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THE PANDEMIC- COVID 19- A RACE OF PHARMACEUTICALS

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ABSTRACT

Corona virus disease (COVID-19) is caused by SARS-COV2 and it represents global public health concern and World Health Organization (WHO) declares public health emergency. Special attention is focused to reduce community transmission of COVID-19 have been implemented to control the current outbreak. COVID-19 develops intestinal symptoms like diarrhea, while low percentage of MERS-CoV or SARS-CoV patients had diarrhea. As the race to find the treatments to cure COVID-19 accelerates, the WHO announced to compare treatment strategies in a streamlined clinical trial design that doctors around the world can join. There is no specific treatment for disease caused by COVID-19. However, many of the clinical symptoms can be treated and therefore treatment based on the patient's clinical condition. Identification of novel chemotherapeutic drugs for treating COVID-19 infections is urgently warranted.

Keywords: Corona virus, COVID-19, Severe acute respirator syndrome Corona virus 2

Introduction

Corona virus is defined as group of viruses belonging to family Corona viridae which are prominently responsible to cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The first incident of this pandemic disease was found in Wuhan China at end of 2019, where it results its outcomes in the form of severe respiratory illness and pneumonia. The name of this pandemic virus has been coined from a Latin word corona which means crown. The truthiness of this word was evidently described from its structure and it is called a novel virus because this virus does not resemble formerly. It was believed that this virus originates from the bats as they are host of replication of viruses on large scale and get transmitted into pangolins. From pangolins it was being transferred to humans. To define the etiology of this virus around 103 SARS – COV 2 genomes have been studied and established the phylogenetic relation that exists between the genomic scale and virus. More extensive research studies were carried and found that this corona virus is an enveloped virion which has been composed by using two single stranded polymorphs which are composed using adenine, guanine, cytosine and uracil. These nucleotides helps in the mutation of virus in two featured shape as S form and L form originated from the host cell S. It was reported that L form is more fatal to people than S form because it mutated very fast and easily transmissible. After various study this virus was

used to be coined by new term which is SARS-COV 2 (Severe acute respirator syndrome Coronavirus 2). The SARS COV 2 has a club of surface proteins which are spherical in shape called as spikes Sohrabi C.

Hierarchical organogram of COVID- 19

Genera	Roboviria
Phylum	IncertaeSedis
Order	Nidovirales
Family	Coronaviridae
Sub family	Orthocoronaviridae

History of origin: The Novel virus is closely resembled to SARS virus of 2002. First case of this pandemic drug arises firstly in 2002-2003. It was firstly identified and mentioned in a study report of Canada in which study was included around 500 patients who depict the symptoms like flu. Among various examined people only 17-18 cases are found infected with corona virus strain and confirmed using evaluation by polymerase chain reaction test. At that time corona was considered not so fatal till 2002. Later, in 2003 a new report outwards in which they have mentioned the spread of the deadly disease among various countries such as United States America, Hong Kong, Singapore, Thailand, Vietnam and in Taiwan with mortality rate of more than 1000 patients. During that time due to the prevalence of this pandemic situation that year was declared as black year for microbiologist (Silverstein, Stroud, *et al.*, 2020). A couple of

years later a new corona species MERS (Middle East Respiratory Syndrome) arises in 2012. Again a bat was a host of animal virus mutation get firstly transferred to camel and then intermediate to human. The total no of cases in 2012, was reported to be around 3300 with a death rate of 2500 reported. In this case fatality rate was found to around 34% (Nishiura, Jung, *et al.*, 2020). Later in 2019, again a new species of this virus get emerged which was identified as novel disease somehow different form earlier species due to the characteristic feature of enveloped virion originates firstly from china in wuhan. The novel virus was emerged to known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease caused by this virus is called coronavirus disease 2019 (COVID-19). In March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic (Banerjee, Kulcsar *et al.*, 2019).

Clinical feature / symptoms

1. Cough
2. Fever
3. Sore throat
4. Dyspnea (shortness of breath)
5. Bi lateral infiltrates on chest X- rays.

Incubation Period- It was reported from the research studies that for the onset of symptoms the virus takes around 2 to 14 days with a median day of start are the 5th day of this incubation time. The spread of virus varies from person to person depending on various factors such as age, medical history and gender. It was observed that the average age for the vulnerable for disease was found to be around 55. It was also evidently reported that people with a previous history of any disease such a diabetes, hypertension, etc. cover the major part of prevalence of this disease. The gender composition with different anatomical structures also play a vital role in spread of virus and found that among the affected population around 67% of the male were found as compared to women with a minor percentage of around 33% only (5-6).

Structure of corona virus: Novel corona virus is unique and different from other viruses because they bears surface protein layer which carry spikes on it. Spikes present on the surface are used to bind the virus to cell receptor and helps in entry of the virus in human body. Spike present on its surface of SARS – COV 2 are quite different from SARS- COV. Due to this property virus is very lethal and no existing vaccine is effective for this. By elaborating in detail about its structure it was found that structure was found to contain four structural proteins present as SEMN which are notated as S stands for spike, E stands for envelope, M stands for membrane and N stands for nucleocapsid (Holmes,2003).

S protein: allows the virus to attach host cells containing receptor binding domain which recognizes a specific receptor ie angiotensin converting enzyme receptor 2 (ACE-2), which is present in lungs, hearts, kidneys and intestines. Spike protein also has two functional supplements as S1 and S2. S1 binds to host cell receptor and S2 mediates the fusion of the virus in cell membranes. S Proteins are also responsible for the shape of the virus in the form of crown.

M protein: Membrane Protein: Membrane protein was found to form the viral envelope. It most abundant on the viral surface and defines the shape of the viral envelope. It

also acts a central organizer for the corona virus assembly and interacts with the other structural proteins.

E Protein: Envelope Protein: It is smallest among the mentioned proteins. It is responsible for the release of virus. During virus replication it acts as intercellular trafficking and plays a major role in spread of virus. As E protein are of two types E1 and E2. E1 helps in the matrix glycoprotein trans membrane Protein. E2 is peplogenic fusion with the humans. Viral envelope contains a layer of fats which when come in contact with the soap form micelles and get removed. This is the utmost reason for advising to frequently wash your hands with soap.

N Protein- Surface protein (Nucleocapsid protein): These are also known as nucleocapsid Protein bearing a capsid shell which contains the genetic material of the virus. Inside the capsid shells there are N protein and nucleocapsids. The N protein binds to single strand of the RNA which carries all genetic information for replication. The N protein appears to be multifunctional as cyst for virus organ for replication and therefore increasing the viral particles. N protein also forms complex with RNA and assist in viral assembly.

HE Protein – Hemaglutir Esterase: S protein in combination with HE protein facilitates the entry of virus in host cells. HE is a peplomer which plays a prime role in the hemagltuination.

Pathogenesis of COVID 19 virus

It is single stranded RNA genome which works by hijacking the cells of the body and replicating them in the cytoplasm. Once it entered into the cells the virus particle get uncoated and attach To RNA genome which was present in the cytoplasm and attached to ribosomes for translation. Viruses can be spread to new cells by the respiratory tract passage. Once entering into passage it moves across the tract it will target to alveoli in the lungs where they get bound by type 2 nemroside. In lungs alveoli, there are two types of cell linings which play a different role in their mode of action as type 1 and type 2. The type 1 nemroside are used for the exchange of gases (like carbon dioxide exhale and oxygen inhale) and the type 2 helps in the production of surfactants. The prime role of surfactant is to decrease the surface tension in the alveoli and reduce the collapsing pressure. Moving ahead as mentioned in the structure of genome that it carries different types of receptor protein which are known to performs different actions. Among them one is spikes protein coined as S- receptor. As the name suggests that it have spikes on its surface which helps in the attachment of antigen to a specific receptor which is angiotensin converting enzyme 2 (ACE- 2) and help to release a single stranded organelle into the cytoplasm of the cell. Once the organelle is released, which is used by the host cellribosomes to convert m- RNA into proteins. Using this phenomenon of translation, single strand RNA get converted into specific protein molecules to form different poly proteins. The single stranded RNA also has the ability to bind with another enzyme that is RNA dependent (RNA- D) RNA polymerase where it uses single stranded RNA to produce more copies of single stranded RNA. At end the, newly formed ploy proteins have to decode it into various parts to form new species of host. This can be achieved by action of poly-proteins in the presence of a specific enzyme proteinase which converted them into a number of viral components such as nucleic capsids, enzymes and spike proteins. Now by concluding all it was

found that when we combine single stranded nucleic acid with these fragments of polyproteins which will leads to formation of a new corona virus (Mousavizadeh, Ghasemi,2020)

Second approach is to inhibit the formation of type 2 nemroside. As a result of these inhibitions they release specific inflammatory mediators and release active oxygen radicals species and proteases which in turn activates the macrophages. Once the macrophages get activated they release specific cytokines such as Interleukin 1, Interleukin 6 and TNF-alpha. These released cytokines got released in blood stream and activates the endothelial cell, the endothelial cells causing contractions leads to dilation of smooth muscles. Fluids and plasma starts leaking from the interstitial spaces. The discharged fluids get accumulated outside the alveoli and cause the contraction of alveoli. The excess accumulation of fluids will be responsible for enhanced activity of surfactant leads to increases the collapsing pressure which results in alveolar edema and alveolar collapse. The excess amount of fluid accumulated around the alveoli also hinders the respiratory gases exchange and leads to hypoxia. Hypoxia results in induced partial pressure which leads to stimulation of chemoreceptors and trigger the reflux system by stimulating the sympathetic nervous system which in turn increase heart rate and respiration rate.

Third pathway of impairment is due to interleukin secretions. As in human body mainly two types of interleukins were secreted interleukin 1 and interleukin 6 which can travel across the blood and reaches to central nervous system (CNS). In the CNS, hypothalamus is present which are responsible to control our body temperature. Interlkiu1 and 6 in higher concentration interact with hypothalamus to release specific prostaglandins such as PGE 2, which impairs with the thermostat and increase your body temperature and causes fever (Yuki, Fujiogi *et al.*, 2020).

Fourth pathway of consequence is due to inflammation of lungs. The inflamed lungs starts secreting and leaching its membrane by discharge of oozing of fluids from its surface into blood stream having inflammatory responses which were carried all over the body. This inflammation of the lungs leads to systemic inflammatory response syndrome (SIRS) which can leads to systemic shock. These inflammations also spread across the circulatory system where they causing the increased capillary permeability. The secreted fluids also starts get accumulated in the tissue spaces and decrease the overall blood volume. Due to that increase blood volume leads to vasodilation of the vessels due to which peripheral resistance got decreased. Both decrease in blood volume and peripheral resistance make the person hypertensive with a very lower rate of blood pressure. As result of hypotensive the perfusion of blood to multiple organs got decreased and can lead to multisystem organ failure (MSOF) (10-11).

Testing methods for the determination of COVID 19

Not various rapid testing techniques have been established till date, which fulfills the promising outcomes. There are recommended methods of detection exist are discussed below as Real Time Polymerase Chain Reaction, Nucleic Acid Amplification Test, Antibody Testing, Medical imaging etc. The sample for all these tests have been collected from the respiratory tract and respiratory secretions in the form of sputum, Bronchi alveolar lavage, Tracheal

aspirate or from upper respiratory secretions such as nasal or throat Swab. The collected samples were further processed for testing and assay.

Real time polymerase chain reaction (RT-PCR): RT-PCR is defined as Real time polymerase chain reaction. For this test sample can be collected from sputum, nasopharyngeal swab, aspirate and serology. In this method, detection was done at molecular level for confirmation of COVID-19. The outcomes of the result arise within few hours to 2 days. This RT-PCR test performed with throat swabs is only reliable for detection in the in the first week of the disease because in later days the virus might disappears in the throat and move forward into lungs where they reproduce and multiply to form more. For those people who are tested in second week, the samples were taken by alternate means by acting a little bit deeper in airways by using suction catheter and sputum. Results are confirmed by interpretation of the genetic fingerprint of the virus i.e. RNA. RT-PCR tests acts as gold standard in diagnosing COVID-19, which are validated by World health organization. On the basis of this detection of COVID 19 are confirmed (Lan, Xu *et al.*, 2020).

Nucleic acid amplification test (NAAT)

Nucleic acid amplification test is very expensive one but quite similar to RT-PCR test. In this test using the detection of unique sequences of RNA are used to determine whether the sequencing is necessary or not. In this test samples were generally collected from the nasopharyngeal swabs in case of person reported with severe infection and pneumonia sample should be collected from the lower respiratory secretions. Collected samples were processed and tested for SARS- COV-2 in this method the RNA was extracted from the sample DNA and converted to PCR by using amplification with specific primers of SARS- COV-2. Due to sequencing of the genetic material and presence of viral RNA in the respiratory tract sample confirms the presence of infection in patients with SARS-COV-2. When the presence of viral RNA is less in amount it can leads to false negative results also. For confirmation secondary test should be also done (Xie, Jiang *et al.*, 2020).

Antibody Testing (Serology)

The antibodies were produced by the immune system of our body in the form of proteins which helps us to combat us from the infections and diseases. The antibodies have ability to bind with the foreign particles which are found on the surface of the pathogen as antigen. When an antibody binds to an antigen and denatures the pathogen directly or indirectly. In this method the whole blood sample was used. It was assumed that the person infected with SARS-CoV-2 antigens have developed antibodies against it by using antigen antibody interaction phenomenon. The change in color was considered as an indicative mark to confirm the test or presence of virus. If change in color was observed marks the test positive. One of the major drawbacks of this test that only amount of antibodies can be determined. If antibodies were found in the sample specimens it confirms that person have been exposed to SARS-CoV-2 and developed immunity against SARS-CoV-2 infection. The time taken by antibodies to develop varies from 1 to 2 weeks. This test can lead to misleading false results because in earlier stages antibodies might not get developed (Long, Liu *et al.*, 2020).

Chest x ray – It is used to determine the bilateral pulmonary infiltrates.

CT Scan- This test is done to determine ground glass opacities and multi lobar consolidations.

Loop mediated Isothermal amplification assays- It is the newly designed test used for the determination of COVID by using the isothermal nucleic acid amplification technology instead of PCR. This method was proved to be simpler and effective with positive result in a short time span of around 5 to 15 minutes duration (Singhal,2020).

Treatment approaches

Herbal Strategies: Due to the alarming rise of this pandemic disease grabs everyone on a stake health with a rising no of cases of fatal deaths and hundreds of people infected every day. This disease mainly target and easily communicated in person having poor immunity profile and odes not able to make sufficient antibodies within the time to combat the virus replication and protect their health. With no definite cure in sight of this infectious disease till date reported only few of the compounds were used to boost your immunity and health. Some of those listed compounds are discussed with their activity.

Garlic-are biologically known as *Allium sativum* L. is a widely used as spice in the food additives. Garlic was found to be used for medicinal properties such as immunomodulatory, protective, antioxidant, antifungal and antibacterial. The consumption of garlic was done to boost your health and immunity. Garlic can be used directly by using cloves, efficiently chewed and engulfed with warm water every day or by incorporating sufficient amount in your food and meals.

Cinnamon-Cinnamon well recognized as cinnamomum and zeylanicum. It is widely used flavoring agent in food and delicacies all over the world. Cinnamon contains active constituents such as cinnamaldehyde, cinnamate and cinnamic acid, eugenol, L-borneol, caryophyllene oxide. Which are being known to have significant pharmacological benefits as antiviral antimicrobial antioxidant.

Yoghurt-Yogurt was processed by inoculation mechanism using the various strains culture of *Lactobacillus bulgaricus* and *Streptococcus thermophilus*. The main active constituent which was found in curd was a probiotic which was found to be effective against the mild respiratory infections which are caused by influenza virus. It also used to treat bacterial, yeast and fungal infections in the pediatrics and preventing urinary tract infections.

Liquorice root (Mulethi): Liquorice also known as *glycyrrhizaglabra* Linn is a commonly used ayurvedic medicine since ancient era. Studies and research reported that *glycyrrhizaglabra* Linn possesses antibacterial, antioxidant, antimalarial, antispasmodic, anti-inflammatory and anti-hyper glycemc properties due to the presence of these phytoconstituents such as glycyrrhizin, isoliquiritigenin and isoliquiritin, liquiritigenin and liquiriti, it is often used as an anti-tussive to soothe sore throat and expectorant in cough.

Amla: Amla also known as *Emblca officinalis* or Indian gooseberry used as a medical plant in Ayurveda. It is well known that amla fruit was effective medicine as diuretic, anti-pyretic, hair tonic, ulcer preventive, antioxidant. The reported activities were exhibited due to presence of various

phytochemicals such as phyllembein, quercetin and ascorbic acid.

Giloy: Glioy also known as *Tinosproia cordifolia* widely used in treatment of various ailments such as skin disease, diabetes helminthiasis, heart diseases, leprosy, rheumatoid arthritis. It was found to boost the immune system of body. The pharmacological activities of the plant is due to its chemical constituents like diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds, essential oils, a mixture of fatty acids, and polysaccharides and is present in a different part of the plant body, including root, stem.

Shilajit: Shilajit is a natural substance found mainly in the Himalayas mainly formed due to the gradual decomposition of certain plants which undergo decomposition by the microbes. It is a potent and very safe dietary supplement which was used for restoring the energetic balance and potentially able to prevent several diseases. Shilajit was found to contains fulvicacid, humic acid, hippuric acid and benzopyrones which are extensively used in various pharmacological properties such as antidiabetic, Immunomodulatory, anti-anxiety, antiviral activity, anti-inflammatory, analgesic, antioxidant and memory enhancer.

Neem: Neem also known as *Azadirachta indica* is the fast growing evergreen tree found mainly in India, Africa and America. This tree is well known for its medicinal properties as antibacterial. Antifungal due to presence of these chemical constituents such as nimbin, nimbanene, 6-desacetylnimthebinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid.

As mentioned above plant and their derivative constituents are used to alleviate immunity and wellbeing of people to combat the serious concern of Corona virus (18-19).

Currently used drugs and ongoing clinical trials for the treatment of COVID-19:

The spread of COVID 19 concerns people all throughout the world. It has compelled the government to take decisions like complete lock down in all the countries and the economy of the countries is at higher risk. Schools, education system, manufacturing units, daily wage workers are worse affected out of this. Wherever the world is facing trouble due to lockdowns, the pharmaceuticals are getting the chance to enhance their potential. They are facing a big challenge because the whole world is relying on them. Various pharmaceutical organizations such as Medicago, Clover, GSK, National Institute of Health (NIH) etc are trying to find the treatment as well as prevention of the COVID-19. Some out of these have found the suitable candidates and are in the process of clinical trials to bring those candidates in the market. In spite of fastening the process and eliminating all the unnecessary steps, it will take upto 1 year or 1.5 year to bring those formulations in the market. At present, none of the drug is approved by US food and drug administration for the treatment of COVID-19 specifically but here are the data of some drugs, which are being utilized in treatment of the same. The data has been taken from National Institute of Health (NIH) (Health, 2020).

Repurposing the current antiviral strategies and vaccinations could act as a promising treatment. Hu *et al.*, has mentioned in Nature Nanotechnology recently that

chloroquine, which is being used and had been approved by US Food and Drug Administration for the treatment of malaria also works by inhibition of endocytosis of nanoparticles which are of the same size as that of virus so can be used for the treatment of COVID-19. Undoubtedly, chloroquine is already being used for the treatment of corona virus disease in China since February, 2020. However, this drug is not been approved by USFDA for the clinical use in COVID-19, so care should be taken while administration and therapy should be monitored especially for the prolonged QTc interval, as suggested by NIH (Health, 2020).

Favipiravir is another antiviral medication which is showing to have good clinical efficiency in the treatment of COVID 19 and has been also included in the treatment plan. In Japan, it is being used to treat the patients with mild to moderate symptoms. Glenmark, India is performing clinical trials on the generic version of Favipiravir and recently, it has entered in clinical trial phase III. Drug Controller General of India (DCGI) has provided the approval for the conduct of clinical trials on this drug. Favipiravir, is a patented product of the Japanese company Fujifilm Toyama Chemical Co Ltd., Japan with a brand name of Avigan (Lipworth, Chan *et al.*, 2020).

Favilavir is another antiviral drug which is approved by National Medical Products administration, China for the treatment of COVID-19. The drug was efficient to treat the animals in pre clinical trials and even passed the clinical trial involving 70 patients. The clinical trials are being conducted in Shenzhen, Guangdong Province.

Remdesivir, is another investigational antiviral drug which is being investigated for the treatment of COVID 19. This drug is under clinical trials. It resulted in shortening the period of recovery in COVID patients. The emergency use of this medicine had call for the distribution of Remdesivir in the US and was administered intravenously by the health care workers. Based on the current emergency use and the results provided, USFDA is of view that this medicine can proven to be safe and effective against this deadlier infection. However, some of the side effects observed by Remdesivir therapy include liver inflammation which calls for the enhanced levels of liver enzymes, BP fluctuations; shivering, nausea and vomiting etc. Immune based therapy is also recommended by NIH. However, insufficient data is there to either use for or against the use of immunoglobulins for the treatment of COVID-19. Some of the examples are there like interleukin-6 inhibitors (Sarilumab, Siltuximab and Tocilizumabetc), Interleukin-1 inhibitors (Anakinra). However, except in milieu of clinical trial data, NIH panel has recommended not to use the other immunomodulators such as Interferons (because they lack in efficiency for the treatment of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) and Janus Kinase Inhibitors (Baricitinib) because of its broad potential for immunosuppression (Cao, Wang *et al.*, 2020).

The surface receptors for Severe acute respiratory syndrome corona virus 2 (SARS Cov 2) are angiotensin converting enzyme 2 (ACE 2) receptors. Therapies like ACE inhibitors or angiotensin receptors blockers (ARBs) can be used for these treatments. The hypothesis is that the modulation of the receptors with these medications may suppress or enhance the SARS Cov 2. The studies depicting the role of these medications for the SARS Cov 2 are under

clinical trials (Lisziewicz, Lori, 2020). HMG-CoA Reductase Inhibitors can prove to be useful for the prevention of cardiovascular disease and plays a potential role in the management of patients with SARS Cov 2. It was observed that they can reduce the mortality rate of the patients due to cardiovascular disease in COVID 19 patients especially who possess the history of severe infections such as influenza and pneumonia.

Many other companies like Takeda Pharmaceuticals have started developing the plasma driven therapy and Eli Lilly, Biogen/Vir and Regeneron have started working on the antibody based therapies. However, to use these therapies clinically, adequate clinical testing is required. To win the race of COVID 19, it is essential to slow down the multiplication rate and spread rate of the virus otherwise it could results in higher death rate. Many countries are following the most effective route of alleviation which is the identification and isolation of the infected or suspected patients. South Korea had scaled up the production of testing kits which helped them to come out of the problem, which the whole world is facing now. The government of South Korea had approved the four companies for the production of testing kits following the infection outbreak in China. Within a week, they were capable of conducting 20,000 tests per day. The same strategy is now getting followed in USA.

Companies working on the formulation of Corona virus Vaccines or antivirals along with their stage of development/testing: The following is the list of companies across the world which is working day and night, for the treatment of COVID 19.

Entos Pharmaceuticals: Entos pharmaceuticals is working on the development of Fusogenix DNA vaccine by utilizing the fusogenix platform. Fusogenix platform is nothing but a proteo lipid type vehicle which has the ability to directly introduce the genetic payload into the cells of the host. Payload containing multiple protein epitopes in an optimized concentration is being derived by utilizing the SARS CoV 2 proteins. It will work by stimulating the immune system of the host and enhance their immunity to fight with the pandemic.

University of Oxford: Oxford university has got success in the development of vaccine namely ChAdOx1 nCoV-19 for the treatment of Covid 19. This vaccine is an adenovirus vaccine vector which is developed by the Jenner Institute of Oxford University. The testing of ChAdOx1 nCoV-19 in the form of clinical trials is under process. The university has planned the conduct of clinical trials in Thames Valley Region and will enroll approx 510 volunteers of 18-55 years of age for the conduction of clinical trials (Lipworth, Chan *et al.*, 2020).

Roivant Sciences: Roivant sciences is working on the development of Gilmsilumab, a monoclonal antibody under clinical stage. This antibody targets the granulocyte macrophage colony stimulating factor (GM-CSF) which is found in high levels in the serum of Covid 19 patients. Targeting of GM-CSF is expected to lessen the lung damage and thereby reducing the no. of deaths in Covid 19 patients.

Altimmune: To develop the single dose vaccine for Covid 19, altimmune has collaborated with University of Alabama at Birmingham (UAB). The developed vaccine will be administered via intranasal route. Currently, they are working

on immunogenicity studies to develop the phase 1 clinical trial data.

MabBiopharma: A neutralizing antibody namely TJM2 has been developed by MabBiopharma with the mission to treat the severe cases of Covid 19. This will target GM-CSF which is responsible for the acute and chronic inflammation.

Medicago: Medicago has produced the virus like particles (VLPs) of the corona virus and drug candidates are being produced by the company. In collaboration with Laval University's Infectious disease Research Centre, this company is trying to develop the antibodies against SARS-Cov 2 virus. Canadian Institute for Health Research (CIHR) is funding the research.

Airway Therapeutics: AT-100 is an novel human recombinant protein developed by Airway Therapeutics and it is being explored by the company for the treatment of Covid 19. In preclinical studies, the drug has shown to reduce the inflammation and infection in the lungs and also generated the immunity against various respiratory diseases.

Tiziana Life sciences: Tiziana life sciences is also working on the development of monoclonal antibody namely TZLS-501 which is a human based anti interleukin- 6 receptor (IL-6R) attacking antibody which helps to prevent the lung damage and also enhances the levels of interleukin-6.

OyaGen: The investigational new drug product of the company is OYA1 which was developed for treating the cancer, initially but derelict due to the lack of efficacy. Further, the company has decided to conduct research on the same product for the treatment of corona virus infection. OYA1 has been found to be more effective than chlorpromazine HCl for the inhibition of replication of SARS CoV 2 in cell culture.

Algernon Pharmaceuticals: This company has also announced the exploration of their product NP-120 (Ifenprodil) as a treatment for Covid 19. Ifenprodil is an N methyl-d-aspartate (NDMA) receptor glutamate receptor antagonist which is sold under the name of Cerocal. This drug has improved the survivability of mice which was infected with H5N1.

Moderna and Vaccine Research Center: Moderna and Vaccine Research Centre which are the units of National Institute of Allergy and Infectious Diseases (NIAID) are working under collaboration for the treatment of corona virus infection. The prepared vaccine will be able to target the spike proteins of the corona virus.

Takeda Pharmaceutical Company: This company has shared their plans to develop the plasma derived therapy as a treatment against the corona virus infection. This therapy will be used to treat the higher risk patients. The therapy will be anti-SARS-CoV 2 polyclonal hyperimmune globulin therapy (H-IG). Concentrated pathogen specific antibodies derived from plasma of the recovered patients will be utilized under this therapy. These antibodies will be able to generate the immune response when injected to a new patient.

Serum Institute of India (SII): SII in collaboration with Codagenix, a US based biopharmaceutical company, is developing a treatment for the cure of Covid 19 infection. They are using a vaccine strain similar to the original virus. The developed vaccine is under preclinical stage while it will take further 6 months to start with the clinical trials. The

companies are expecting to launch the medicine in early 2022 (Antunes Filho, dos Santos, *et al.*).

Zydu Cadila: An accelerated research programme has been announced by *Zydu cadila* for the development of vaccine for Covid 19, which will use the involvement of 2 novel approaches. The first approach will involve the production of DNA vaccine against the viral membrane protein of virus while in the second approach, live attenuated recombinant measles virus vectored vaccine (rMV) will be developed.

Nano Viricides: This is a clinical stage company which is also working for the development of treatment for Covid 19. This company is utilizing the concept of nanoviricide technology. The company will develop ligands which will bind to the virus in the same way as cognate receptor and will attack the various proteins present in the virus.

Along with these companies, many more companies are also there who are working hard to get the promising treatment of corona virus infection. Along with the vaccine and treatment, there is a need to follow the principles of social distancing and daily cleansing as suggested by World Health Organization (WHO). The race against COVID-19 will therefore be won only if science is supported by the necessary social behavior.

Discussion and Conclusion

For the above literature it was reported about the basic epidemiology and etiology of Covid 19 along with its various mechanism of action in different pathways. The structure of Covid 19 is well elaborated with different types of receptors present on its surface which acts in different modes of actions. Along with it various elaborative methods of determination were discussed and mentioned their role in diagnosis and mitigation of the disease. By concluding all along with race of pharmaceuticals from herbals to current research of allopathic medicines which were used for uplifting immune systems and strength.

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