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A REVIEW ON CORONAVIRUS – THE PANDEMIC CAUSING GLOBAL CRISIS

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ABSTRACT

The word COVID - 19 is abbreviated as CO – Corona, VI – Virus, D – Disease and 19 indicates the year it emerged. The occurrence of coronavirus disease had been confirmed in around 210 countries and territories. The virus had infected 9,360,758 people worldwide. The most severely affected countries include USA, Brazil, U.K, Russia, Spain and India is inching towards the most affected country. Telangana confirms 9,553 confirmed cases till June 24-2020. A pandemic is an epidemic of an infectious disease which spreads across large regions and countries affecting many people. The 2019- 2020 Covid –19 pandemic is expected to have negative effect on the global economy, for years to come with a drop in GDP accompained by increase in unemployment around the world. The basic strategies in the control of an outbreak are containment and mitigation. Another strategy called as suppression strategy includes stringent population – wide social distancing, isolation of cases and quarantine can be considered.

INTRODUCTION

Coronavirus belongs to the family Coronaviridae. Club-shaped glycoprotein spikes in the envelope give the viruses a crown like appearance. Coronaviridae is generally considered to contain two genera, Coronavirus and Torovirus, which differ in nucleocapsid morphology, the former being helical and the latter being tubular. Coronaviruses constitute the subfamily Orthocoronavirinae, in the family Coronaviridae, order Nidovirales, and realm Riboviria.

STRUCTURE:

Coronaviruses are large, roughly spherical, particles with bulbous surface projections. The average diameter of the virus particles is around 125 nm (.125 μm). The diameter of the envelope is 85 nm And the spikes are 20 nm long. The viral envelope consists of a lipid bilayer, in which the membrane (M), envelope (E) and spike(S) structural proteins are anchored. The ratio of E: S: M in the lipid bilayer is approximately 1:20:300. On average a coronavirus particle has 74 surface spikes. The coronavirus surface spikes are homotrimers of the S protein, which is composed of an S1and S2 subunit. The homotrimeric S protein is a class I fusion protein which mediates the receptor binding and membrane fusion between the virus and host cell. The S1 subunit forms the head of the spike and has the receptor binding domain (RBD). The S2 subunit forms the stem which anchors the spike in the viral envelope and on protease activation enables fusion. The E and M protein are important in forming the viral envelope and maintaining its structural shape.

Inside the envelope, there is the nucleocapsid, which is formed from multiple copies of the nucleocapsid (N) protein, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation. The lipid bilayer envelope, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell. Coronaviruses contain a positive-sense, single-stranded RNA genome. The genome size for coronaviruses ranges from 26.4 to 31.7 kilobases.The genome size is one of the largest among RNA viruses.

Four human coronaviruses produce symptoms that are generally mild:

1. Human coronavirus OC43 (HCoV-OC43), β-CoV
2. Human coronavirus HKU1 (HCoV-HKU1), β-CoV
3. Human coronavirus 229E (HCoV-229E), α-CoV
4. Human coronavirus NL63 (HCoV-NL63), α-CoV

Three human coronaviruses produce symptoms that are potentially severe:

1. Middle East respiratory syndrome-related coronavirus (MERS-CoV), β-CoV
2. Severe acute respiratory syndrome coronavirus (SARS-CoV), β-CoV
3. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), β-CoV

COMMON COLD:

The human coronaviruses HCoV-OC43, HCoV-HKU1, HCoV-229E, and HCoV-NL63 continually circulate in the human population and produce the generally mild symptoms of the common cold in adults and children.

SEVERE ACUTE RESPIRATORY SYNDROME (SARS):

In 2003, following the outbreak of severe acute respiratory syndrome (SARS) which had begun the prior year in Asia, the World Health Organization (WHO) issued that a novel coronavirus identified by a number of laboratories was the causative agent for SARS. The virus was officially named the SARS coronavirus (SARS-CoV)

MIDDLE EAST RESPIRATORY SYNDROME (MERS):

In September 2012, a new type of coronavirus was identified, initially called Novel Coronavirus 2012, and now officially named Middle East respiratory syndrome coronavirus (MERS-CoV). After the Dutch Erasmus Medical Centre sequenced the virus, the virus was given a new name, Human Coronavirus—Erasmus Medical Centre (HCoV-EMC). The final name for the virus is Middle East respiratory syndrome coronavirus (MERS-CoV).

CORONAVIRUS DISEASE 2019 (COVID – 19):

In December 2019, a pneumonia outbreak was reported in Wuhan, China. On 31 December 2019, the outbreak was traced to a novel strain of coronavirus, which was given the interim name 2019-nCoV by the World Health Organization (WHO), later renamed SARS-CoV-2 by the International Committee on Taxonomy of Viruses. In late 2019 a virus apparently closely related to SARS coronavirus emerged in Wuhan, China. The virus, later named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), caused an illness known as COVID-19, which was similar to SARS and was being characterized primarily by fever and respiratory symptoms. The virus was likewise highly contagious. By early 2020 it had spread throughout regions of China and had reached the United States and Europe, having been carried by travelers from affected regions. In March the World Health Organization declared the outbreak a pandemic, and travel to, from, and within many countries was severely restricted in an effort to control its spread. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the strain of coronavirus that causes coronavirus disease 2019 (COVID-19), the respiratory illness responsible for the COVID-19 pandemic. Colloquially known as simply the coronavirus, it was previously referred to by its provisional name, 2019 novel coronavirus (2019-nCoV),

and has also been called human coronavirus 2019 (HCoV-19 or hCoV-19). The World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020. SARS-CoV-2 is a positive-sense single-stranded RNA virus that is contagious in humans. As described by the U.S. National Institutes of Health, it is the successor to SARS-CoV-1, the strain that caused the 2002–2004 SARS outbreak.

HISTORY OF CORONAVIRUS AND ITS EVOLUTION:

Most of us will be infected with a coronavirus at least once in our life. This might be a worrying fact as heard of only one coronavirus, SARS-CoV-2, the cause of the disease known as COVID- 19. There is much more to coronaviruses than SARS-CoV-2. Coronaviruses are actually a family of hundreds of viruses. Most of these infect animals. Occasionally, viruses that infect one species can mutate in such a way that allows them to start infecting another species. This is called "cross-species transmission" or "spillover". The first coronavirus was discovered in chickens in the 1930s. It was a few decades until the first human coronaviruses were identified in the 1960s. Scientists first identified a human coronavirus in 1965. It causes common cold. Later researchers found a group of similar human and animal viruses and named them after their crown-like appearance. Seven coronaviruses have the ability to cause disease in humans. Four are endemic and usually cause mild disease, but three can cause much more serious and even fatal disease. Coronaviruses can be found all over the world and are responsible for about 10-15% of common colds, mostly during the winter. The coronaviruses that cause mild to moderate disease in humans are called: 229E, OC43, NL63 and HKU1. The first coronaviruses discovered that are able to infect humans are 229E and OC43. Both of these viruses usually result in the common cold and rarely cause severe disease on their own. They are often detected at the same time as other respiratory infections. In 2004, NL63 was detected for the first time in a baby suffering from bronchiolitis (a lower respiratory tract infection) in the Netherlands. It was later named HKU1 and has been found to be present in populations around the world.

Deadlier strains:

But not all coronaviruses cause mild disease. Sars (severe acute respiratory syndrome) caused by SARS-CoV was first detected in November 2002. The cause of this outbreak wasn't confirmed until 2003 when the genome of the virus was identified by Canada's National Microbiology Laboratory. The one that causes SARS emerged in southern China in 2002 and quickly spread to 28 other countries. More than 8,000 people were infected by July 2003. A small outbreak in2004. This coronavirus causes fever, headache, and respiratory problems such as cough and shortness of breath. Sars bears many similarities to the current pandemic of COVID-19. Older people were much more likely to suffer severe disease and symptoms include fever, cough, muscle pain and sore throat. A decade later, in 2012, there was another outbreak involving a newly identified coronavirus: MERS-CoV. The first case of Middle East respiratory syndrome (Mers) occurred in Saudi Arabia. There were two further Mers outbreaks: South Korea in 2015 and Saudi Arabia in 2018. There are a handful of Mers cases every year, but the outbreaks are usually well contained. One of the main challenges in containing the SARS-CoV-2 outbreak is that symptoms can be very mild – some people may not even show any symptoms at all – but can still infect other people. SARS-CoV-2 is not as deadly as either Sars or Mers, but because it can spread undetected, the numbers of people it will infect and the numbers that will die will be higher than any coronavirus we have ever encountered. Virus that was first detected in Wuhan, China, in late 2019 and has set off a global pandemic.

WHERE DID CORONAVIRUS ORIGINATE:

Experts say SARS-CoV-2 originated in bats. That's also how the coronaviruses behind Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) got started. SARS-CoV-2 made the jump to

humans at one of Wuhan's open-air "wet markets." They're where customers buy fresh meat and fish, including animals that are killed on the spot. Some wet markets sell wild or banned species. Crowded conditions can let viruses from different animals swap genes. Sometimes the virus changes so much it can start to infect and spread among people. As Sars- CoV- 2 spreaded both inside and outside China, it infected people who have had no direct contact with animals.

IMPLICATIONS OF CORONAVIRUS ON OTHER DISEASES:

DIABETES AND CORONAVIRUS:

Early studies have shown that about 25% of patients with severe COVID-19 infections h ad diabetes. Those with diabetes were more likely to have serious complications because of high blood sugar, it weakens the immune system and makes it less able to fight off infections.coronavirus infection is even higher due to another condition, like heart or lung disease. COVID-19 infection could be at greater risk for diabetes complications like diabetic ketoacidosis (DKA). DKA happens when high levels of acids called ketones build up in your blood. It can be very serious. New coronavirus have a dangerous body-wide response to it, called sepsis. To treat sepsis, the body's fluid and electrolyte levels should be managed. DKA causes loss of electrolytes, which can make sepsis harder to control.

HIV AND CORONAVIRUS:

COVID-19 is new so there isn't much data on how COVID-19 affecting HIV specifically. But the new coronavirus impacts the respiratory system, If HIV is well-controlled by antiretroviral therapy (ART) suppressing HIV and having normal CD4 counts then covid- 19 is not harmful.Other types of coronaviruses, such as those that caused SARS and MERS, did not have a major impact on people with HIV. But if HIV is advanced or isn't under good control with antiretroviral therapy (ART), then the immune system will have a harder time defending against infections, possibly including COVID-19. In that case, COVID-19, may be more likely to have serious complications. ASTHMA &

CORONAVIRUS:

COVID-19 is a respiratory disease caused by a coronavirus. It can affect lungs, throat, and nose. people who have asthma, infection with the virus could lead to an asthma attack, pneumonia, or other serious lung disease. Asthma doesn't raise the chances of getting infected with the coronavirus that causes COVID-19. But if you get sick, your symptoms could be worse than other people's because of trouble breathing.

Signs and Symptoms of Coronavirus and Asthma:

Common COVID-19 symptoms include:

- Fever, Fatigue, Dry cough, Loss of appetite, Body aches, Shortness of breath.
- Symptoms of Asthma include:
- Chest tightness, Coughing, Shortness of breath, A whistling or wheezing sound when you breathe out.

MULTIPLE SCLEROSIS (MS) AND CORONAVIRUS:

MS itself doesn't enhance the chances of COVID-19, the respiratory disease caused by a new kind of coronavirus, But having MS certain things affect how it responds to the virus. They include: Age, other health conditions and the kind of MS medicines prescribed. National and international health organizations are following developments about the virus and working to make the best recommendations. People with MS who are at high risk are:

- Have medical conditions like lung disease or heart disease.
- Age older than 6
- Aren't able to move around much.

MULTIPLE MYELOMA AND CORONAVIRUS:

Blood cancers like non-Hodgkin's lymphoma and multiple myeloma may pose the most risk for COVID-19. Blood cancers affect

body's infection-fighting white blood cells. Multiple myeloma is a cancer of white blood cells called plasma cells. That weakens the immune system. Treatments such as chemotherapy and bone marrow transplants knock down the immunity even more. A study published in February of people who were hospitalized with COVID-19 found that those who have any type of cancer or had cancer before were several times more likely to suffer. But that study was done on only 18 people with cancers, so it's unclear if larger samples might lead to the same findings.

CROHN'S DISEASE AND CORONAVIRUS:

Having Crohn's doesn't make you more likely to get exposed to the new coronavirus. It includes people who take medications that suppress, or weaken, their immune system. Many things can lower immunity, including chronic illness, recent surgery, or medication. Some, but not all, Crohn's drugs suppresses body's immune response. So far, researchers haven't done any specific research on COVID-19 and people with Crohn's. But there's already some expert advice for people with inflammatory bowel diseases such as Crohn's. These drugs don't affect the immune system:

- Balsalazide (Colazal, Giazo)
- Mesalamine (Apriso, Asacol, Delzicol, Lialda, Pentasa)
- Olsalazine (Dipentum)
- Sulfasalazine (Azulfidine)

Immunomodulator drugs do affect the immune system. They include:

- 6-mercaptopurine (Purinethol, Purixan)
- Azathioprine (Azasan, Imuran)
- Cyclosporine (Gengraf, Neoral, Sandimmune)
- Methotrexate (Rheumatrex, Trexall)

Biologic and biosimilar drugs also suppress the immune system. These include:

- Adalimumab (Humira) and its biosimilars Amjevita, Cyltezo, and Hyrimoz
- Certolizumab pegol (Cimzia)
- Golimumab (Simponi)
- Infliximab (Remicade) and its biosimilars Inflectra, IXIFI, Renflexis
- Natalizumab (Tysabri)
- Vedolizumab (Entyvio)
- Ustekinumab (Stelara)

RHEUMATOID ARTHRITIS AND CORONAVIRUS:

Rheumatoid arthritis (RA) is more likely to cause certain infections. It may cause higher chance of getting COVID-19. Symptoms could be more serious than someone who doesn't have RA. RA can increase the chances of getting any kind of infection. There's also some evidence that respiratory infections spread by viruses, like COVID-19, may raise the risk of getting RA. One study showed that women and older people who'd had other kinds of coronaviruses were more likely to get RA after they'd been sick. But more research is needed to know whether COVID-19 can actually trigger RA. There's no vaccine or treatment for the virus yet. But some researchers think that certain RA drugs might help. They include:

- Chloroquine
- Hydroxychloroquine (Plaquenil)

GLOBAL RESEARCH ON CORONAVIRUS:

Global research database: WHO is gathering the latest international multilingual scientific findings and knowledge on COVID-19. The global literature cited in the WHO COVID-19 database is updated daily. Other resources on coronavirus disease (COVID-19):

- BMJ
- Cambridge University Press
- Centers for Disease Control and Prevention

- Chinese Medical Association
- Cochrane
- Elsevier
- European Centre for Disease Prevention and Control (ECDC)
- JAMA Network
- The Lancet
- LITCOVID: US National Library of Medicine
- New England Journal of Medicine
- Oxford University Press
- PLOS
- Public Health England
- Science
- Springer Nature
- SSRN (Preprints)
- Wiley

DEVELOPMENT OF CORONAVIRUS VACCINES BY PHARMACEUTICALS:

1. Glaxosmithkline and China based partner Clover biopharmaceuticals has initiated phase –I study to develop a covid-19 vaccine and it was announced in February 2020.
2. The agreement between AstraZeneca and Biomedical advanced research and development authority (BARDA) will develop and manufacture the vaccine.
3. Glenmark drug Favipiravir used to treat moderate covid-19 infections is available in indian market under the brand name Fabiflu.
4. Hetero received regulatory approval to manufacture and market antiviral drug Remdesivir for treating coronavirus under the brand name Covifor in India.
5. Cipla launches generic Remdesivir under the brand name Cipremi for covid- 19 by USFDA
6. CSIR gets nod for phase III trials of antiviral drug Umifenovir.
7. Clinical trials of a Russian coronavirus vaccine developed by Moscow based Gamaleya research institute i.e liquid and powder for injection will be tested.
8. Biotech firm Curevac launches human trials of an experimental coronavirus vaccine in Germany.
9. The AZD1222 vaccine jointly developed by british pharma giant AstraZenecea and Oxford University begins human trials.
10. Patanjali launches Coronil tablets-Ayurvedic treatment for coronavirus.
11. Nigerian scientists have discovered vaccine for novel coronavirus. It was developed by scientists from Nigerian Universities under the aegis of covid-19 research group developed locally for Africans as published on June 22-2020.

MUTATIONS RESPONSIBLE FOR STABILITY IN COVID –19 & BEING PANDEMIC:

A variant of the SARS-CoV-2 virus, which is responsible for coronavirus pandemic sweeping the world, has been found in multiple studies to have a very tiny mutation in its genetic code. This variant is primarily circulating through Europe and the United States, according to a study released by Scripps Research, and the genetic tweak significantly increases the virus' ability to infect cells in a host. "Viruses with this mutation were much more infectious than those without the mutation in the cell culture system we used," virologist Hyeryun Choe has stated. The researchers found out that the mutation caused a marked increase in the number of spikes on the viral surface. The spikes are a very important part of the virus' architecture and it allows the virus to bind to cells and enter them, starting the process of infection. The number or density of functional spikes on the virus is 4 or 5 times greater due to this mutation. The spikes, which are easily the most noticeable feature of the coronavirus in its now-popular illustrations, give it a crown-like appearance. They also give the virus its ability to latch onto a cell through specific receptors that it attaches to the ACE2 receptors. In the

mutant virus, the "D614G" mutation [where the amino acid at position 614 is changed from aspartic acid (D), to glycine (G)] gives these spikes more flexibility in their "backbone", co-author of the study Michael Farzan, co- chairman of the Scripps Research Department of Immunology and Microbiology stated.

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