your hands if you touch the front of the mask.

- A mask shouldn't be worn by a child under 2 years old, a person who has trouble breathing, or a person who can't remove the mask on their own.

12. Self-quarantine if sick

Call your doctor if you have any symptoms. Stay home until you recover. Avoid sitting, sleeping, or eating with your loved ones even if you live in the same home.

Figure; 13 Stay home stay safe.

Stay physically fit. Exercise regulary. Eat a nutritious diet. Don't smoke Wear a mask and wash your hands as much as possible. If you need urgent medical care, wear a mask and let them know you may have COVID-19.

6. Types Of Treatment

6.1 Allopathic Treatment

In the allopathic approach, treatment in coronavirus included intravenous infusion of fluid, oxygen therapy, and life support system in critical cases. It was advisable if anyone prevails symptoms of the virus like flu, fever, and breathlessness, they should contact the doctor immediately. This virus is similar to the human immunodeficiency virus (HIV) in terms of virus replication and proteins. Different administrating drugs were found to clear and handle in vitro action against SARS-CoV and MERS-CoV.

Name of Drugs

1. **Ritonavir 100 mg**

Figure: 14 Protease inhibitors;

2. Remdesivir 100 ml

Figure; 15 Anti covid Agents

3. Oseltamivir 75 mg

Figure; 15 Anti-Influenza virus or Anti covid-19 Drugs

4. Sputnik V COVID-19 vaccine

Figure; 16 sputnik v covid-19

6.2 Herbals Treatment

The current pandemic of COVID-19 that is spreading across countries originated in Wuhan, China.

The single cause of this highly communicable disease is a novel coronavirus, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is the seventh known virus of the Coronaviridae family capable of infecting humans.

The latest report from the World Health Organization cited that there are now over 19 million confirmed cases and over 700,000 deaths worldwide caused by this virus. The United States of America now has the highest number of COVID-19 cases (over 4 million cases), followed by Brazil (almost 3 million cases) and India (over 2 million cases).

The fast propagation of this disease is mainly through close contact with infected individuals via respiratory droplets from either sneezing or coughing. Furthermore, there are two other ways of transmitting the virus, including contact and aerosol transmission.

Among infected patients, COVID-19 shows various unspecific symptoms, ranging from mild to

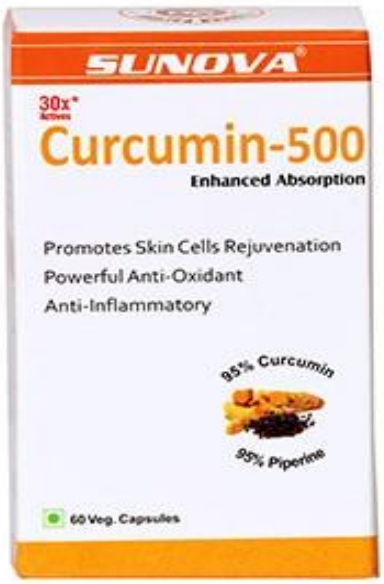
severe. A report from Huang et al. mentioned that fever (98%) is the most frequent manifestation that is reported by patients, followed by cough (76%), myalgia or fatigue (44%), sputum production (28%), and headache (8%). Also, some fatal cases have been reported in certain patients experiencing progressive respiratory failure due to the virus activity that attacks the alveolar epithelial cells. This damage is initiated by the receptor-binding domain (RBD) attachment of the virus to the receptor on the respiratory tract, known as the angiotensin-converting enzyme-2 (ACE2) receptor. Humans have many ACE2 receptors in their respiratory tracts, which increase their susceptibility to COVID-19. This molecular mechanism may partly explain why the incidence rate of this disease is increasing rapidly. Afterwards, viruses infecting humans can lead to subsequent inflammatory processes and the release of numerous proinflammatory cytokines that are responsible for the clinical appearance of inflammation. Some of these proinflammatory cytokines, including IL-2, IL-7, IL-10, G-CSF, IP-10, MCP-1, MIP-1a, and TNF-α, are highly elevated in the blood of severely ill COVID-19 patients. Thus, there may be an association between this elevated level of cytokines and the severity of a patient's manifestations.

Currently, there is no specific treatment for COVID-19. Furthermore, people in the community and researchers are trying to find the best way to cure or prevent the disease, including using herbal medicine. Since the immune status of patients plays an essential role in COVID-19 infection, an herbal medicine, which has an immunomodulatory effect, could have potential as a preventive measure and even therapeutic agent for patients with COVID-19 infection. A recent trend in the community is the consumption of herbal medicines containing certain active compounds, which have antimicrobial or antiviral, anti-inflammatory, and immune stimulatory activities, such as echinacea, quinine, and curcumin. These herbal compounds are assumed to have the capacity to modulate the immune response and, therefore, they are believed to have beneficial effects on preventing or treating COVID-19

Name of drug

Curcumin 500 mg: Curcumin is the main active ingredient in turmeric. Turmeric is native to Southeast Asia, but is popular all over the world. It is perhaps most popular in India, where it is one of the main spices in curry powders. Its flavor is warm and bitter, and it has a striking yellow color.

Turmeric has been reported to have many health benefits. Its use as a medicine dates back nearly 4000 years. Over the past few decades, modern medicine has increased research into turmeric's reputation for healing. Curcumin is at the heart of the research, as it's the source of many of turmeric's healthful properties



Figure; 17 curcumin

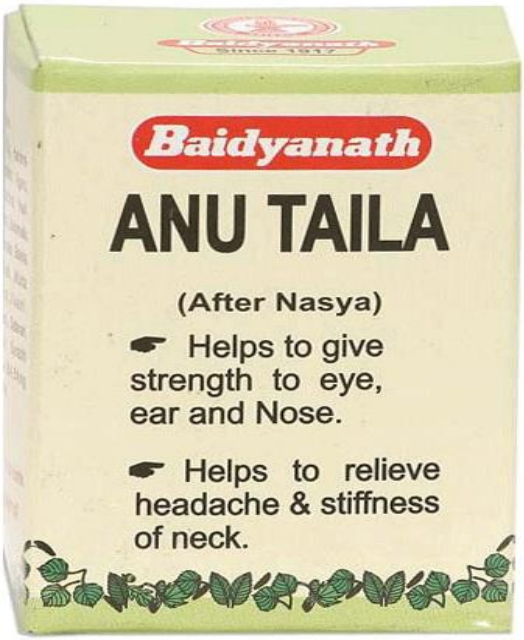
Echinacea 860 mg

Figure; 18 Echinacea

Shatavari

Figure; 19 Shatavari

Anu tail 10 ml



Figure; 20 Anu tail

Scientific Reasoning for Anu Taila

COVID-19 causes viraemia after entering the body and the main clinical manifestations are fever, pharyngalgia, fatigue, diarrhoea and other non-specific symptoms. Based on the clinical symptoms observed in the COVID-19 patients, the preventive medication should be aimed in reducing the inflammation of the respiratory tract through anti-inflammatory activity, and reduction of hypercoagulable state. In the traditional Ayurveda Anu taila is used for Nyasa processes (nasal drops) involving reduction of nasal passage inflammation, sinusitis and that of respiratory tract. These polyherbal components of Anu Taila have been described to have anti-inflammatory potential through amelioration of pro-inflammatory cytokines such as IL-1β, TNF-α, IFN-γ, IP-10, MCP-1, IL-4, and IL-8. Plants extracts obtained from Anu Taila component plants have been found to have direct effects on the respiratory tract, for example: Aegle marmelos, Asparagus recemosus, Aquilaria agallocha, Cedrus deodara, Cinnamomum verum, Coleus vettiveroides, Cyperus esculentus, Cyperus rotundus, Desmodium gangeticum, Elettaria cardamomum, Embelia ribes, Glycyrrhiza Glabra, Nelumbo nucifera, Ocimum sanctum, and Pogostemon cablin. While most of the studies have been performed on lung epithelial cells, it closely represents the cellular composition of the nasal passage. Hence, Anu taila can be used as a potential polyherbal medicine for COVID-19 related ailments.

Coronil

Figure; 21 Coronil Coronil Tablet :

Giloy, Ashwagandha, Tulsi. Swasari Vati, Mulethi, Kakdasinghi, Rudanti, Sounth,

7. Conclusion

There are hundreds of coronaviruses, most of which circulate in animals. Only seven of these viruses infect humans and four of them cause symptoms of the common cold. But, three times in the last 20 years, a coronavirus has jumped from animals to humans to cause severe disease.

SARS, a beta coronavirus emerged in 2002 and was controlled mainly by aggressive public health measures. There have been no new cases since 2004. MERS emerged in 2012, still exists in camels, and can infect people who have close contact with them.

COVID-19, a new and sometimes deadly respiratory illness that is believed to have originated in a live animal market in China, has spread rapidly throughout that country and the world.

The new coronavirus was first detected in Wuhan, China in December 2019. Tens of thousands of people were infected in China, with the virus spreading easily from person-to-person in many parts of that country.

The novel coronavirus infections were at first associated with travel from Wuhan, but the virus has now established itself in 177 countries and territories around the world in a rapidly expanding pandemic. Health officials in the United States and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, testing, quarantines and travel restrictions. Scientists are working to find medications to treat the disease and to develop a vaccine.

The World Health Organization declared the novel coronavirus outbreak “a public health emergency of international concern” on January 30. On March 11, 2020 after sustained spread of the disease outside of China, the World Health Organization declared the COVID-19 epidemic a pandemic. Public health measures like ones implemented in China and now around the world will hopefully blunt the spread of the virus while treatments and a vaccine are developed to stop it.

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