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An Update On Novel Coronavirus: Conquering World

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ABSTRACT

It was in late 2019 when the world got alarming news of the fatal virus that took birth in the seafood market of China (Wuhan) and a few months later pandemic was announced by WHO. This virus was named novel coronavirus (SARS-CoV 2) which has its clinical features similar to "pneumonia" including human to human contact. According to its genomic structure, it belongs to betacoronavirus having a crown-like presence and is a positive-sense RNA virus. Meanwhile, as per the reports, the treatment options contain the use of some antiviral drugs like Lopinavir, Ritonavir, Remdesivir, including Ayurvedic System of Medicine. In this pandemic situation, the pharmacists play a vital role in providing medical services to the patients. All over the world, many pharmaceutical firms have collaborated to develop the vaccine to combat COVID-19 as soon as possible and will soon make the world corona free. This coordination globally, has helped and fasten the development of vaccine with several vaccine candidates initiating human trials. The mental health of people has been affected to a great extent. This review explains the structure, manifestations and how Covid-19 led to the global emergency. The fatal effect of virus on three countries- Italy, USA and India are also described.

Keywords: Coronavirus, Pandemic, Remdesivir, Wuhan city, Pneumonia

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INTRODUCTION

Covid-19 or Novel Coronavirus is a viral disease that is extremely deadly and infectious. Humans have been exposed to many viruses and the year 2019 ended with one new virus called as Novel Coronavirus. The severe acute respiratory syndrome (SARS) which emerged in 2002-2003 has a strain named SARS-CoV. The year 2019 came up with a new strain of SARS which is SARS-CoV 2 which emerged into Covid-19. The most recent virus which is Middle East respiratory syndrome coronavirus (MERS-CoV) was initially recognized in Saudi Arabia in 2012 The present situation relates to such viruses that have become one of the biggest pandemic started from a seafood market in Wuhan district of China during December 2019 and from then a big number of patients in china started coming to the hospital with some similar kind of respiratory infections¹.

It was on December 31st, 2019 when china informed WHO about this epidemic, and then the orders were sent to close down the seafood market in Wuhan. Various samples were collected from the seafood market and got tested in the labs which came out to be positive, this implies that the virus took birth in the market itself. Within a few days only, there were a huge number of cases and some of them didn't come from the animal market which also indicates the presence of human to human contact. Eventually, the virus started building its mark in whole china, and other countries like the USA, London, Thailand, and Italy also came to its reach. The Chinese government had to make certain strict decisions to stop human to human contact, and they announced the lockdown in the country².

This virus produces its symptoms within 14 days as per the study, because of which many countries started isolating people who were suspected to be infected by corona. Initially, many infected countries opened up quarantine centers, started various online awareness programs to teach people about self-isolation, social distancing.

STRUCTURE OF SARS- COV-2

Coronaviruses belong to coronaviridae family, the subfamily of which is divided into four genera based on genomic structure and phylogenetic analysis- alphacoronaviruses, betacoronaviruses, gammacoronaviruses, and deltacoronaviruses³. The seventh member of Coronaviruses family infecting humans, SARS-CoV-2 is a single-stranded, positive-sense RNA virus with a genome length of 26 to 32 kilobases(kb). It is an oval or round-shaped virus with 60-140nm of diameter with an appearance of a crown(4). SARS-CoV-2 binds to the angiotensin-converting enzyme 2 (ACE2) receptor in the human lung and has 89% nucleotide similarity to SARS-like coronaviruses ^{3,5}.

Coronaviruses genome comprises at least 6 open reading frames (ORFs). ORF1a/b is the first open reading frame which is about two-thirds of the whole viral genome, encodes for 16 non-structural proteins (NSPs), and translates two polyproteins-pp1a and pp1ab. The remaining ORFs in the genome encode four structural proteins, including spike (S) glycoprotein, nucleocapsid (N) protein, envelope (E) protein, membrane (M)protein, and several accessory proteins interfering with the immune response of the host ^{6,7}.

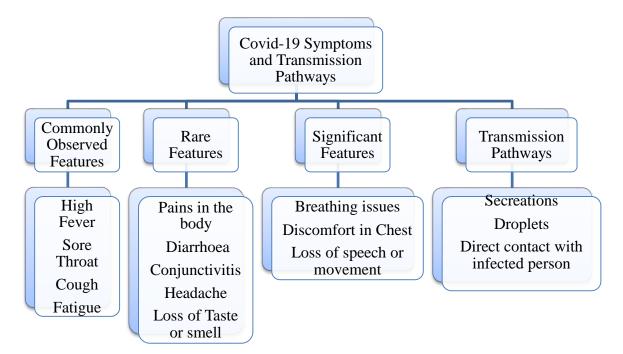
The S protein monomer has 1273 amino acids and is a homotrimer with two subunits – S1 subunit defined with N- terminal domain (NTD) and C-terminal domain (CTD) and S2 subunit have fusion peptides that mediate fusion between virus and host cell membrane. The CTD has a receptor-binding domain (RBD)^{8,9}.

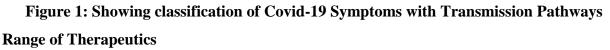
Manifestations

The initial stages of COVID-19 showed clinical features similar to pneumonia. More and more patients were studied and the clinical manifestations were respiratory-related.

The most commonly observed symptoms are high fever, cough, sore throat, fatigue. Some rare lists of symptoms are pains in the body, diarrhoea, conjunctivitis, and headache, loss of taste, or smell. The significant or the major list includes breathing issues, discomfort in the chest, and loss of speech and movement. The way of transmission is through any kind of secretions, droplets, close and direct contact with an infected person (Figure 1). As per the recent examination, it takes around 1-14 days to develop symptoms of COVID 19 in an individual. The most suspected individuals are elderly with some or other chronic diseases like diabetes, hypertension. These individuals were easily catching the viral infection as per the reports and also leading to deaths. Apart from elderly patients, neonates were also kept under special attention because of the low immune system.

Some of the clinical characteristics seen in hospitalized patients were reduced or normal amount of white blood cells and in serious cases, there was an increase in neutrophil count, creatinine, and blood urea levels⁷.





All over the world, scientists are trying hard to find possible medicines that can help in combating this deadly viral infection. Although the research to find vaccines is still in its process but the world can still find positive hopes with the use of certain drugs.

With the help of recent investigation, researchers were able to find around 30 possible agents including natural, western, and traditional Chinese medicines which were tested in the laboratory and provided preliminary success against COVID 19. National Health Commission issued its latest guidelines regarding the use of antiviral drugs which has potential in treating viral infection. The drugs are IFN- α , lopinavir, ritonavir, and ribavirin. Another antiviral drug that has gained a lot of attention is Favipiravir. This drug is going through clinical trials and the results of its efficacy are still to be judged¹⁰.

Remdesivir, which is the most commonly used anti-viral drug and also shown its capability in controlling Ebola virus infection. It is now been tested to provide its efficacy to treat the most deadly coronavirus. Its anti-viral nature can fight against various RNA virus and consequently, it exhibits promising initial in-vitro testing results in the control of coronavirus. Amongst various anti-viral drugs, remdesevir, lopinavir, and ritonavir are considered to be the most probable drugs for the management of severe cases of COVID-19¹¹.

The antimalarial drug chloroquine along with its derivative hydroxychloroquine has emerged as a potential agent to treat COVID-19. Because of their anti-viral and anti-inflammatory properties, they are being considered to kill this virus. During the in vitro studies, their antiviral capacity and

also potential to prevent the growth of various viruses including the coronavirus was also identified in the cell culture line¹².

Also, an Interleukin (IL)-6 receptor antagonist Tocilizumab which is used for the treatment of rheumatoid arthritis was used to treat serious 21 COVID-19 patients in China. It was found out that almost 19 patients were given a discharge from the hospital with the use of Tocilizumab. With this, Tocilizumab got approval from the US Food and Drug Administration for the phase III clinical trial in hospitalized patients suffering from the serious COVID-19 infection. Simultaneously, like Tocilizumab one more IL-6 receptor antagonist Sarilumab is also undergoing clinical trials to measure its success in serious cases¹³.

With the use of these drugs, researchers also suggested Convalescent plasma therapy for fighting against COVID-19. WHO had recommended in 2014 to preserve the convalescent plasma of the patients recovered from the Ebola Virus for future use during emergencies. With this perspective, it was suggested to use the convalescent plasma of the recovered patients from the virus to treat the infected ones¹⁴.

Recent Updates as per WHO

Recent news regarding Covid-19 was updated by WHO. The most demanded and used drug Hydroxychloroquine clinical trials have been stopped to check its efficacy against Covid-19. All the researchers and primary investigators have agreed upon this decision. All the facts and figures obtained from the relevant sources do not provide efficient data to combat Covid-19. Also, there will be no further randomization of patients on Hydroxychloroquine in Solidarity trial.

The drug Dexamethasone, belonging to corticosteroid category was under clinical trials in UK. Initial trial results showed some positive details that can make this drug a lifesaving candidate for Covid-19. The mortality rate got reduced by one-third for patients on ventilator and one-fifth for patients requiring only oxygen.

Vaccine Status

The surge in COVID – 19 cases globally has made vaccine development against SARS – CoV - 2 crucial and the development process is to be accelerated. Several pharmaceutical companies and various research universities are evaluating a range of platforms including viral vector vaccine (replicating and non - replicating), virus-like particle, nucleic acid vaccines, recombinant protein to see for the scope of an effective vaccine against COVID – 19. The development of vaccines against SARS – CoV - 2 poses various challenges, the first being designing antigen ensuring optimal immune response¹⁵. The fragments of S – protein that can be used as antigens include full-length S – protein, RBD domain, S1 subunit, and N – terminal domain⁸. The earlier experience

with vaccines developed for SARS and MERS has also posed a challenge by raising concerns regarding elevating lung disease directly or due to antibody-dependent enhancement¹⁵. Coalition for Epidemic Preparedness Innovations (CEPI) is engaged with global health authorities to support vaccine development against SARS – $CoV - 2^{16}$.

As per the landscape of vaccine candidates provided by the World Health Organization (WHO) on September 9, 2020, there are 145 vaccine candidates in the preclinical evaluation and 35 in clinical evaluation. Two Indian vaccine candidates COVAXIN from Bharat Biotech in collaboration with Indian Council of Medical Research (ICMR) – National Institute of Virology (NIV) and ZyCoV-D from Zydus Cadila are among the many which are in clinical trials.

The novel approach for the development of vaccines i.e. nucleic acid vaccines provides flexibility for antigenic manipulation. These types of vaccines are developed based on viral sequence Several companies are working to develop nucleic acid-based vaccines including Inovio pharmaceuticals (based on DNA) and Moderna, BioNTech, and Pfizer (working collaboratively), CureVac (based on mRNA).

The recombinant protein technology is also used for developing vaccines against SARS – CoV - 2. These are recombinant subunit vaccines that elicit response against S protein which prevents its binding with host ACE2 receptor. These vaccines take a longer time to develop than nucleic acid vaccines and require potent adjuvant but are commercially robust. The University of Queensland is working on this type of vaccine and is funded by CEPI. Novavax is also aiming to develop a potential subunit vaccine wherein it has developed immunogenic virus-like nanoparticles^{8,17}.

Viral vector uniquely integrates their genetic material with the host genome and hence efficiently mediate gene transfer. Viral vector vaccines use viral vectors like adenovirus and encode gene of interest into a suitable vector. The University of Oxford and AstraZeneca is developing non – replicating viral vector vaccine which has entered clinical trials¹⁷.

The Pharmacist at the Frontline

Pharmacists are one of the healthcare workers who are constantly working for building and growing our medical world. Even coronavirus was not able to stop them from providing services to the people.

From providing masks, hand sanitizers, medicines, emergency aid, they are dedicated to provide essential services to as many people as possible. They are putting their efforts into making people aware to improve public health through various immunization programs, online health improvement programs, classes on medication, hygiene training, testing, and screenings. Apart from this, various pharmacists in pharmaceutical firms are working hard to design the vaccine to fight against this virus¹⁸.

In many countries, the pharmacist has united to contribute their attempt in prevention, preparedness, response, and recovery of Covid-19. They have started home deliveries of the medicines by associating with Red Cross society and some workers to provide people assistance. Online prescriptions are being sent through emails, and other social media means so that human to human contact is avoided as much as possible and medical consultation continues¹⁹.

The clinical Pharmacists prepared an information formulary containing the list of essential drugs that healthcare workers can use for the treatment of COVID-19. This formulary also contained information about the use, amount of dose, side effects, preventive measures, special instructions for elderly patients, pregnant women, and children. The role of pharmacist never ends; due to this pandemic telemedicine counseling was launched to provide people with online consultations. There are many quarantine people with mild to chronic illness and requires medical treatment. In these cases, telemedicine comes in play and provides professional online consultation to the people²⁰.

Pharmacist and other Healthcare workers of our society risk their life in saving the life of people. They have come out to be as a hero serving their country people without any selfishness. Their dedication and generous efforts to stop the transmission of the Covid-19 can only be possible when the whole world starts supporting them, following their pathways and guidelines, and bringing a change in their own space. They are most easily available healthcare providers, as they are always present in their Pharmacy shops. People can seek advice from them regarding their medication, or any kind of medical assistance in absence of doctors. During this Covid-19 crisis, many pharmacists have got themselves trained out of their qualification to help the doctors in emergencies. People all around the world, should spread awareness through online means about the preventive measures of Covid-19 and how to deal with it. This can reduce the work load of many Healthcare workers around the globe and they can also sit back and relax for some time.

COVID-19 ON THREE MAJOR COUNTRIES

Italy

After China, the country which suffered the most was Italy. Although with such good medical care and facilities, Italy was not able to cope up with the tsunami of coronavirus patients. This started when the government of Italy announced Red Zone on February 22nd in some of the regions of Lombardy district after the detection of the first case in the country. This red zone was then

extended to the whole Lombardy district on March 8th. Consequently, the government announced the Lockdown in the country on March 21st to combat with the coronavirus²¹.

The epidemic has contributed to the recession, mental stress amongst people because of the effect on the economy. Also, in Hospitals, the stress was at its peak because of medical care facilities falling short. The beds in hospitals were almost occupied and the number of patients was increasing. The number of healthcare workers was getting short so the government decided to add more of the Doctors, nurses, and other medical staff to cope up with the outbreak. The medical authority decided to call all the retired doctors and students who are under training and have completed their medical degree to overcome the shortages²².

Also, a huge shortage of personal protective equipment occurred for the healthcare workers, which led to the exposure of the nurses, doctors to the virus. Some of the major preventive actions were implemented like no unnecessary visitor in hospitals, usage of online consultation with doctors, isolating people in their homes for not so serious cases, awareness programs at the online platform²³.

USA

It was on January 20th when the US discovered its first case of coronavirus in Washington. The man had returned from Wuhan (China) and a few days after returning he experienced cold and fever. His nasal and oral swabs were taken to test for corona which came out to be positive²⁴.

More and more cases started coming and the President of USA announced on March 13, 2020, a complete lockdown in the country. This emergency included many preventive actions to fight against the coronavirus. This includes closure of all kinds of public meetings, theatres, bars, schools. Also, the offices were asked to work through the home. There should not be any group gatherings comprising of more than 50 people²⁵.

The US reached up to 1,345,000 reported cases and 80,554 deaths till the date of 11th May 2020. Various agencies started building up measures to reduce the spread of the virus-like reducing human to human contact by promoting social distancing²⁶.

Some of the laboratory results were examined to get an insight into how children and adults are responding to COVID-19. It was found out that severe cases of corona came in adults more than in children. To get more accurate data the symptoms, the number of hospitalizations were also compared to the adults and children²⁷.

India

Covid-19 is like thunderstorms which started in China and slowly build its roots in India. The beautiful country India discovered its first case on 30th January 2020 which had a history with

China. From then it started to make its mark in many regions of India. This alarming news made the health officials and medical authorities worried and they started planning measures²⁸.

Till March the cases reached till 563, and as a precautionary measure, the Prime Minister of India Shri Narendra Modi announced nationwide lockdown for three weeks started from 24th March 2020 midnight. He had also given orders to close all the government offices. People can only move out in case of any emergency. All the airports were closed, people who had international travel history were isolated. India was most worried about the spread of the virus amongst the economically weaker section of people. These people might not be able to quarantine themselves or face some other issues²⁹.

After 21 days of lockdown, the government of India extended these lockdowns to prevent human to human contact. The government helped the economically weaker sections of the country by providing food, and other essential services to them.

Through Advertisements, social media platforms people were made aware of social distancing, wearing masks, washing hands as much as possible, using alcohol-based sanitizer, don't meet any person who is suffering from cold, fever or any kind of similar symptom to corona. Online consultations from doctors were recommended. Some of the precautionary measures for healthcare workers were implemented like usage of personal protective equipment which includes wearing triple layer masks, gloves, eyewear, head cap, shoe cover. The usage of disposable medical equipment was also recommended³⁰.

INDIAN SYSTEM OF MEDICINE – AYURVEDA ON COVID-19

The emergence of Covid-19 has led many researchers to start building newer therapeutic options to kill the coronavirus from human life forever. Indian systems of medicine are one of the oldest and natural systems which are highly recommended for various treatment options. Homeopathy, Ayurveda, Siddha, Unani play an important role as a treatment option worldwide. These systems of medicines utilize natural excipients like plants, minerals and have less or no side effects, unlike the other synthetic medicinal system³¹. Ayurveda recommends fewer medicines and provides actions for a healthy lifestyle. To deal with coronavirus, one has to have powerful immunity; Ayurveda helps in building immunity by Charaka Samhita. This helps in understanding how immunity can kill the illness as well as slow down its growth. To stop the entry of the virus Ayurveda suggest some of its therapeutic course of actions like drinking hot water and eating hot food, regular gargling using medicated water, intake of steam. These actions help in fighting against mild symptoms in an individual^{32.}

The government of India announced some guidelines about the use of Ayurveda for enhancing immunity and for personal care during these Crisis. The guidelines suggested performing Yoga which could help in increasing fitness, consumption of some Indian authentic spices like cumin, garlic, turmeric for enhancing the nutritional level of the body, drinking of the most commonly consumed herbal tea in India containing cinnamon, black pepper, ginger, basil which is great for reducing cough and respiratory problems, and honey and clove powder usage can reduce throat related issues³³.

A lot of research is still going on the potential of Ayurveda to treat Covid-19. One of the researches implies the usage of Ayurveda Rasayana, which has been investigated for its immunomodulator and rejuvenation effects. After many clinical, animal, and in-vitro studies it was considered a potential candidate for the treatment of Covid-19³⁴. Most talked drug of the Ayurveda Rasayana is Ashwagandha (scientific name- Withania Somnifera) which is a great immunity booster and anti-inflammatory in nature. Also, one of its formulations was analyzed and it exhibits similar efficacy as shown by Hydroxychloroquine. Guduchi, Shatavari, Amalaki are also considered as a potential candidate to combat Covid-19³⁵.

Various states of India like Gujarat, Kerala have started the treatment of asymptomatic patients of Covid-19 using Ayurvedic medicines. Other states of India have also initiated the use of Ayurvedic Medicines after seeing its potential³⁶.

The most famous and therapeutic plant of Ayurveda is Tulsi (Basil). This plant is also worshipped in India. Because of its medicinal values almost every house in India has this plant. Tulsi provides with multiple benefits ranging from anti-inflammatory, used in Rheumatoid arthritis, rich in antioxidants, diabetes. It also effectively works against the fever and cough which are the common symptoms of Covid-19.Earlier it was used for treating various viruses like Vaccinia virus, Infectious Brusal Disease Virus, Newcastle Disease Virus³⁷.

The use of Ayurveda has extended the approach of treatment towards the Covid-19. This Indian system of medicine should be followed and implemented in this time of crisis. Ayush Healthcare System is working since this pandemic started and is continuously providing the essential data of Ayurvedic Drugs which could further help in the advancement of the treatement³⁸.

Effect of Covid-19 on Mental Health

COVID-19 and its consequences, in the long run, have become a major concern globally. The virus is not only affecting the physical health of the people but also it has a severe impact on their mental health. The daily routines, activities, and way of living have changed due to lockdown, and people are advised to stay indoors which has led to anxiety, insomnia, loneliness, frustration, irritability.

The virus outbreak has led to an increment in cases of domestic violence and mental illness. People have a sense of fear of avoidance, getting isolated, and also fear meeting other people^{39,40}.

The concern regarding the spread of infection from people who are suspected COVID-19 positive has made people anxious. Moreover, the effect of COVID-19 on the economy and uncertainty surrounding the situation like fear of losing their jobs, financial struggles, death of relatives has increased suicidal behavior^{39,40}. Two cases of suicide attempts were reported in India. In both cases, there was a fear that they might have developed COVID-19 infection due to the people they met. The thought that they might infect their family members, made them isolate themselves. They learned that the infection is having a high mortality rate and may cause a painful death. The anxiety and depression that they faced during this pandemic led them to take gruesome steps, harming themselves and their families^{41,42}.

The way having food and sleeping is important, similarly, interacting socially is a basic human requirement. The current pandemic situation and measures taken to contain the virus have confined people to their homes leading to insufficient social interaction, majorly affecting adolescents. Adolescence is a phase where an individual develops socially and psychologically. It is also a phase that is very vulnerable to mental illnesses⁴³.

Healthcare professionals all around the world are working to keep people healthy under such extreme and challenging conditions and have to make difficult decisions that keep them at constant risk of moral injury or mental health issues. To cope with the stress they suffer from, they should be prepared well with the situations they might face without comforting them with any false reassurances⁴⁴.

In the current scenario of the pandemic, people have a constant fear of getting infected and this threat fills them with negative emotions that are contagious to mental health. Behavioral changes can be intensified by social networks in a harmful or beneficial way. To understand this, on one hand, where meeting people can spread COVID-19 infection, on the other hand, some people can create awareness about social distancing and washing hands. A sense of belief, cooperation, and compliance are required to fight a pandemic. Patients should trust their healthcare providers and comply with the instructions and healthcare policies that aim to contain the virus⁴⁵.

Amidst all negativity and fear, people trusted their government that they would implement all the measures that are required to fight the pandemic and that no person would be deprived of basic and essential amenities. It was suggested to practice social distancing and hands should be washed frequently with soap⁴⁶.

To avoid any kind of mental stress, people should indulge themselves in some kind of activities so that they get busy and don't find time to overthink or think negatively. Special care, attention and counselling should be provided to elderly and children. Mental Peace comes with a brave and positive nature.

Category	Drugs	Route of Administration
Anti-Viral	IFN-α, Lopinavir, ritonavir,	IFN- α: Vapour Inhalation
	ribavirin, Favipiravir and	Ribavirin: Intravenous
	Remdesivir	Favipiravir: Oral (Fabiflu by
		Glenmark Pharmaceuticals)
		Lopinavir, Ritonavir: Oral
		Redesivir: Intravenous
Anti-Malarial	Chloroquine/Hydroxychloroquine	Oral
Anti-Rheumatoid/IL-6	Tocilizumab, Sarilumab,	Oral
Receptor antagonist	baricitinib	

FUTURE DIRECTIONS

It is because of Covid-19 that maybe the coming days would not be as normal as earlier. Wearing Masks, Social Distancing, Hygiene maintenance, staying at home, isolating the infected individual, regularly washing your hands for at least 20seconds are some of the activities which have become part of life. These courses of action are helping globally to reduce transmission. The development of vaccine will also take more time to come in the market, research on animal models are being done to judge the efficacy and safety of the vaccine⁴⁷. Till then, online awareness programs, telemedicine, Staying Home, implementing to the guidelines given by the higher authorities should be followed judiciously.

Our safety is in our hands. Nobody can force us to move out of our secured areas.

CONCLUSION

Originating from the seafood market in Wuhan and being declared as a pandemic by WHO, COVID - 19 has affected many countries across the world. The infants, elderly people, and people with co-morbidities require more care and attention. The novel coronavirus outbreak has challenged the economy and health authorities of the world. The pharmaceutical companies are working on different types of vaccines and drugs to develop an effective treatment to cure this disease. Outbreaks like this have occurred in the past and will continue in the future so dealing with the current situation is one aspect of the pandemic but one should be prepared for future outbreaks like this.

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