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CORONAVIRUS: A REVIEW

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Abstract: With the development and spread of the novel coronavirus a new public health disaster is being caused is endangering the whole globe. The illness is transferred by inhalation or contact with infected droplets, with a 2 to 14-day incubation period. Common symptoms include fever, cough, sore throat, dyspnea, and exhaustion. As of February 14, 2020, 49,053 laboratory-confirmed illnesses and 1,381 deaths had been reported worldwide. In reaction to the perceived risk of catching sickness, several countries have developed a variety of control measures. To summarize what we know about the virus and the present outbreak, we did a literature review of publicly available material. The protein of coronavirus, its life cycle, non-structural proteins, symptoms, and techniques for doing in-silico research on COVID, its relationship with the neurological system, detection strategies, and current treatments are all discussed in this literature review.

Keywords: Coronavirus, structural proteins, symptoms, diagnosis, Drug repurposing, diagnosis, detection, medicines.

INTRODUCTION:

The China Health Authority notified the World Health Organization (WHO) in December 2019 of several instances of pneumonia of unknown cause in Wuhan City, situated in Hubei Province in central China. Swab test from patients' throat revealed new coronavirus, and WHO classifies it as Coronavirus-2019 at first (Hui *et al.,* 2020). Coronavirus Study Group renamed this infectious agent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and WHO renamed the ailment caused due to this pathogen as coronavirus disease 2019 (COVID-19). Coronavirus has a significant mortality rate (Burkhi, 2020). In China, 9720 people were sick, of which 213 died, and 106 people were afflicted in 19 different countries (Zhou *et al.,* 2020). In essence, coronavirus is a class of positive and uni-stranded RNA virus that has a deep assortment and enclosure and spikes like surface protrusions which give it a crown-like appearance when viewed in the electron microscope and based on appearance, is referred to as coronavirus (Singhal, 2020). Fever, weakness, and cough were the fundamental manifestations of COVID-19, which were seen to be similar to SARS-CoV and MER patients (Liu *et al.,* 2020). The pathogen belongs to the subfamily Orthocoronavirinae, Coronaviridae family, order Nidovirales. Members of Coronavirinae subfamily are classified into four genera: viruses that can infect Homo sapiens are classified as α- and β-coronaviruses. Gamma coronavirus and delta-coronavirus is discovered uniquely in the animals as Gamma-coronavirus encompass viruses that infect whales and birds while Delta-coronavirus includes infections that are secluded from pigs and birds (Harapan *et al.,* 2020). The illness is strongly connected to group of SARS-like beta-coronaviruses found in the bats lately in China, according to phylogenetic examination of the whole viral genome (Hu *et al.,* 2018) The bat was surmised as a virus natural repository host based on sequencing and development investigations (Giovanetti *et al.,* 2020, Paraskevis *et al.,* 2020). Because Wuhan's marketed bats were not available and comparative buildups of virus receptor were seen in numerous species. Turtles, pangolins, and snakes were proposed as elective transitional hosts (Liu *et al.,* 2020, Zhang *et al.,* 2020). As an emergent intense respiratory irresistible disease, COVID-19 spreads through the respiratory tract by globules, respiratory discharges, and spit (Li *et al.,* 2020, Rothe *et al.,* 2020). The Angiotensin-Converting Enzyme 2 receptor is abundant throughout the respiratory system as well as in the salivary gland epithelial cells that have been exhibited to be SARS-CoV early targets (Yang *et al.,* 2020). Transmission route of Coronavirus can be seen in figure 1 (Dhama *et al.,* 2020). Coronaviruses contain a 30-kb un-segmented, single-stranded, positive-sense RNA genome encased by a 5-cap and 3-poly (A) tail. The SARS-CoV-2 genome is 29,891 bp long and has a GC content of 38%. They are comprised of an envelope containing a viral nucleocapsid with a helical symmetry of these capsids. Some other genes are also known additional genes. These genes are mixed with structural genes (HE). The positive-sense genome of coronavirus works as mRNA and is translated to 1a/1ab (pp1a/1ab) polyprotein. Then a replication

transcription complex (RTC) is made up of nonstructural proteins (Nsps), coded by the polyprotein gene in double membrane vesicles (DMV). Later, Subgenomic RNA is arranged by the RTC through a process of discontinuous transcription (Fehr *et al.,* 2015, Chan *et al.,* 2020, Brian *et al.,* 2020).

CORONAVIRUS STRUCTURAL PROTEINS:

Spike proteins, nucleocapsid proteins, envelope proteins, and membrane proteins are major structural proteins. The viral genome's 3" end encodes all of these structural proteins (Wang *et al.,* 2020).

- **S-Glycoprotein:** it is multi-role class I viral transmembrane a protein having a lot of different functions. The amino acid of protein varies between 1,160 and 1,400 (Belouzard *et al.,* 2015). It gives a crown like similar appearance when it sits in a trimming position on the virion's surface. By interacting with multiple host cell receptors, infectious virion particles are able to enter the cell with the help of S protein (Beniac *et al.,* 2006). These proteins have two domains: a big ectodomain and a small endodomain (Millet *et al.,* 2014). Ectodomains are differentiated into two subsets, S1 and S2, and have akin domain layout in all Coronavirus S proteins. The S1 subunit aids in host's receptor binding, while the other subunit aids in melting. The former subunit is also separated in 2 domains i.e. N-terminal and C-terminal domain. NTD and CTD serve as binding domains for receptors (Belouzard *et al.,* 2015, Li *et al.,* 2016). The S-protein can connect with ACE2 receptor present on host's cell surface (Tortorici *et al.,* 2019). At the boundary of many CoVs, the spike is divided into S1-S2 subunits (Kirchdoerfer *et al.,* 2016). The TMPRSS2 (Millet *et al.,* 2015) as well as cathepsin (Simmons *et al.,* 2005) induce the trimmer S protein to be cleaved.
- **M Protein:** Most protein-protein interactions are facilitated by the protein M, which is necessary for coronavirus assembly. When the proteins M and E are expressed together, they create virus-like particles (VLPs), which form coronavirus envelopes. It has three transmembrane domains, with a short amino end on the outside and a long carboxy terminus on the interior (Arndt *et al.,* 2010). M monomer has a molecular mass ranging from 25 to 30 kDa. The tiny N-terminal as well as C-terminal endodomain found interior or on intracellular membrane of cytoplasma make up a substantial percentage of this molecule (Kuo *et al.,* 2016). It resides as a dimer with two distinct configurations, according to one research, this allows it to increase membrane curvature and adhere to the nucleocapsid (Neuman *et al.,* 2011).
- **E Protein:** It is most enigmatic protein. It is smallest of the critical structural proteins; vary in size from 8-12 kDa (Masters, 2006). These proteins are substantially less abundant in the virion. These proteins act as viroporins (ion channels) and perform a variety of roles in the assembly, pathogenesis, and release of virus (Nieto *et al.,* 2014, Castaño *et al.,* 2018). E proteins are tiny integrated membrane polypeptides with the same general structure among coronaviruses: a brief hydrophilic N-terminus, a huge hydrophobic area, and a big hydrophilic C-terminal tail (Schoeman *et al.,* 2019).
- **N Protein:** It's a nucleocapsid protein that's found in helical nucleocapsids. It consists of two well-preserved, separately plying domain, N and C-terminal. In vitro, both domains can bind to RNA, although each domain has its own binding mechanism. This protein contributes a variety of roles, including assisting in the creation of complexes during viral assembly, facilitating M protein interaction, and promoting virus transcription efficiency (Chang *et al.,* 2006, Hurst *et al.,* 2009).

CORONAVIRUS LIFE CYCLE: S-proteins interact with host receptors, causing viruses to first attach to host cells. Because S proteins have 2 subunits, the S1 subunit, which promotes receptor binding, and the S2 subunit which promotes virion and cell membrane binding, due massive structural changes in S2 subunit. The SARS-CoV receptor is Angiotensin-converting enzyme 2 that is found primarily in epithelial cells of the lung and small intestine, and in other tissues (Hamming *et al.,* 2004) This is followed by another proteolytic cleavage by TMPRRS2, cathepsin or protease that permits the virus to enter the host cell's cytoplasm (Kleine *et al.,* 2018, Park *et al.,* 2016). A fusion peptide is then broken up at S2 and an antiparallel six-helix group is formed when two heptad repeats are combined in S2. The fusion of viral and cellular membranes results in the viral genome being transported to the cytoplasm (White *et al.,* 2016). The next stage of this life cycle is the translation of the replicase gene from virion genomic RNA. Rep1a and rep1b, two enormous ORFS encoded by the replicase enzyme, which express pp1a and pp1ab (Baranov *et al.,* 2005). pp1a and pp1ab Polyproteins include the nsps 1–11 and 1–16 respectively. Polyprotein cleavage mechanisms may be classified into two categories that separate these polyproteins into individual Nsps. The first kind includes one or two papain-like proteases located inside Nsp3 that perform particular separations of Nsp1, 2, and 3. Left 11 cleavages are performed by the primary protease (Mpro), Nsp5. Large number of Nsps then congregates in the replicase-transcriptase complex to provide perfect environment for RNA synthesis (Neuman *et al.,* 2014). RTC is anchored to intracellular membranes by several transmembrane helices seen in Nsp-3, 6, 4 and rep 1a products (Oostra *et al.,* 2008). Nsp3 is the most prevalent of all RTC proteins. A hypervariable acidic N-terminal region (Ubl1) and greatly conserved C-terminal region (Y domain) are responsible for the protein's structure (Neuman *et al.,* 2008). The genome is bound to RTC via Ubl1's interaction with the SR region of N protein, which promotes the development of the RNA synthesis initiation complex (Hurst *et al.,* 2010, Keane *et al.,* 2013). The following stage is the translation and assembly of the viral replicase complex. There are both genome and subgenomic RNAs that are synthesised during viral RNA production. For structural and auxiliary genes, sub-genomic RNAs act as messenger RNAs (mRNAs) and viral RNA replication requires several cis-acting sequences (Brown *et al.,* 2007). The viral structural proteins are translated and incorporated into the endoplasmic reticulum after replication and

transcription. These proteins are then secreted to the endoplasmic reticulum-Golgi intermediate compartment (ERGIC), where N proteins wrap viral genomes by bridging into ERGIC membranes containing viral structural proteins, resulting in mature virions. M mediates protein-protein interactions in the formation of coronaviruses. Virions are assembled and transported to the cell surface in vesicles before being released by exocytosis (Wong *et al.*, 2015). The entrance of the coronavirus into the target cell is the first critical step in the replication cycle. In this stage, S glycoprotein binds efficiently to a protein-receptor which is present on surface of cell. On the virion surface, the S protein of coronavirus is found as a trimer. It is a glycoprotein of type 1 which involves S1 and S2 subunits. The stalk is formed by the expanded S2 portions of the spike trimer, which are principally responsible for initiating the fusion of the viral envelope and target cell membranes. The S1-NTD largely promotes viral binding and entry by interacting with glycans on the host cell surface (Li, 2016, Hulswit *et al.*, 2016). The N- and C-terminal domains of S1 region are thought to be receptor binding regions (Walls *et al.*, 2016). To enter host cells, the S1-CTD of most known alphacoronaviruses interacts with aminopeptidase N. The alphacoronavirus HCoV-NL63, on the other hand, makes use of angiotensin-converting enzyme 2 (ACE2), a type-I membrane glycoprotein with a large N-terminal ectodomain composed of two alpha-helical lobes (Wu *et al.*, 2009).

CORONAVIRUS AND NON-STRUCTURAL PROTEINS:

The largest genome containing structural, accessory gene, extensive replicase and nonstructural proteins are of coronavirus (Gorbalenya *et al.*, 2020). The ORF1a/b portion of virus genome, which then translated in pp1a (Nsp1-11) and pp1ab (Nsp1-16), makes up two-thirds of the genome (Cui *et al.*, 2019). Along with viral RNA and Nsp1-16, four structural proteins are used to accelerate virus replication within host cells: envelope (E), matrix (M), phosphoprotein nuclear capsule (N), and spikes (S) (Kang *et al.*, 2020). 16 nonstructural proteins are produced from severing ORF1ab Gene that cause polypeptide expression (Yoshimoto, 2020). NSP3 and NSP5 are two protease enzymes generated from ORF1ab. NSP13 is a guanosine N7-methyltransferase, NSP14 is an endoribonuclease, and nsp16 is a 2′-O-ribose methyltransferase. Functions of these proteins are: NSP3 and NSP5 act as proteases. Nsp13, 14, 15 and 16 are enzymes involved in viral RNA post-translational modification, or 5′-capping modification as well as enable viral RNA to evade the host's inborn immune system. NSP12 is required for RNA replication. ADP-ribose phosphatase activity (NSP5) is required for posttranslational modification and NSP14/NSP15 for exoribonuclease/ endoribonuclease activity (Yoshimoto, 2021). NSPs 1 to 3 are severed by papain-like protease (Nsp3), and 3CLPro, or 3-chymotrypsinlike proteinase, cuts the C-terminus from nsp4 to 16 in coronaviruses (Serrano *et al.*, 2009). In the Nsp virus-encoded replication/transcription complex, the virus replicates and transcribes itself. All of RTC components are encoded by the gene replicase (Orf1a and Orf1b). Early RTC is an essential step in the maintenance and synthesis cycle of subgenomic mRNA with SARS-CoV-2. The RTC is made up of several proteins, including the nonstructural proteins Nsp3, Nsp4, and Nsp6, which help develop sites for synthesis of viral RNA Nsp5: the salient protease, the Nsp7–Nsp8 primase complex, Nsp12: the prime RNA-dependent RNA polymerase, the helicase/triphosphatase (Nsp13), the exoribonuclease (Nsp 14), the endonuclease (Nsp15) and the N7- and 2′O- methyltransferases (Nsp10/Nsp16) (Angelini *et al.*, 2013).

CLINICAL MANIFESTATIONS:

SARS-CoV major symptoms range from mild to life-threatening in severity. The virus takes 4.6 days to evolve (Chiu *et al.*, 2003). Estimated average duration of symptoms is ten days (Donnelly *et al.*, 2003). Coronavirus symptoms include fever, a dry cough, myalgia, dyspnea, headache, sore throat, sputum production, and rhinorrhea (Booth *et al.*, 2003, Chan et al., 2003). The infection can be further characterized by abnormal lung scan findings. Small percentage of patients experience respiratory failure, multiple failures of organs and demise (Chiu *et al.*, 2003). Acute Respiratory Distress Syndrome, cytokine storm, and coagulation dysfunction are more likely in the elderly and those with underlying conditions such as hypertension, chronic obstructive pulmonary disease, diabetes, and cardiovascular disease, among others (Huang *et al.*, 2020, Chen *et al.*, 2020). According to the researchers, SARS-COV-2 causes an inflammatory reaction in the lower airway, which might lead to lung injury (Lee *et al.*, 2003). The lung is the most affected organ. During imaging investigations employing computer tomography or X-rays, lesions can be identified in several lung lobes (Lin *et al.*, 2020). When virus particles infiltrate the respiratory mucosa, they trigger immune responses and a cytokine storm (Assiri *et al.*, 2013). The first anti-viral defense barrier is IFN-β secretion as shown in Figure 1.3. In the case of coronavirus, viral replication and the consequent suppression of adaptive immune responses may reduce IFN- production. Furthermore, viral replication produces hyperinflammation, which results in a high production of pro-inflammatory cytokines and chemokines, particularly by neutrophils and monocytes/macrophages (Prompetchara *et al.*, 2020, Cheung *et al.*, 2005). A "cytokine storm" is seen in severe cases of COVID-19 patient, which amplifies immune responses and leads to viral sepsis and ARDS. Some elderly people and others with fundamental ailments die as a result of these intensifications (Huang *et al.*, 2020). The innate immune system perceives viral ‘molecular patterns (Akira *et al.*, 2006) whereas adaptive immune system obliterates virus-tainted cells utilizing T and B cells that contain pathogen-specific antibodies. Hindering virus replication, advancing virus expulsion, initiating tissue repair, and setting off a long-lasting adaptive immune response to viruses are all part of a well-regulated immune response (Li *et al.*, 2020). T cells are exposed to CoV antigens by infected cells. As a result of this process, T cells are activated and differentiated, and cytokines associated with various T cell subsets (Th1/Th17) are produced. Cytokines attract lymphocytes and leukocytes to the infection site. Adaptive immunity is mediated by a fraction of developed T cells, as well as the activation of B and plasma cells, which produce monoclonal antibodies. Immune cell activation increases the production of chemokines and other cytokines, which create a pro-inflammatory response and attract cells like neutrophils and macrophages to infection sites. As a result, damage molecules such as matrix metalloproteinases and reactive oxygen species (ROS) are released by these cells. The term

"cytokine earthquake" refers to the secretion of large amounts of immune mediators, which leads to more extreme conditions. Immune responses must be controlled in order to clear the infection (Tizaoui *et al.,* 2020). The ACE2 receptor is richly present all through the respiratory tract as well as in the salivary gland epithelial cells that have been exhibited to be SARS-CoV early targets (Yang *et al.,* 2020). A risk map for 2019-nCoV infection was created by Zou *et al.,* using scRNA-seq data from organs like nasal mucosa, the respiratory tract, bronchus, and lung. AT2 cells in the lungs and respiratory epithelial cells have significant ACE2 expression according to researcher's discovery (Zou *et al.,* 2020). On the other hand, genes involved in viral procedure, such as viral life cycle, viral assembly, and viral genome replication, were highly expressed in ACE2-expressing AECII according to gene ontology enrichment analysis. Corona viral replication in the lung is therefore enhanced by AECII that expresses ACE2. This suggests that the respiratory system is a sensitive site for SARS-CoV-2 infection (Zhao *et al.,* 2020).

STRATEGIES USED TO CONDUCT IN SILICO RESEARCH ON COVID-19: Researchers all around the world have used a diverse range of tactics and procedures to conduct a number of research initiatives that focus SARS-CoV-2 protein as a potential target to identify potential inhibitors for treatments of COVID-19. Natural chemicals that can act as inhibitors were extracted from natural sources, drug repurposing and other techniques were the most prevalent strategy. The literature review drew on data from public databases such as Pubmed and Google Scholar. Different enzymes of SARS-COV-2 were targeted, but RNA polymerase or the main viral protease, 3CLpro, were the primary targets since these proteins play an important function in virus reproduction and transcription, according to the prior literatures analysis (Froggatt *et al.,* 2020, Mohammad *et al.,* 2020).

In-silico Drug repurposing studies: The fatal contagious disease COVID-19 currently has no therapeutic options accessible (COVID-19). Drug repurposing, in contrast to de novo drug discovery, is a process for exploring new uses for licensed or experimental drugs. It is a very successful drug discovery technique since it requires less time and money to find a therapeutic agent (Singh *et al.,* 2020). Many researchers have used this technique to identify prospective new pharmaceuticals from existing treatments that have already been approved. For instance, to investigate known medicines against coronavirus 3CL hydrolase and protease enzymes, Elmezayen *et al.,* used this technique in May 2021 in which they discovered protease inhibitors using the ZINC15 database. In the beginning, the 3D structure of the human TMPRSS2 gene was produced using a homology modelling technique. The results revealed possible Mpro enzyme inhibitors that were Talampicillin, Lurasidone, ZINC000000702323 and ZINC000012481889. In addition, Rubitecan and Loprazolam medicines, as well as chemicals ZINC000015988935 and ZINC000103558522, have been found as promising inhibitors of TMPRSS2 (Elmezayen *et al.,* 2021). Maffucci *et al.,* nearly evaluated 3000 compounds against the Mpro and the S-protein, in 2020. When combined with ritonavir, indinavir, atazanavir, and lopinavir were found to alleviate the symptoms of mild-to-moderate SARS-CoV-2 infection. Polymyxin B, colistin, and daptomycin, as well as terlipressin, lypressin, and thymopentin, were effective against SARS-Cov-2 RBD (Maffucci *et al.,* 2021). In order to overcome in silico virtual screening's limitations, Trezza *et al.,* applied a strong in silico technique to pharmacological repurposing in 2020. To find a Spike protein - ACE2 interaction inhibitor, they coupled and integrated docking simulations with other techniques. Lumacaftor and Simeprevir bind to the receptor binding region of Spike protein with great affinity, preventing ACE2 receptor engagement, according to findings (Trezza *et al.,* 2020). Sachdeva *et al.,* also used numerous antimalarial medications for repurposing against the S-protein and the Mpro in October 2020. DOX can be a promising candidate for COVID-19, according to the in silico technique report (Sachdeva *et al.,* 2020). In order to discover a cure for this disease, many researchers repurposed FDA-approved medicines. Kumar *et al.,* for example, used molecular docking-based virtual screening to screen FDA approved antiviral medicines against the Mpro in 2020. Top three medicines were subjected to further molecular dynamic simulations to determine their binding affinity and stability in the Mpro active site. In docking tests, the top 10 medications were found to have strong binding affinity, whereas the top three medications, Lopinavir/Ritonavir, Tipranavir, and Raltegravir, were evaluated for conformational stability in the active region of the SARS-CoV-2 Mpro protein (Kumar *et al.,* 2020). Similarly, The Nsp13 and Nsp14 helicases of SARS-CoV-2 were modelled in silico, and FDA-approved antiviral medicines were repurposed as dual inhibitors by Gurung in 2020. In this, comparative homology modeling approach was utilized to develop in-silico model of Nsp13 helicase and Nsp14 protein of coronavirus and then these model structures were validated. FDA-licensed antiviral medicines were screened virtually using these models. Simeprevir, Paritaprevir and Grazoprevir were discovered as leads. They were identified as potential duo target inhibitors because they demonstrated more binding affinity to both Nsp13 helicase and Nsp14 than the reference (Gurung *et al.,* 2020). A Coronavirus disease was predicted to be treatable with Dextromethorphan coupled with Prednisolone and Dexamethasone which are in 2020 by Sarkar *et al.,* using in silico screening. They utilized tertiary structure of major protease (Mpro) of Coronavirus as the target in their investigation and repurposed three common cold medications to act as anti-covid agents: dextromethorphan, prednisolone, and dexamethasone (Sarkar *et al.,* 2020).

In-silico approach to find novel lead compounds derived from natural sources: Many researchers are concentrating their efforts on discovering novel natural-source lead compounds that act as inhibitors for coronavirus different enzymes and proteins. Natural flavonoids and synthesised indole chalcones were the focus of Vijayakumar *et al.,* studies in 2020. They went after RNA dependent RNA polymerase, Mpro that is main protease, and Spike protein. According to findings, 30 substances out of twenty three natural flavonoids and twenty five synthetic indole chalcones have capability of deactivating Mpro and perhaps reducing Mpro function efficiency. Quercetin is known to impede contact sites on the viral spike, while Cyanidin may impair RNA polymerase function. These findings imply that flavonoids and their pharmacological cousins, indole chalcones, can combat SARS-CoV-2 (Vijayakumar *et al.,* 2020). Likewise, by employing an in silico technique, various African plant

alkaloids and terpenoids were tested to see if they could behave as possible inhibitors of the coronavirus 3CLPro. Inhibitors 3CLpro-referenced were compared to the docking scores (Lopinavir and Ritonavir). According to this ligand-protein interaction study, greater than half of the top 20 alkaloids and terpenoids interacted well with coronaviruses 3CLpro, with binding affinities that surpassed those of lopinavir and ritonavir (Gyebi *et al.,* 2021). Maya *et al.,* used an in silico technique to target S-CoV-2 Mpro by using natural compounds from Centella asiatica. In this study, 11 C. asiatica molecules were docked with Mpro and their pharmacokinetic properties were evaluated. Asiatate 6 was recommended for further investigation as Mpro inhibitor in light of these results (Maya *et al.,* 2021).

COVID-19 AND NERVOUS SYSTEM: COVID-19 has been linked to a variety of neurological symptoms, according to the research. As per study, greater than 35 percent COVID-19 sufferers experience neurological symptom. Certain patients might develop symptoms as the illness worsens (Jiang *et al.,* 2020). The neurological indications and symptoms were divided into two categories: those related to the central nervous system and to peripheral nervous system (Niazkar *et al.,* 2020). A principal docking receptor for SARS-CoV-2 is ACE-2 which has been found in human brain vessels as well (Hoffmann *et al.,* 2020). There are a plethora of possible brain entry routes including Nervous System Invasion, Nervous System Invasion, Blood-Brain Barrier Invasion, and so on. This virus can infect neuron and cause neuronal death, according to experiments in human ACE2 transgenic mice. In brain cells derived from human pluripotent stem cells, dopaminergic neurons were extremely vulnerable to SARS-CoV-2 infection (Yang *et al.,* 2020). Blood borne virus commonly enters brain through the blood-brain barrier (Bergmann *et al.,* 2006). Cytokines that are associated with SARS-CoV-2, such as interleukin 6, 1b, 17, and tumour necrosis factor (TNF), disrupt the BBB, potentially allowing the virus to enter the body (Erickson *et al.,* 2018). COVID-19 has been linked to a number of CNS symptoms, according to the literature. With prevalence ranging from 6.5 to 23 percent in various studies, the most frequent CNS symptom is headache (Rodriguez *et al.,* 2020). 138 patients that were hospitalized with this illness were having dizziness (13 patients) or headache (9 patients) in a research (Wang *et al.,* 2020). The patients that are more likely to experience disease severely might appear with encephalopathy as well as confusion (Filatov *et al.,* 2020). An estimated 9.0 percent of COVID-19 participants expressed perplexity in study (Chen *et al.,* 2020). Patients with severe condition, cerebrovascular disorders are one of the most common ailments. CVDs such as acute ischemic stroke can also be caused by COVID-19 (Wang *et al.,* 2020, Morelli *et al.,* 2020). Some COVID-19-infected critically sick individuals have a strong tendency to form blood clots (Violi *et al.,* 2020). COVID-19's PNS signs and symptoms are milder. SARS-COV-2 is distinguished by anosmia, ageusia, which are common PNS symptoms. These symptoms may be accompanied by nasal symptoms such as nasal obstruction or excessive nasal discharge (Vaira *et al.,* 2020). TMPRSS2 and ACE2 are expressed in sustentacular cells, allowing coronavirus to transneuronally spread in brain via olfactory pathway and infiltrate the olfactory neuroepithelium resulting in anosmia (Xydakis *et al.,* 2020, Moein *et al.,* 2020).

DETECTION OF COVID-19: COVID-19 must be diagnosed accurately in order to be controlled. COVID-19 can be diagnosed using a variety of different methods. In general, molecular techniques, serology, and viral culture are used as diagnostic tools. Patient's first laboratory examinations include a complete blood count, coagulation testing and serum biochemistry tests. SARS-CoV-2 is likely to target lymphocytes (especially T cells) in most patients, according to laboratory testing as there was a considerable reduction of total lymphocytes in the vast majority of patients. Reduced lymphocyte counts could be used to diagnose SARS-CoV-2 infection and severity (Li *et al.,* 2020). Diagnosis is also made using infrared sensors and thermal scanning technology. It is necessary for pre-diagnosis screening. A thermal camera are installed detect people with a rising body temperature. Such cameras must be able to scan a distance of at least 10 metres. It has since been expanded to other hospital entrances and departments. Infrared radiation is detected and captured as heat by thermal cameras, which then converts it to a visual image (Lee *et al.,* 2020). The NAAT (Nucleic acid amplification test) is used to confirm the illness using nasal swabs or blood samples using a real-time fluorescence polymerase chain reaction (Wu *et al.,* 2020). The US Food and Drug Administration (FDA) and other regulatory agencies have granted the use of COVID-19 diagnostic kits based on RT-PCR technology for emergency purposes. As the first commercial diagnostic kit to perform tests ranging from moderate to high complexity, Cobas SARS-CoV-2 set the bar high (Lippi *et al.,* 2020). Due to the limitations of Nucleic acid amplification test, Chinese scientists have proposed that CT imaging be utilized for diagnosing COVID-19 in the current circumstances (Ai *et al.,* 2020). It was proven in one study in which the patient had a sore throat and was feeling exhausted. Previously his Fluorescent Real Time Polymerase Chain Reaction test of sputum yielded negative COVID-19 results for first six days but later when he undergone chest CT scan, This indicated a number of peripheral ground-glass opacities in both lungs, with greater involvement in the left upper lobe and liner segment of the left lung. According to this group, ground-glass opacities in the lungs progressed after three days of hospitalization due to COVID-19 (Huang *et al.,* 2020). New COVID-19 diagnosis and treatment technique include using CRISPR/Cas13 (Nguyen *et al.,* 2020).

CURRENT MEDICATION FOR TREATING COVID-19:

According to studies from the World Health Organization, Food and Drug Administration and the Centers for Disease Control and Prevention, no effective drug, therapy, or vaccine for the prevention and treatment of SARS-CoV-2 infection has yet been produced or licensed. However, the current medications used to treat COVID-19 individuals include Remdesivir, Chloroquine, Hydroxychloroquine etc (Samudrala *et al.,* 2020). SARS-CoV and MERS-CoV are among the viruses that Remdesivir (RDV) has been shown to have antiviral activity against (Gordon *et al.,* 2020). Analogue nucleotide Remdesivir has been shown to be a potent RNA polymerase inhibitor. Remdesivir has been authorized for treatment by the Food and Drug Administration in roughly 250 COVID-19-infected patients after it was evaluated on three patients in the United States and demonstrated

improvement in symptoms without substantial side effects. It drastically lowered mortality rate with 64 percent of cases showing improvement (Jean *et al.,* 2020). Covid-19 sufferers are also treated with chloroquine these days. The medicine chloroquine has already been authorized for the treatment of malaria, arthritis, and lupus by the FDA (Touret *et al.,* 2020). As per the existing research, the weak base chloroquine raises acidity levels in the TGN and lysosomal vesicles, resulting in the malfunctioning of enzymes required for processing of freshly generated viral proteins (Savarino *et al.,* 2003). SARS-CoV-2 infection can be treated more effectively and safely with hydroxychloroquine, a chloroquine hydroxy derivative. Animal investigations have revealed that it is less toxic than chloroquine (Liu *et al.,* 2020). Phazinecarboxamide derivatives and analogues, known as Favipiravir and RdRp is effectively and precisely blocked by this medication (McKee *et al.,* 2020). Protease inhibitors were previously used to treat HIV patients and the US Food and Drug Administration had authorised its usage (USFDA). Protease enzymes are principally responsible for the synthesis of structural and functional proteins from polypeptides such as pp1ab and pp1a, which aid in viral replication. 3-chymotrypsin-like enzyme, which is necessary for replication and synthesis of structural proteins, has been shown to be inhibited by protease inhibitors like lopinavir/ritonavir in in vitro studies of coronaviruses (de Wilde *et al.,* 2014).

CONCLUSION:

The current COVID-19 outbreak is unquestionably a worldwide health concern. Despite substantial advances in our knowledge of the pathogen, how it infects cells and causes disease, as well as clinical indications of illness, viral outbreak are expected to persist in future. Because the speed with which the disease is spreading, the illness monitoring system should be given more attention by governments throughout the world. As a result, efforts should be made, in addition to the present outbreak, to create comprehensive methods to minimize future zoonotic epidemics.

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