

COVID-19: A novel strain challenging the human race

Abstract

Diseases are not new to the humans' as we have learnt to cope up with a variety of contagion and contagious infections. Way back in the 18th century cowpox was a terrorizing clinical condition and as time progressed, the era of rabies and TB was an issue of health concern. But time has been the eternal evidence to validate the fight of mankind against these clinical manifestations. However, over the last few months, the world is being taken by a swing by an invisible, nanoscopic biological particle which was later named as COVID-19 or in short form is represented as nCoV-19 where n designate the uniqueness of the virus and is rightly called as novel corona virus 19 (nCoV-19). Though the outbreak of the pandemic gained its pace in 2020, it was initially discovered in December 2019 in the Wuhan province of China. Hence the virus is represented with 19 as a suffix. The disease which initially started as an epidemic soon started its universal form and became a severe pandemic all over the globe. The current article is an attempt to comprehend the facets of COVID-19 otherwise called as novel corona virus which is very often compared to the SARS outbreak in 2002 in China. The article also attempts to disclose various measures undertaken by the government and private firms to curb the intensity of the contagion. The current article emphasizes on clinical signs and epidemiological characteristics of novel corona virus disease and endeavors to brief out the possible steps to curd the rapid spreading of the disease.

Keywords: corona virus, COVID-19, nCoV-19, quarantine and social distancing, signs and symptoms of COVID-19, nCoV-19 treatment

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Introduction

Over the course of time, human beings have adjusted to cope up with situations and circumstances that have confronted them at every point of their lives. A very similar scenario is being experienced by people all over the globe because of a nanoscopic biological particle that has taken the world by its stride. The most common discussion over the last few months on a global scale has been the COVID pandemic and India was not an exception to its outbreak. COVID-19 is a newly discovered disease caused by corona virus. Though several theories have attempted to validate the claim that the global pandemic started as an epidemic in the Wuhan province of china during September 2019, the formal authentication on the contagion was not known till November 2019. It was in December 2019 when the causal agent was officially named as 2019 novel corona virus infection otherwise called as 2019-nCoV which stands for novel corona virus.¹ The 2019 novel corona virus emerged in the Wuhan province of China and has become a global issue of health concern. The disease is one of its own kinds and is considered to be zoonotic in nature. Though its existence is known to the scientific community over the last few decades, the current contagion is a novel strain and was not discovered in the past. The initial discovery of corona virus was in 1930s when an acute respiratory infection of domesticated chicken was shown to cause a condition known as infectious bronchitis and the virus was named as infectious bronchitis virus.² The clinical manifestation has resulted in a mortality rate up to 40-90% in the infected chickens. The virus responsible for causing infectious bronchitis was successfully isolated and cultivated in the later years by Fred Beaudette and Charles Hudson.³ In the later years two more animal corona viruses were discovered in mouse and pig that were known for causing hepatitis and gastroenteritis in mouse and pig. The viruses were named as mouse hepatitis virus (MHV) and transmissible gastroenteritis virus

(TGEV) and it was later known that these viruses (IBV, MHV and TGEV) were related to each other.^{4,5}

However, it was in the 1960s when human corona viruses were discovered and were isolated using different methods in the UK and US.^{6,7} Researchers at the common cold unit of British Medical Research Council in 1960 have isolated a common cold virus B814 from a boy.^{8,9} However, it was not until 1965 when an appropriate method of cultivating the virus was successfully implemented by Tyrrell and Byone by serially passing the novel virus through the organ culture of human embryonic trachea.¹⁰ Bertil Hoorn is credited to have discovered the new method of cultivating the virus which can be inoculated in to volunteers through intranasal route. Ether treatment has successfully inactivated the virus which indicates the presence of lipid envelope.^{11,12} During the course of time, Dorothy Hamre and John Procknow at the University of Chicago have isolated a cold causing virus in the medial students that were cultivated on the kidney tissue culture cells.¹³ Further studies on these strains have revealed affiliated facts from the context of their morphology and structure. Electron microscopic studies have disclosed distinctive morphological assets like surface spikes on the virus and viral envelope. Striking revelations were made in the later years from the context of morphology among these viruses which has validated the morphological similarities among the viral strains isolated from humans with those isolated from chicken and pigs which in turn has provided the scientific evidence of these belonging to the same family of viruses.

Further insights on COVID-19

Based on the kind of clinical manifestation caused, it was renamed n 7th January 2020 as SARS corona virus (severe acute respiratory syndrome corona virus) by International committee on Taxonomy

of Viruses (ICTV). ICTV indeed has put forth the claim to validate the role of the virus in causing a disease called as COVID-19 otherwise called as corona virus disease 2019. The WHO (World Health Organization) has then initiated the urge to instigate global public health emergency. The WHO has proclaimed the necessity of a worldwide health emergency from the context of dire consequences as a result of susceptible health systems. On 30th January 2020, the world health organization declared community health crisis on a global scale that could compromise the health structure in several countries leading to the outbreak of the contagion.^{14,15} The prevalence of the epidemic was so rapid that it soon spread to other countries from China and was declared as a severe pandemic claiming lives. As of 26th March 4, 60,000 have tested positive which has increased to a staggered number

of 2.9 million over a span of one month. The number of positive cases of COVID as of 26th April is over 2.9 million with over 2, 00,000 deaths on a global scale.^{16,17} As a matter of fact, the pandemic has changed the life style of people by influencing their daily routine. It could be rightly said the pandemic also had a psychological impact people in addition to biological manifestations. It could be rightly said that the current situation has triggered the circumstantial behavior in humans. This statement could be substantiated from the present scenario that has indeed forced people to acclimatize to a contrasting life style different from what it used to be in the recent past. One of the main issues related to the disease is the lack of a suitable vaccine or medicine to counteract the efficacy of the disease (Figure 1).

GLOBAL COVID 19 POSITIVE CASES

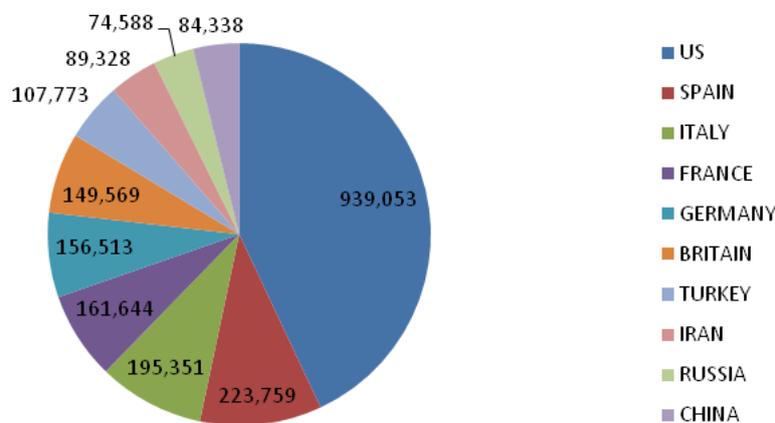


Figure 1 The above pie illustration depicts the global COVID 19 positive cases as on 26th April 2020.¹⁶

Hence, the only way to lessen the wide spread of the disease is by limiting public gathering and lockdown is the easiest way to achieve social distancing. The fact of people getting stranded at different regions in the country cannot be denied as the fear of the disease and imposed quarantine measures have provoked legal bodies and authorized organizations to employ drastic steps to contain the contagion. Several sectors all over the world ranging from industries to academics have been severely hampered and have gone in to dormancy for the last couple of months. In simple terms, the clinical condition has taken the entire globe in to a state of stagnation.

What is corona virus?

Viruses are quite hostile biological entities. Entity can be applied to a living or a non living unit. As a matter of fact viruses are generally considered a cellular and require a compatible host for its sustenance; they are biological because they are made up of bio-molecules. Though the novel corona virus is a newly discovered virus, corona viruses are a group of viruses that are associated with mammals and birds. It is known for causing mild to lethal respiratory tract infections in humans. Placid symptoms in humans include common cold while under severe circumstances can lead to multiple organ failure. The extent of severity in humans depends on their medical history. It has been found that elder adults and people with an existing medical condition are susceptible to the disease.¹⁸ They are enveloped viruses comprising of a positive sense single stranded RNA as its genome that is encased in a protein capsid. The nucleocapsid exhibits a

helical symmetry. The genome of the virus is considered to be one of the largest among viruses which consists of 26 to 32 kilobases. The electron micrographic images of the virus shows club shaped spike like projections from its surface which resembles solar corona. Hence they are widely known as corona virus.^{19,20} The first attempts to study human corona virus was made by June Almeida and David Tyrrell who pioneered in the observatory studies on human corona virus and the name “corona” was coined by these pioneers. The term corona virus also has its Latin and Greek connection as the word corona was derived Latin which means crown.²¹ The virus is considered to be zoonotic in nature as it was first discovered in domesticated chickens that suffered from acute respiratory infection. It was then disclosed that the infection among the domesticated chickens was caused by infectious bronchitis virus (IBV).²² The infection in new born chicks was characterized gasping and listlessness and the mortality rate was up to 90%. It was not until the 1940s when two more strains of the viruses were discovered in mouse and pigs respectively. Two more animal corona viruses, mouse hepatitis virus (MHV) and transmissible gastroenteritis virus (TGV) were isolated from mouse and pigs respectively. However, it was not known that all these three viruses were related.²³⁻²⁵

Human corona virus

Human corona viruses were discovered in the 1960s and were isolated using unique techniques in UK and US. Though the general technique employed for cultivating viruses were of no use for corona

virus isolation, Tyrrell and Byone in 1965 successfully isolated the virus. Their method involved the serial passing of the virus through the organ cultures of human embryonic trachea.²⁶ New methods of isolating the virus were introduced and the viral inoculation in to humans was done through intranasal route in volunteers which cold and the virus was inactivated by injecting ether which indicated the presence of lipid envelope.

Different strains of novel viruses inoculated in to volunteers caused cold and the inactivation of these different strains were possible by ether treatment.^{27,28} Further studies have disclosed various insights which revealed the morphological relatedness between the IBV (infectious bronchitis virus that was isolated in chicken) and MHV (mouse hepatitis virus). However, the IBV group was later known to be called as corona virus due to their distinctive morphological features. The virus is considered to be pleomorphic and is capable of altering its biological abilities and is made of a lipid bilayer envelope which comprises of bulbous surface projections. The lipid bilayer envelope

anchors the vital proteins like the membrane and the structural spike proteins which will assist in the viral attachment to the host. Certain strains of corona virus also exhibit shorter spike like surface protein called hemagglutinin esterase (ET) commonly abbreviated as HE.²⁹

Microbiology and genome of the virus

Corona virus is a large pleomorphic spherical particle with spiked bulbous surface projection with a diameter of 120nm. The dimensions of envelope and spike are 80nm and 20nm respectively. The envelope is made of lipid bilayer membrane that is studded with the spike like projection which allows the virus attachment to a compatible host.^{30,31} The viral envelope comprises of structural proteins that are anchored to the surface membrane and the nucleocapsid is encased within the envelope. The nucleocapsid surrounded by the envelope consists of multiple copies of nucleocapsid proteins that are bound to a positive sense single stranded RNA genome which resembles beads on a string confirmation. The virus is protected by the envelope and membrane proteins in the absence of host cell (Figure 2 & 3).^{32,33}

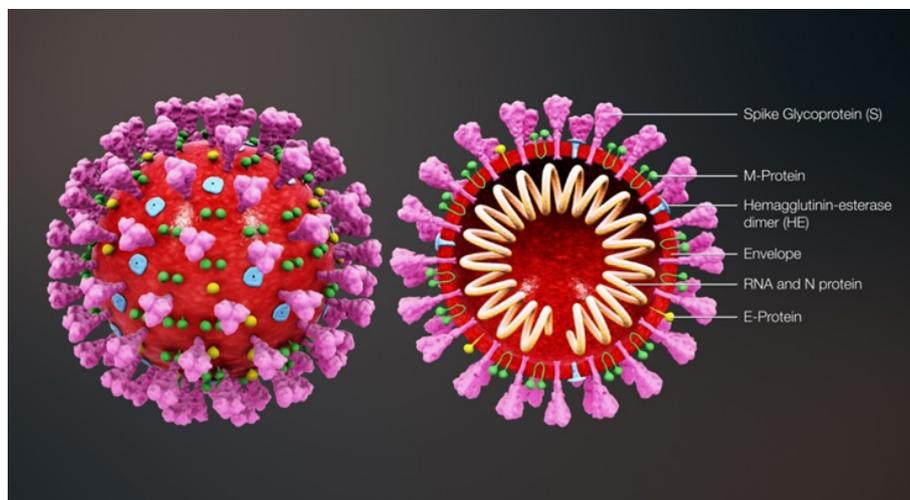


Figure 2 Diagrammatic illustration of Corona virus.³³

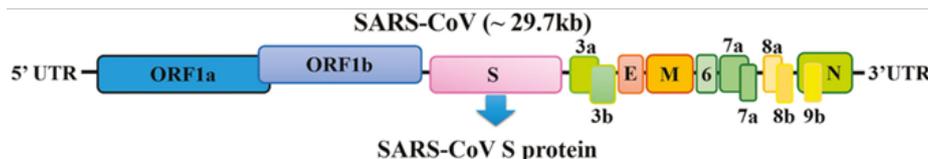


Figure 3 Illustrating the viral transcript.³⁴

The genome of the virus is made of positive sense single stranded RNA and its size ranges from 26 to 32 kilobases and is considered as one of the largest among RNA viruses. The genome is also known to possess a methylated cap at the 5 prime end and poly a tail at the 3 prime end. The genome of the virus consists of untranslated regions at the 5 and 3 prime end which has its prominence in the regulation of the translation process of different structural genes of virus. In addition to reading frames that encode for viral structural proteins like spike, membrane, envelope and nucleocapsid, there are reading frames for accessory proteins and their functions depends on the specific corona virus.^{19,30}

Pathophysiology

The COVID 19 belongs to a sub family of coronavirinae comprising of SS RNA as its genetic material. The viruses of this family are known for causing cold like symptoms which under

severe circumstances can lead to SARS (severe acute respiratory syndrome) and is also known for Middle East syndrome (MES). In 2019, a new strain of the virus originated from China is responsible for the worldwide outbreak of the pandemic. Further studies from the context of structural and genomic facets on COVID 19 have disclosed its genomic relatedness to previously identified corona virus that was responsible for an outbreak in 2003.³⁵ The composition of SARS corona virus is well defined and structural studies have further disclosed the binding of 14 residues with the human angiotnsin converting enzyme 2. This enzyme is attached to the outer surface of cells in lungs, heart, kidneys, intestines, arteries and they play a very vital role in monitoring the blood pressure by regulating the body fluid potential.³⁶ Eight amino acids in COVID 19 were conserved and the thought of it mild impact on humans was ruled out after the global outbreak of SARS CoV. However, the insights of pathophysiology is yet to be fully understood as the research on COVID 19 is still going on

but its genomic resemblance to SARS CoV partially explains the role of COVID 19 in causing respiratory manifestations.³⁷

Symptoms and causes

The infected patient exhibited symptoms ranging from dry cough, fever, sour throat to septic shock, pulmonary edema, multiple organ failure, pneumonia and ARDS (acute respiratory distress syndrome).³⁸ Older adults and patients with prior health complications are highly susceptible to CoV infections. Patients with the history of digestive, respiratory and endocrine diseases need special attention as the possibility of clinical severity is high among them.¹⁸ Signs and symptoms of corona virus disease 19 (COVID-19) appear between 2 to 14 days in an individual after exposure. The time from the entry of the virus till the appearance of clinical signs is called as incubation time. Apart from breathing difficulties, fever and cough, persistence of other signs like sore throat, diarrhea, tiredness and severe vomiting have been related to COVID19.

Certain sources have also disclosed the persistence of severe abdominal pain, dizziness, anorexia and dyspnoea.³⁹ Though the virus is considered to be zoonotic, its wide outbreak in humans has been an issue of serious concern. The outbreak of SARS-CoV from cats to humans in China (2002) and MERS-CoV from Camels to humans in the Middle East (2012) strongly validates the zoonotic nature of the virus. However, the recent reports have substantiated the transmission of the disease from human to human through infected droplets or contact. Studies have disclosed the persistence of the virus for few hours in the air when an infected person sneezes or coughs. Nevertheless, the virus may not be able to stay for longer durations in air because of the heavy nature of the discharged droplets which falls on the ground or any object. If these droplets get deposited on any article the spread of the disease occurs by mere contact with these articles or objects. People with a travel history of COVID 19 affected areas serve as main perpetrators in spreading the disease.⁴⁰ The only remedy to safeguard ourselves from the contagion is by maintaining social distancing and following quarantine measures to ensure the curbing of the pandemic. Personal hygiene is one of the vital facets that can be affiliated to the pandemic and people compromising on their personal hygiene are susceptible to the disease.

Clinical signs and symptoms

Measures to curb COVID-19

The outbreak of nCoV-19 pandemic has been declared as a medical emergency from the context of people health and has been proclaimed as public health emergency of international concern. While a lot is yet to be disclosed, certain facts on the disease have elaborated the measures to evade the contagion. Many vital facts on CoV-19 are not fully understood but steps like social distancing and personal hygiene has been proven to be useful. It is a widely accepted truth that the transmission occurs on coming in contact with the respiratory droplets and any basic measure like use of masks or tissue papers avoids the release of the infected droplets in the air or on to articles which serves as prime means of infection. As a matter of fact discharge of infected droplets through sneezing and coughing can be avoided by using a mask or a tissue paper. Individuals can also get infected by touching the contaminated surfaces. Self inoculation of the contagion is possible by rubbing the nose, ears and mouth after coming in contact with contaminated surfaces and objects. As COVID-19 continues to spread among communities, there is an urge to curb

its occurrence by appropriate measures. The measures employed could range from personal hygiene maintained by an individual to legal steps implemented by the official bodies and organization to introduce quarantine in order to prevent the spread of nCoV-19. In fact, community transmission of the disease can be reduced to a greater extent by maintaining social distancing and strict quarantine strategies. The protection of children and older adults are of prime importance because of their higher susceptibility to COVID-19. Appropriate measures are necessary to prevent the outbreak in the school settings following the lockdown period (Figure 4).

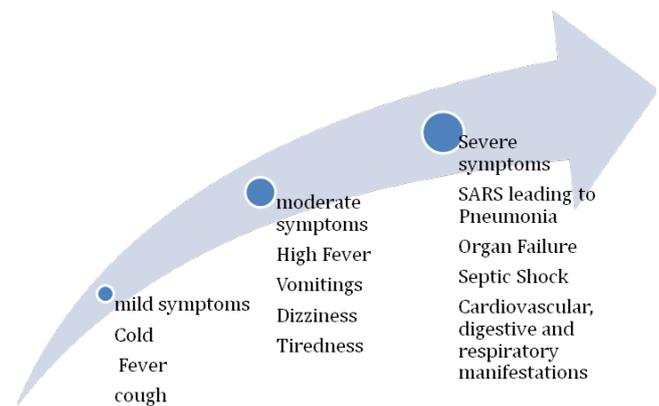


Figure 4 Diagrammatic illustration of COVID-19 symptoms.

Every area with the school premises and other educational organizations should be thoroughly sterilized to ensure safety. However, it is a global fact that COVID-19 does not differentiate among races or ethnicities but young children and older adults should be provided with extra care because of their susceptibility. Several studies have validated the prominence of safety measures to evade the contagion and many organizations have undertaken programs to enlighten the severity of the disease. Apart from government other private firms and industries have come forward with their part of effort to curb the intensity of nCoV-19 through their financial assistance. The COVID-19 disease may be restricted by following quarantine measures like isolation, social distancing and early stage detection.⁴¹ The ministry of health, family and welfare of the Indian government has closely monitored the extent of positive cases in India and has strengthened the health infrastructure to minimize the outbreak of the disease. Many influential leaders including the honorable prime minister have urged the citizens to maintain strict quarantine measures through social distancing and janatha curfew. The effective measures were followed all over the world in an attempt to reduce the outbreak of the disease. The national and state health authorities are constantly monitoring the health infrastructure and the associated measures employed to ensure safety among people. The authorities are also regularly reviewing the public health initiatives including diagnostics and preventive remedies. The national center for disease control (NCDC) has initiated appropriate measures and has started the strategic health operation centers which served as a major platform for answering public queries. Many official organizations and legal bodies are in constant correspondence with the world health organization to resolve the health emergency crisis. Several official bodies like ministry of health, family and welfare, national center for disease control, Indian council of medical research and ministry of information are in talks with the world health organization through the WHO joint monitoring group. Since January 2020, WHO joint monitoring group has been providing technical assistance, guidance

and useful resources to official bodies like ministry of health, family and welfare, national center for disease control, Indian council of medical research and ministry of information.

Indian council of medical research has taken every effort to provide the insights on the pandemic and has taken the initiative of introducing the best possible techniques to perform nCoV-19 screening.

The government of India over the last three months has implemented the following steps to evade the outbreak of the contagion⁴²⁻⁴⁵

- a. Enhancement of public health facilities and infrastructure
- b. Regular follow-ups in case of positive cases
- c. Setting up of nationwide diagnostic centers and hospitals specialized in COVID-19 treatment
- d. Scrutinizing every entry and exit points thoroughly to segregate the positive cases
- e. Setting up of health awareness camps
- f. Strategic health operation centers initiated by national center for disease control
- g. Stringent surveillance of the check-in points at airports
- h. Fortification of the travel advisory guidelines
- i. Setting up of additional research lab apart from medical camps to speed up the screening process (Figure 5 & 6)
- j. Help line centers and control rooms for assisting people by creating awareness
- k. As on 6th February 2020, 11 more labs were set up to cope up with the crisis situation
- l. Updated travel guidelines were put in to practice and visas for foreign nations travelling from China were suspended
- m. Passengers were screened at the airport and doubtful cases were quarantined for diagnosis
- n. Over 1100 flights covering 121000 passengers were screened as on the first week of February 2020 at the airports
- o. Risk communications were strengthened to sort out miscommunication and false propaganda

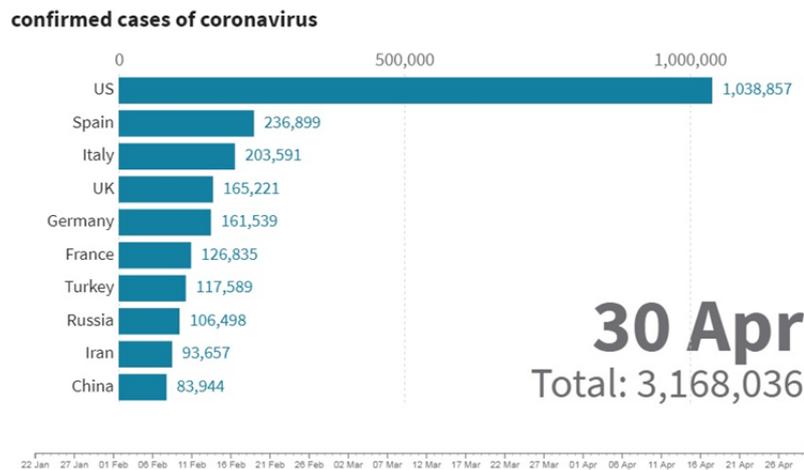


Figure 5 Horizontal bars graphically depicting the number of COVID-19 positive cases as of 30th April 2020.⁴⁹



Figure 6 Diagrammatic illustration of the extent of COVID-19 severity in humans.

Diagnosis and potential treatment

It is a widely known fact that the initial symptoms include fever, dry cough, breathing discomfort, vomiting, diarrhea and myalgia and patients with the history of medical illness are highly susceptible and are liable to kidney failures and ARDS (Acute respiratory distress

syndrome). In an attempt to cope up with the crisis the ministry of health, family and welfare along with world health organization has issued major clinical guidelines and epidemiological insights related to COVID-19.^{46,47} Individuals suspected of positive signs to nCoV-19 are screened through stringent laboratory tests and procedures and are kept in quarantine for 14 days which is considered as the incubation

period of the virus. Clinical tests on suspected patients are performed multiple times to ensure the presence of the disease because the virus has reached a stage where it can be non symptomatic. The non symptomatic nature of the disease has indeed posed a greater level challenge because it would be difficult to confirm the presence of the virus in the patient at this stage. However, molecular analysis and techniques are of great importance from the context of diagnosis and identification of the clinical condition. COVID-19 infection can be confirmed through genome sequencing and phylogenetic analysis of bronchoalveolar lavage or the fluid from the lower respiratory tract.⁴⁸ As of now there is no specific vaccine or treatment for COVID-19. Effective antiviral treatment is yet to be discovered but attempts are being made to come out with an effective vaccine. Plasma is being collected from those who have recovered from the illness and research activities for productive outcomes are on its way. Certain reports have claimed the significance of interferon α and lopinavir/ritonavir among SARS patients.

Reports suggest the efficiency of these drugs in lowering the mortality rate among SARS infected patients.⁵⁰ Several other drugs like tenofovir, disoproxil, lamivudine are recommended as they serve as DNA synthesis inhibitors. Chloroquin was helpful to some extent⁵¹ but according to WHO there is no specific vaccine or medicine for COVID-19. Several clinical trials are being conducted in order to derive a suitable way to counteract the contagion. Attempts are being made by using RT PCT kits to comprehend the virus and ICMR in collaboration with Bharat Biotech (which is a pharmaceutical firm) has started the clinical trial on volunteers using plasma so sort out the antibodies against the disease.

FDA employed measures⁵²

The food and drug administration have taken appropriate measures to cope up with the ongoing health emergency and created special emergency programs for possible therapies which has been named as the Corona virus Treatment Acceleration Program (CTAP). The program employs every possible method to treat the patients in an efficient manner with a check on the efficacy of the employed method to counteract the disease. The clinical trials are currently going on in order to gain knowledge about COVID-19.

The measures employed to counteract COVID-19 through CTAP are as follows

- a. Evaluation of new drugs and biological therapies
- b. Employment of scientists and other staff officials to speed up the process
- c. Prioritization of interactions based on scientific merits of the product for development plans
- d. Provision of rapid protocols within 24 hours of submission in some cases
- e. Working with applicants and other regulatory agencies to accelerate the quality assessment of products used in COVID-19 treatment
- f. Ensure the product supply to new sites without any disruption

Clinical trials⁵³

Clinical trials are being influenced by COVID-19 pandemic due to challenges arising from self isolation, site closures, travel restrictions and discrepancies in the supply of vital products. These challenges

may lead to intricacies from the context of protocols, procedures and administrative aspects. FDA is vigorously enduring its hard work to provide the transparency needed to help ensure the wellbeing of clinical trial participants, maintain acquiescence with good clinical practice (GCP), and minimize risks to trial integrity during the COVID-19 pandemic. The FDA is organizing the propagation of information and suggestions from CDER (Center for drug evaluation and research) /FDA to domestic and international stakeholders regarding the conduct of clinical trials during the COVID-19 pandemic. The prime intention is to ensure appropriate input and consistency of information within CDER and across centers. COVID-19-related inquiries from stakeholders in accordance to regulatory measures and human health safety were addressed appropriately. FDA is also maintaining a tracking system for inquiries and responses connected to the conduct of clinical trials affected by COVID-19.

How to protect ourselves and people around us?⁵⁴

1. Have Know the spread of the disease

- a. The virus is thought to spread mainly from person to person (people who are in close contact)
- b. Spreads through respiratory droplets when an infected person coughs, sneezes
- c. Objects with contaminated droplets also serve as a mode of spreading the disease
- d. Recent studies have revealed the presence of non symptomatic COVID-19 that spreads among people

2. Washing hands can be beneficial

- a. Washing hands frequently with soap for about 20 seconds have proven to be a good practice
- b. Alcohol hand sanitizer with 60% alcohol can be used if water and soap is not available
- c. Touching of nose, mouth and eyes should be avoided

3. Avoid close contact (maintain social distancing)

- a. Avoid close contact with those who have tested positive for COVID-19
- b. Maintain social distancing and follow self quarantine measures
- c. People without symptoms may harbor the virus, so we have to maintain self isolation to help prevent the spreading of the disease
- d. Maintain distance from those who are highly susceptible to the contagion like older adults and special care should be taken for those who are highly vulnerable to the disease

4. Covering of mouth and nose with a cloth cover or mask

- a. Everyone should cover their mouth and nose with a mask or a cloth when they are in public
- b. Cloth covering or mask is not recommended for children below 2 yrs as it might result in breathing discomfort and special care should be taken to safe guard young children
- c. Minimum distance of 6 feet should be maintained among people as the use of face mask is not a substitute for social distancing

5. Cover your mouth while cough and sneeze

- a. We are supposed to cover our mouth with our elbow in the absence of a cloth or a face mask
- b. The used masks and tissues should be safely discarded
- c. Washing of hands after coughing or sneezing with soap or alcohol sanitizer

6. Personal hygiene

- a. Clean and disinfect surfaces, objects, articles on a daily basis
- b. Cleaning of door knobs, laptop, key board, phone, sink etc
- c. Use of disinfectant consisting of sodium hypochlorite

Discussion

Microorganisms and humans have coexisted since the dawn of the time. Over the eons, microorganism and humans have indeed been an integral aspect of the nature. Humans have been employing microorganisms for research which has in turn provided answers to many human queries from the context of health and well being. Microorganisms are not of research prominence but are an integral part of human system which comprises of fulltime and part time pathogens. However the human system has always been able to maintain the ecological niche to ensure well being and our immune system plays a vital role in protecting us from foreign invaders. But over the last few months the entire human race has come under the scanner because of a novel contagion that was not known to mankind in the past. Though the novel disease causing agent is often compared to some of its members that are known to cause similar kind of clinical manifestation, it is regarded as novel because of its ability to rapidly spread among people which differentiates it from its earlier contenders. The virus that is commonly called a COVID-19 is a pleomorphic, mutating virus and is known for contact spreading. Though the disease started as an epidemic in the Wuhan province of China, it soon spread all over the world resulting in a pandemic condition. Young children and older adults are highly susceptible to the disease which targets the respiratory system. The initial symptoms of the disease causes cold like signs associated with fever and cough which in later stages transforms in severe acute respiratory syndrome causing severe respiratory manifestation and under further stages can lead to death because of multiple organ failure.

Several reports have claimed the significance of ivermectin in inhibiting the replication of SARS-CoV *in vitro*. The treatment is capable of producing an impact of 5000 fold reduction in viral development within 48hrs under lab conditions in cell cultures. This drug has been approved by FDA for parasitic infections and is therefore regarded as a prime solution for COVID infection. World health organization (WHO) also has included ivermectin on the list of essential medicines and regards ivermectin as a possible option against COVID infection.⁵⁵ Ivermectin has been very commonly used as an option for parasitic infections but recent developments have substantiated the significance of the drug in an affirmative manner against viruses. Several studies have validated the prominence of the drug against viruses in lab conditions (*in vitro* conditions).^{56,57} The drug was originally identified as an inhibitor of HIV-1 (human immunodeficiency virus-1) integrase protein and importin responsible for nuclear import.⁵⁸ Ivermectin has since been validated to inhibit viral proteins capable of nuclear import and HIV-1 replication. Though other actions of ivermectin have been demonstrated, it is known for the inhibition of viral nuclear import in the host.⁵⁹ Studies

have also substantiated the role of ivermectin in inhibiting viral proteins like the large tumor antigen protein of simian virus SV40 and the non structural protein of dengue virus (DENV).⁶⁰ In the recent past, researchers have validated the role of ivermectin in limiting the infections caused by RNA viruses which have been demonstrated in case of dengue virus and influenza virus and is known to possess broad spectrum activity.⁶¹ It is a widely known fact that the current pandemic caused by nCoV-19 is an RNA containing virus (positive sense RNA) which causes respiratory affiliated manifestations leading to viral pneumonia in critical stages. The virus comprises of single stranded RNA as its genome and causes severe acute respiratory syndrome. Studies on SARS corona virus have revealed certain proteins that play a vital role in the sustenance and development of the virus.

Studies on SARS-CoV proteins have revealed a potential role for IMP α / β 1 during infection in signal-dependent nucleocytoplasmic shuttling of the SARS-CoV Nucleocapsid protein.^{62,63} Further insights on SARS CoV proteins have disclosed the significance of SARS-CoV accessory protein ORF6 in antagonizing the antiviral activity of the STAT1 transcription factor by sequestering IMP α / β 1 on the rough ER/ Golgi membrane.⁶⁴ Based on the above insights, the reports suggested that ivermectin's nuclear transport inhibitory activity may be effective against SARS-CoV-2.

Conclusion

Microorganisms and humans are inseparable because major biological processes in our system cannot be coordinated without the assistance of these invisible creatures but the darker side of their bad reputation from the context of human well being cannot be ignored. As a matter of fact the coexistence of humans with microorganisms has had a very long history over the course of time. The prominence of microorganisms in research for human betterment cannot be denied as they have led to productive outcomes of scientific significance. Hence it could be rightly said that microorganism and humans are essential aspect of the nature. Use of microorganisms in research has provided answers to many human queries from the perspective of health and well being. Several organizations have attempted to curb the incidence of the disease by creating awareness. Legal bodies and authorized firms have undertaken appropriate measures to safeguard the people. Extensive screening at various entry and exit points were carried out for the isolation of patients with positive COVID-19 symptoms and the isolated patients were sent to quarantine centers installed at different places. There is a lot of speculation about how the virus actually spreads and some sources claim the viability of virus in the air which cannot be denied because they spread through infected droplets released from patients through coughing, sneezing, talking etc. Recent studies also validate the spread of the disease by person to person contact.

Several studies have demonstrated scientific measures to disclose a suitable drug for the contagion and FDA in collaboration with the world health organization have taken essential scientific measure through *in vitro* procedures. The use of ivermectin has been approved by the FDA and further tests are going on for further insights and the mechanism of counteracting the virus. Several studies have disclosed the ability of the drug to inhibit the virus by interfering with the viral replication process. However, further validation through clinical trials and lab procedures are needed for comprehending the mechanism of drug action and the response in humans to the drug. In addition, steps like social distancing and self quarantine measures also have had an impact on the extent of COVID-19 spread. Plasma treatment have been suggested by authorized organization as an attempt to curb the

incidence of disease but further experiments have to be performed to validate the usefulness of the treatment. There is no effective vaccine or medicine for the contagion but some studies reveal the usefulness of chloroquin and sodium hypochlorite (as a disinfectant for cleaning the objects and floor). However, according to WHO, vaccine is yet to be discovered and quarantine measures like self isolation and social

distancing are currently followed to reduce the community infection. It could be rightly said that staying at homes is not only for our safety but is to safeguard others from getting the infection. This article only attempt to provide a drop of information about the contagion and attempts to furnish details at the primary level as further research is necessary to comprehend COVID-19.

The following are some questions related to COVID-19 which are yet to be answered



Acknowledgments

None.

Conflicts of interest

Authors declare that there is no conflict of interest.

References

1. Prem C, Pragati P, Upendra R, et al. *Epidemic and Challenges of Coronavirus Disease-2019 (COVID-19): India Response*; 2020.
2. Estola T. Coronaviruses, a New Group of Animal RNA Viruses. *Avian Diseases*. 1970;14(2):330–336.
3. Decaro N. Gammacoronavirus. In Tidona C, Darai G (eds.). *Gammacoronavirus: Coronaviridae*. The Springer Index of Viruses. Springer; 2011. 403–413 p.
4. McIntosh K. Corona viruses: A Comparative Review. In Arber W, Haas R, Henle W, et al (eds.). *Current Topics in Microbiology and Immunology*. Berlin, Heidelberg: Springer; 1974. 87 p.
5. Once upon a time there were coronaviruses. *Réalités Biomédicales*; 2020.
6. Kahn JS, McIntosh K. History and recent advances in coronavirus discovery. *Pediatr Infect Dis J*. 2005;24(11 Suppl):S223–S227.
7. Mahase E. Covid-19: Coronavirus was first described in The BMJ in 1965. *BMJ*. 2020;369:m1547.
8. Kendall EJ, Bynoe ML, Tyrrell DA. Virus isolations from common colds occurring in a residential school. *British Medical Journal*. 1962;2(5297):82–86.
9. Richmond C. David Tyrrell. *BMJ: British Medical Journal*. 2005;330(7505):1451.
10. Tyrrell DA, Bynoe ML. Cultivation of a Novel Type of Common-Cold Virus in Organ Cultures. *British Medical Journal*. 1965;1(5448):1467–1470.
11. Tyrrell DA, Fielder M. *Cold Wars: The Fight against the Common Cold*. Oxford University Press; 2002. 93–95 p.
12. Hagan WA, Bruner DW, Gillespie JH, et al. *Hagan and Bruner's Microbiology and Infectious Diseases of Domestic Animals: With Reference to Etiology, Epizootiology, Pathogenesis, Immunity, Diagnosis, and Antimicrobial Susceptibility*. Cornell University Press; 1988. 440 p.
13. Knapp A. *The Secret History of the First Coronavirus*. Forbes; 2020.
14. Lupia T, Scabini S, Pinna SM, et al. 2019-novel coronavirus outbreak: A new challenge. *J Glob Antimicrob Resist*. 2020;21:22–27.
15. Sohrabi C, Alsafi Z, O'Neill N, et al. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). *Int J Surg*. 2020 Apr;76:71–76.
16. <https://www.thestar.com.my/news/regional/2020/04/26/almost-29-million-confirmed-covid-19-cases-worldwide-on-april-26-midday>

17. <https://www.deccanherald.com/international/world-trending/coronavirus-world-o-meter-update-live-country-wise-total-number-of-cases-deaths-april-26-827195.html>
18. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069.
19. Woo PC, Huang Y, Lau SK, et al. Coronavirus genomics and bioinformatics analysis. *Viruses*. 2010;2(8):1804–1820.
20. Almeida JD, Berry DM, Cunningham CH, et al. Virology: Coronaviruses. *Nature*. 1968;220(5168):650.
21. Estola T. Coronaviruses, a New Group of Animal RNA Viruses. *Avian Diseases*. 1970;14(2):330–336.
22. Decaro N. Gammacoronavirus. In Tidona C, Darai G (eds.). *Gammacoronavirus: Coronaviridae*. The Springer Index of Viruses. Springer; 2011. 403–413 p.
23. McIntosh K. Corona viruses: A Comparative Review. In Arber W, Haas R, Henle W, et al (eds.). *Current Topics in Microbiology and Immunology*. Berlin, Heidelberg: Springer; 1974. 87 p.
24. Once upon a time there were coronaviruses. *Réalités Biomédicales*; 2020.
25. Tyrrell DA, Bynoe ML. Cultivation of a Novel Type of Common-Cold Virus in Organ Cultures. *British Medical Journal*. 1965;1(5448):1467–1470.
26. Hagan WA, Bruner DW, Gillespie JH, et al. *Hagan and Bruner's Microbiology and Infectious Diseases of Domestic Animals: With Reference to Etiology, Epizootiology, Pathogenesis, Immunity, Diagnosis, and Antimicrobial Susceptibility*. Cornell University Press; 1988. 440 p.
27. Hamre D, Procknow JJ. A new virus isolated from the human respiratory tract. *Proceedings of the Society for Experimental Biology and Medicine*. 1966;121(1):190–193.
28. de Groot RJ, Baker SC, Baric R, et al. Family Coronaviridae. In King AM, Lefkowitz E, Adams MJ, et al. *Virology Division* (eds.). Ninth Report of the International Committee on Taxonomy of Viruses. Oxford: Elsevier; 2011. 806–828 p.
29. Neuman BW, Adair BD, Yoshioka C, et al. Supramolecular architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy. *Journal of Virology*. 2006;80(16):7918–7928.
30. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. *Methods Mol Biol*. 2015;1282:1–23.
31. Chang CK, Hou MH, Chang CF, et al. The SARS coronavirus nucleocapsid protein-forms and functions. *Antiviral Research*. 2014;103:39–50.
32. Neuman BW, Kiss G, Kunding AH, et al. A structural analysis of M protein in coronavirus assembly and morphology. *Journal of Structural Biology*. 2011;174 (1):11–22.
33. https://upload.wikimedia.org/wikipedia/commons/9/96/3D_medical_animation_coronavirus_structure.jpg
34. https://upload.wikimedia.org/wikipedia/commons/1/11/SARS-CoV_MERS-CoV_genome_organization_and_S-protein_domains.png
35. Lu R, Zhao X, Li J, et al. Genomic characterization and epidemiology of 2019 novel corona virus: implications for virus origins and receptor binding. *The Lancet*. 2020;395(10224):565–574.
36. Hamming I, Timens W, Bulthuis ML, et al. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *The Journal of Pathology*. 2004;203(2):631–637.
37. Fehr AR, Perlman S. *Coronaviruses: an overview of their replication and pathogenesis*. Humana Press: New York, NY; 2015. 23 p.
38. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *The Lancet*. 2020;395(10223):507–513.
39. Coronavirus disease 2019 (COVID-19); Mayo clinic; 2020.
40. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. *Journal of Medical Virology*. 2020;92(4):441–447.
41. World Health Organisation (WHO). Novel coronavirus (2019-nCoV). Situation report-12; 2020.
42. World Health Organisation (WHO). Novel coronavirus (2019-nCoV). Situation report India-3; 2020.
43. World Health Organisation (WHO). Novel coronavirus (2019-nCoV). Situation report India-4; 2020.
44. World Health Organisation (WHO). Novel coronavirus (2019-nCoV). Situation report India- 5; 2020.
45. World Health Organisation (WHO). Novel coronavirus (2019-nCoV). Situation report India-6; 2020.
46. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020;395(10223):497–506.
47. Elsevier, Novel Coronavirus Information Centre; 2020.
48. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*. 2020 Feb 20;382(8):727–733.
49. Gallagher J. *Coronavirus symptoms: What are they and how do I protect myself?*. BBC News; 2020.
50. Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*. 2004;59(3):252–256.
51. Liu W, Morse JS, Lalonde T, et al. Learning from the past: possible urgent prevention and treatment options for severe acute respiratory infections caused by 2019-nCoV. *Chembiochem*. 2020;21(5):730–738.
52. <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/coronavirus-treatment-acceleration-program-ctap>
53. <https://www.fda.gov/drugs/coronavirus-covid-19-drugs/clinical-trial-conduct-during-covid-19-pandemic>
54. <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>
55. Calya L, Druce JD, Catton MG, et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro. *Antiviral Res*. 2020;178:104787.
56. González Canga A, Sahagún Prieto AM, Díez Liébana MJ, et al. The pharmacokinetics and interactions of ivermectin in humans—a mini-review *AAPS J*. 2008;10(1):42–46.
57. Götz V, Magar L, Dornfeld D, et al. Influenza A viruses escape from MxA restriction at the expense of efficient nuclear vRNP import. *Sci Rep*. 2016;6:23138.
58. Wagstaff KM, Rawlinson SM, Hearps AC, et al. An AlphaScreen(R)-based assay for high-throughput screening for specific inhibitors of nuclear import. *J Biomol Screen*. 2011;16(2):192–200.

59. van der Watt PJ, Chi A, Stelma T, et al. Targeting the nuclear import receptor Kpnbeta1 as an anticancer therapeutic. *Mol Cancer Ther.* 2016;15(4):560–573.
60. Wagstaff KM, Sivakumaran H, Heaton SM, et al. Ivermectin is a specific inhibitor of importin alpha/beta-mediated nuclear import able to inhibit replication of HIV-1 and dengue virus. *Biochem J.* 2012;443(3):851–856.
61. Jans DA, Martin AJ, Wagstaff KM. Inhibitors of nuclear transport. *Curr Opin Cell Biol.* 2019;58:50–60.
62. Rowland RR, Chauhan V, Fang Y, et al. Intracellular localization of the severe acute respiratory syndrome coronavirus nucleocapsid protein: absence of nucleolar accumulation during infection and after expression as a recombinant protein in vero cells. *J Virol.* 2005;79(17):11507–11512.
63. Wulan WN, Heydet D, Walker EJ, et al. Nucleocytoplasmic transport of nucleocapsid proteins of enveloped RNA viruses. *Front Microbiol.* 2015;6:553.
64. Frieman M, Yount B, Heise M, et al. Severe acute respiratory syndrome coronavirus ORF6 antagonizes STAT1 function by sequestering nuclear import factors on the rough endoplasmic reticulum/Golgi membrane. *J Virol.* 2007;81(18):9812–9824.