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An Update on Novel Corona Virus COVID-19 Outbreak: A mini review

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ABSTRACT
The current outbreak of COVID-19 which commenced at Wuhan City, Hubei canton, China, which arises and reported in December 2019. That migrated to Thailand, Japan, South Korea, India and a few other nations.Organizations like CDC and WHO are conterminously proving regular updates regarding the coronavirus. SARS is a type of viral pneumonia that is mostly related to severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Denominated SARS-CoV-2 that impacting the lower respiratory tract and manifesting as human pneumonia. Dry cough, fever, vomiting, diarrhea, pneumonia are the clinical features that are observed in the patient suffering from COVID-19. Due to minor qualitative pieces of evidence (mainly purpose controlled trails) is the most consequential constraint of current COV research, As of 09th April , 2020, The World Health Organization (WHO) data represents that more than 1356780 cases have been affirmed. Have been recognized worldwide, with 720219 of cases being detected in the Europe, and keep on increasing in number. In spite of the fact that till presently there's not an affirmed vaccine against the infection, subsequently combination treatment or elective therapies are utilized for the hindrance or to prevent the development of viral growth, Additionally, from the earlier experience of the administration of SERS-CoV and MERS-CoV organizations, numbers of an pharmaceuticals are being utilize within the 2019-nCoV strategy, but the main challenge for this virus is change of protein at functional and structural level, escalated spreading and mutation. In this review we have provided an insight on the origin, symptoms, and pathogenesis, diagnosis and treatment strategies available against COVID19.

Keywords: COVID-19, Wuhan City, SARS and MERS, SARS-CoV-2, pneumonia

INTRODUCTION

The latest coronavirus, originally identified as 2019-nCoV and now formally called as SARS-CoV2 (virus) and COVID-19 (virus) as Severe acute respiratory syndrome (SARS), belongs to the coronavirus family, which owes the title to its surface as crown-like spikes. Most delineate coronavirus square measure available in aves or mammals, especially in bats (https://www.isglobal.org/en/coronavirus).

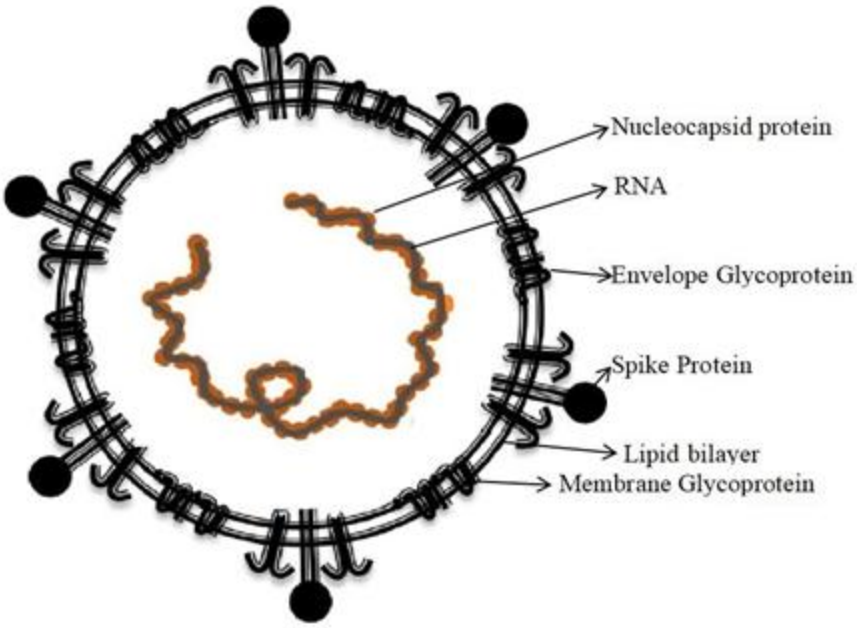

Figure 1: Schematic of coronavirus. The virus consist of nucleocapsid protein (N), which is a structured protein which shapes the genomic RNA complex and it communicates with membrane glycoprotein at virion assembly and improving the quality of transcription of virus. Spike protein (S) is a multipurpose protein that governs the entrance of coronavirus into the host cell. Envelope protein (E), is a small membranous protein that functions in ion-channel and also in the virion assembly. Membrane protein (M) which play a vital role in the viral assembly and to embedded the spike into viral envelope.

As per updates, it is mostly believed that the origin of coronavirus is a "local market" Situated in Wuhan where both dead, as well as live animals like poultry, marmots, snakes, fishes, birds, are sold widely, those markets are likely to be more prone to such viruses although the original animal source is not found yet it is likely to be a bat (1,2) (Figure 1).

Exactly at the tip of December 2019 cases of pneumonia with obscure etiology , cases were reported in Wuhan City, Hubei located in China, that was formally called as coronavirus disease in 2019 by the World Health Organization (WHO), The patient is observed most outstandingly influenced with sign and symptoms like pyrexia, tiredness, cough, and found to be as the bilateral lung infiltrates in imaging. Principally, cases are quickly resolved But others have experienced multiple fatal symptoms, including organ failure, pulmonary oedema, septic shock, extreme condition of pneumonia, and Acute Respiratory Distress Syndrome (ARDS), Nevertheless, people with intensive treatment with other comorbidities such as cerebrovascular, neurological, pulmonary, renal with respiratory problems is more prone to experience dizziness, anorexia and dyspnoea (https://www.isglobal.org/en/coronavirus) (2).

The International Committee on Taxonomy of Viruses rechristened the antecedently name 2019-nCoV as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Although antecedent studies have an affiliation between an area fish and therefore the wild animal market and most of the cases of infection, an denoting doable animal to human transmission afterward In fact, it exposes human to human SARS-CoV-2 transfer through droplets or direct touch and additionally noted that in a study it's according than over 40% of patient plausible hospital-related transmission of SARS-CoV-2(3). There are several committees which states the spread of COVID-19 and the robust therapy options are implemented (4).

SYMPTOMS

As per WHO, The COVID-19 virus influences very different populations throughout a number of

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ways.COVID-19 can be a respiratory illness and most affected.

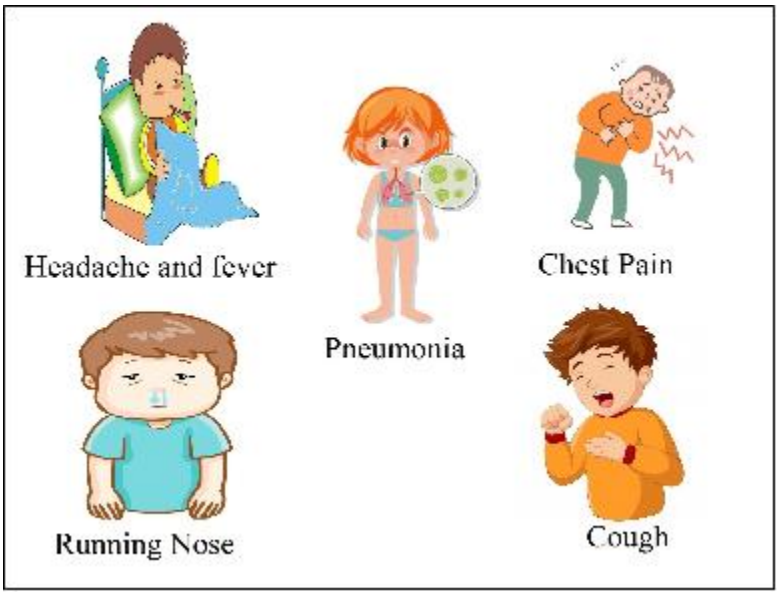

Figure 2: Coronavirus signs that may appear in patients with positive coronavirus diagnosis that could include pyrexia, nasal discernment, coughing, and many other signs.

individuals can experience moderate effects to alleviate and heal without medical care (Figure 2). Individuals who have fundamental restorative conditions and individuals over the last 60 years have the following a higher chance of creating serious illness and indeed passing. Mundane symptoms include pyrexia, lassitude, dry cough. Additional symptoms are: breathlessness, aches and torment, throat congestion, and exceptionally few individuals will report loose bowels, sickness or a runny nasal discerner (https://www.who.int/health-topics/coronavirus#tab=tab_3).

CORONAVIRUS DISEASES:-

Coronavirus Disease (COVID-19) seems to be a viral contagious disease triggered by a newly identified coronavirus. Many patients with COVID-19 infection should include mellow to direct respiratory ailment and rehabilitation without specific care being needed. Older persons and individuals who are at the origin of medical conditions, such as cardiovascular disease, asthma, chronic respiratory condition and cancer are most prone to experience severe illness (https://www.who.int/health-topics/coronavirus#tab=tab_1).

Pathogenesis of few coronavirus are given below

Human coronavirus:(HCoV)

Prior to the introduction of SARS-CoV, two proto-typed human coronavirus, OC43 and 229E, are common cold etiologic agents (3).Since SARS-CoV was identified, two incipient human coronavirus associates with respiratory disease have been reported. HKU1 may be a Group II coronavirus isolated from pneumonia-associated aged patient (4). This virus was difficult to cultivate in cell culture, and a very few data on this virus 'biology is available. HCoV-NL63 is a category-I coronavirus extracted from a seven-monthly infant suffering from bronchiolitis and conjunctivitis within the Netherlands. HCoV-NL63 has been linked with extreme respiratory problems, Upper respiratory infection, pneumonia, and bronchiolitis (5).

Murine coronavirus (MHV)

The strain of murine coronavirus or MHV presents several specific tropisms and degrees of virulence. brain and liver are basically tainted by commonly utilized research facility strains and Hence, offer the species models for encephalitis and hepatitis and the immune-mediated demyelination infection that creates contamination after sometime, cresting almost 1-month post-infection.Viral removal and pathogenesis in the central nervous system are roles of the immune response to MHV infection . For the protection against coronavirus infections both antibody and cell-mediated immune response is

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required. For the clearance of viruses during acute infection, the primary obligation rests with CD8 + and CD4 plus T (6).

Porcine coronavirus

Studies have been done on different porcine coronavirus (7,28,29). In 1946, the transmissible gastroenteritis virus was recognized. It was blamed for the development of fetal diarrhea and viral enteritis in pigs.; the economic loss was a major result as it occur most chronic in neonates with impermanence. In neonates, small intestine epithelial cells have been contaminated with Transmissible Gastroenteritis Virus (TGEV) contributing to possibly lethal gastroenteritis. The upper respiratory system is often infected, though not frequently in the lungs (7).

Avian coronavirus

Particularly infectious infections in poultry is caused by *infectious* bronchitis virus(IBV); As this is transmitted by aerosol, which is of great economic benefit to the poultry industry. It replicates in upper respiratory tissues, as reported in Turkey and pheasants infecting bronchus and severe disease in young animals. Some IBV strains induce more systemic illnesses and replicate in certain tissues, along with the kidney (by occurrence of nephritis), the oviduct (by limiting egg secretion), and the intestines(28). Hens of all ages are vulnerable, but quite young chickens display extreme respiratory symptoms and experience far higher mortality than older ones. The protection mechanism regarding IBV-induced infections is not fully apparent(27,28).

Feline coronavirus (FeCoV)

Two bio-types form the feline coronavirus. During multicat environments, the feline enteric coronavirus (FeCoV), is found mainly in an non-symptomatic carrier condition, which leads to seroconversion. The Feline infectious peritonitis virus (FIPV) which is a less prevalent variant of FeCoV has the potential to reproduce in macrophages and induce an astringent and deadly disease. FeCoV seems to have a virulent form, FIPV which is used for chronic infections. Replication of FIPV primarily occurs in the pharyngeal network's respiratory or intestinal epithelial cells(30). The macrophage infection then contributes to viremia and systemic virus dissemination, together with abdominal and thoracic cavity inflammation that triggers neurological disorders and occasional ocular disorders (7).

Bovine coronavirus (BCoV)

The universal virus BCoV, is diagnosed with serology. BCoV, including calf diarrhea, winter dysentery in adults and respiratory diseases in livestock of all ages, including those with moving fever, induces respiratory as well as peculiar illness(28). When viruses are isolated, bovines either with respiratory or enteric diseases are similar antigenically. The serum antibody correlates with immunity as per Epidemiological studies (7).

VIROLOGY

Coronaviruses is a single-stranded RNA genome(26-32 kb) encloses viruses, with spherical and Usually pleomorphic virions with a diameter of around 80 to 120 nano metres (8),there are total four range of coronavirus genera (a, b, g, d) are known albeit, with human coronavirus (HCoVs) that are detected within the coronavirus (HCoV-229E and NL63) and b coronavirus (MERS-CoV, ARS-CoV, HCoV-OC43, and HCoV-HKU1) genera (https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd). The RNA genome is complexed with the fundamental nucleocapside (N) proteins that make up a spiral capside located inside the viral genome. The coronavirus membrane should contain a minimum of 3 viral proteins (https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd) (Figure 3 A and 3 B).

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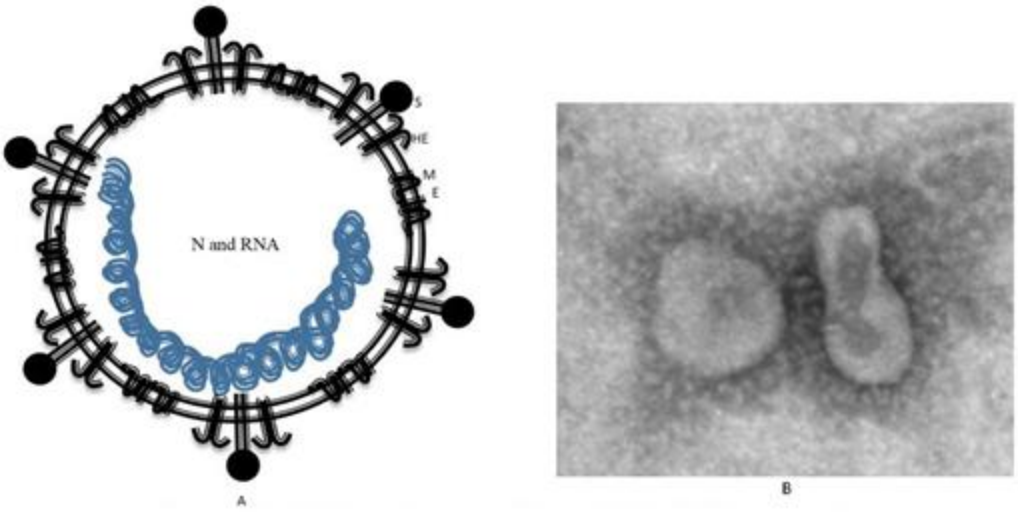

Figure 3: (A) Schematic of virus. The structure include a interior helical RNA protein which is incorporated by glycoprotein,nucleocapsid protein (N), which is a structured protein which shapes the genomic RNA complex and it communicates with membrane glycoprotein at virion assembly and improving the quality of transcription of virus. Spike protein (S) is a multipurpose protein that governs the entrance of coronavirus into the host cell. Envelope protein (E), is a small membranous protein that functions in ion-channel and also in the virion assembly. Membrane protein (M) which play a vital role in the viral assembly and to embedded the spike into viral envelope. (B) MHV particles electron micrograph.

Around 88 per cent of the isolated novel b-CoV demonstrates similarity to the series of 2 severe acute respiratory syndromes (SARS) originating from bat. kind of similar to bat-SL-CoVZXC21, bat-SL-CoVZC45, coronavirus, And 50 per cent identity of the MERS-CoV sequence (8). The International Virus Classification Commission named novel b-CoV as "SARS-CoV-2" (8) (Figure 4).

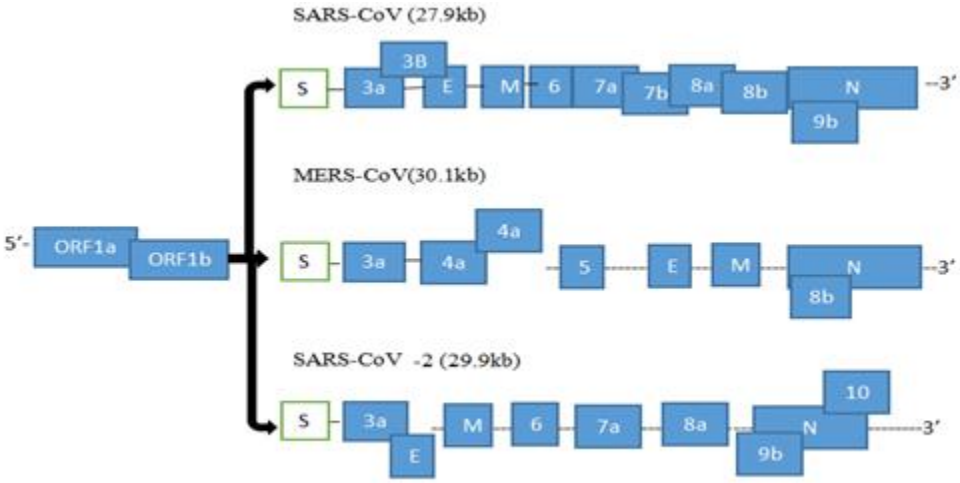

Figure 4: Genomes of SARS-CoV(27.9kb), MERS-CoV(30.1kb), SARS-CoV2(29.9kb). corobavirus consist of 25-33 kb of optimistic-sense single stranded RNA (ssRNA) genome. Mostly the 2/3 of the genomes encodes for 5' - terminal of ORFa/b polyprotein that further takes shape of transcriptase complex.

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Table 1: Different classes of virus alongwith the host on which it act and the infection caused by them.

Class	Virus	Host	Infection caused
I	Human coronavirus 229E	Human	Respiratory Tract
	Porcine respiratory coronavirus	Piglets	Respiratory Disease
	Canine coronavirus	Dogs	Leucopenia, gastroenteritis and diarrhea(2)
	Feline enteric coronavirus	Cats	severe enteritis(3)
	Transmissible Gastroenteritis Virus	Piglets	Respiratory and enteric infection
	Human coronavirus *NL63*	Humans	Severe Acute Respiratory Syndrome (SARS)
II	HCoV-*OC43*	Humans	common cold
	Mouse Hepatitis Virus	Rat	Hepatitis,encephalomyelitis, etc
	Bovine Coronavirus	cattle	Respiratory infection, diarrhoea, rhinitis
	HCoV-*HKU1*	Humans	Upper and lower respiratory infection
	SARS-CoV	Humans	Respiratory Infection
III	Infectious bronchitis virus	Aves	bronchitis

COVID19 SPREADING:

According to WHO, The primary route of communication is through atmosphere, through tiny droplets created when an infected individual coughs or sneeze. It is communicated by directly touching the ocular perceivers, nasal perceiver, or mouth following direct interaction with contaminated surfaces (8).

Recent research shows that indistinct with SARS that has been spread exclusively by people with symptoms, early coronavirus is also spread well before symptoms begin.

This can considerably hinder containment efforts geared toward limiting viral spread (Figure 5).

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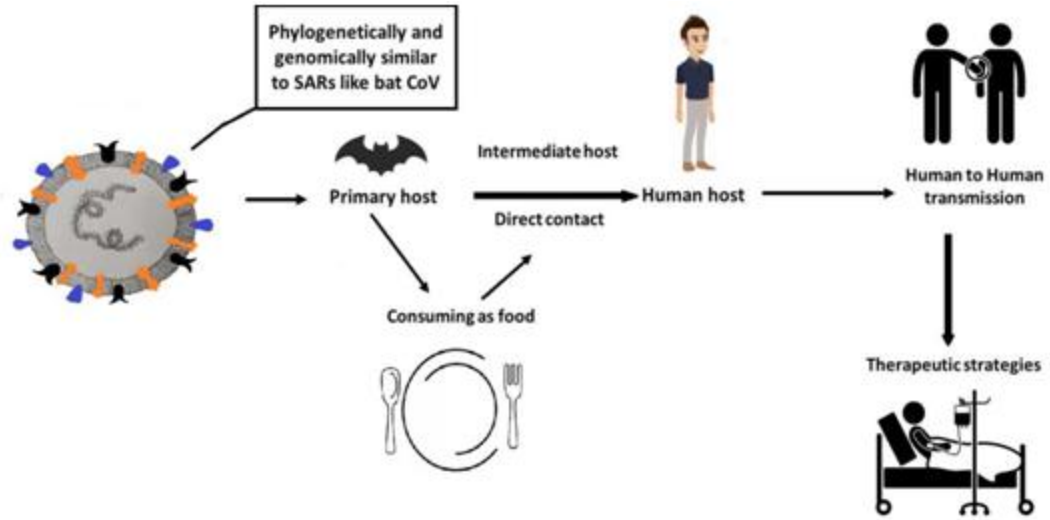

Figure 5: Spreading of coronavirus. The virus is phylogenetically related to SARs example- bat, the virus chooses or grows inside the primary hosts either through physical interaction or through consumption of the primary host as food hosts continues to grow the virus inside the human body and the human body becomes a conduit for the virus to reproduce and propagate in different forms such as direct touch, fluid transmission, needle sharing, etc. Therefore we ought to take the clinical approach to treat and control the disease.

COVID-19 can be communicated with considerable easiness from one person to another .To date, the WHO reports that the virus is between 1.4 and 2.5 in the R0 or simple reproduction amount , though alternative provide approximately vary lies under 2 and 3. Which suggests that each infected person will successively affect 2 to 3 different population, though several "superspreaders" have been identified to infect up to 16 people during this outbreak, The R0 requires to be below 1, to control situation (9).

PREVENTION

To deter infection and slow spread of COVID-19 according to WHO many steps followed like hand wash mostly with sanitizer, disinfectant,soap, water, or scrub with alcohol-predicted rubbings for hand and must set a total gap of 1 meter between you and those that are coughing or physiologically sensitive. Evade physically contacting your face. When coughing or sneezing close the mouth and nasal perceiver. When you feel unwell, sit home. Abstain against cigarettes and other practices which emasculate the lungs. Follow physical distances through refusing non-essential pilgrimages and keeping away from tremendously gigantic communities of citizens (https://www.who.int/health-topics/coronavirus#tab=tab_2).

CURRENT SITUATION

As per organizations like the World Health Organization (WHO), the Centers for Disease Control and Prevention (CDC), and the U.S. Food and Drug Administration (FDA), There are actually no treatments or vaccinations licensed that have been demonstrated to be successful in the diagnosis or prevention of COVID19(10) (Figure 6).

Figure 6: Exposure of coronavirus Globally. This pie chart indicates the number of persons get affected due to the SARS-CoV-2 outbreak till 08th April 2020. as per WHO

CPAM suggests taking lopinavir, ritonavir (2 capsules orally twice daily) with a combination of nebulized alfa-

interferon (5 million units inhaled twice daily) for active antiviral therapy of SARS-CoV-2 (https://www.tal-com.com/health-wellness/here-are-covid-19-drug-therapy-potential-options) (Figure 7).

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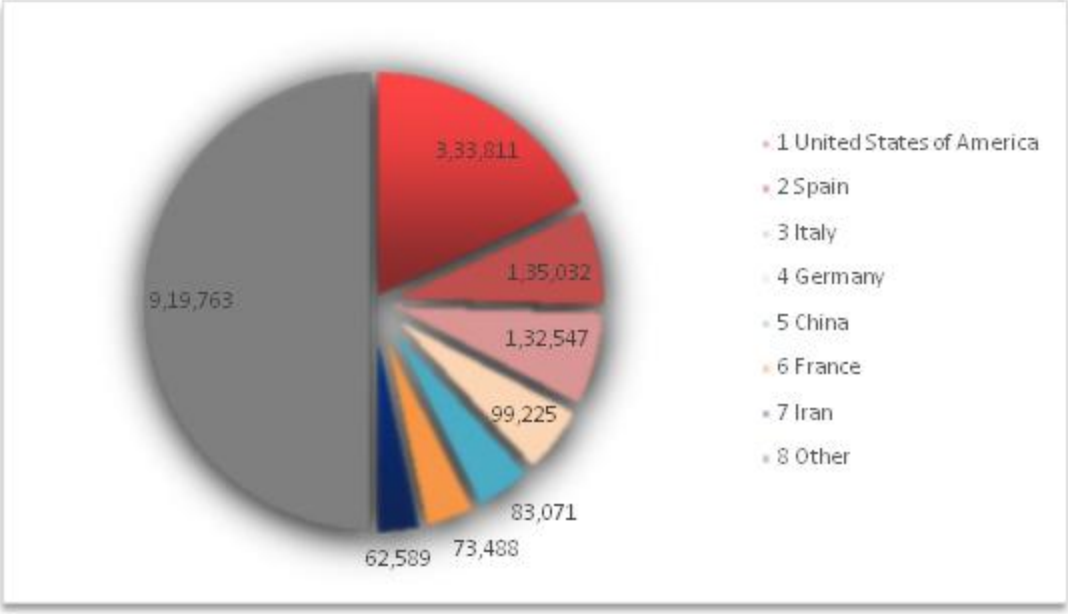

TYPES OF PROTEINS

There are mainly 4 major types of proteins available in the coronavirus structure

A) Spike protein

The coronavirus spike protein (CSP) are the class I protein and helps in binding to the host receptor (11). N-glycosylated spike protein whose measure beneath the CoV species extending in between 1100 to 1450 along with an approximate molecular mass around 220kDa(12). These proteins are extremely glycosylated and possess 20-35 N-glycosylation position. Ectodomain of the CSP share a similar association in two areas: S1 sub-unit mainly responsible for the receptor recognition and S2 sub-unit, which is responsible for the execution of membrane fusion. S1 encourage binding of the large receptor of spike protein(SP) and S2 shapes the structure of the spike stalk. CSP is fusion protein of class 1(13,14) (Figure 8).

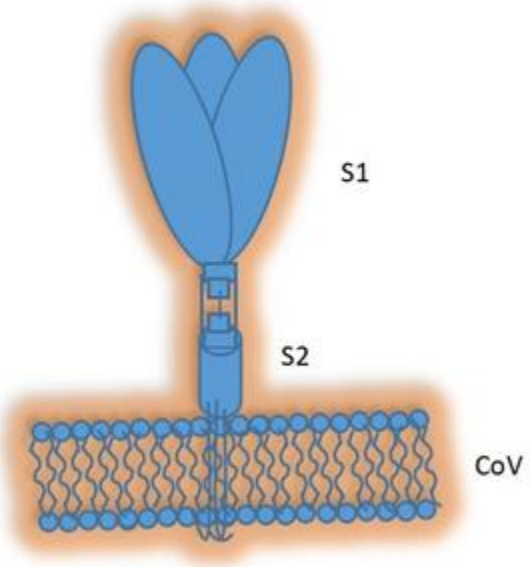

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Figure 7: Spike Protein.Spike protein (S) is a multipurpose protein that governs the entrance of coronavirus into the host cell and it consist generally of S1 unit and S2 unit. The S1 is primarily responsible for binding of receptor while S2 sub-unit is accountable for the fusion of membrane

Betacoronavirus SP sub-unit S1 shows more than one spatial arrangement, which in a general sense is sorted out in four space zones A – D, from which space A and B reaches to function as domain receptor binding.The sub-unit of S2 is emphatically preserved That contains the most protein fragments empowering the combination of infection cells C-terminal domain (CTD) and N-terminal domain (NTD) are the two sub-domains of S1, both CTD and NTD is capable to act like receptor binding protein(RBP) and it is able to bond several sugars and proteins. The CSP is a fusion protein which has a propensity for developing an alpha helical shape and a coiled structure that is processed in the C terminal region in order to create an alpha helical shape, and therefore to be coiled coils (12).

B) Envelope Protein

The Envelope protein contains two discrete domains: a cytoplasmic tail regulated and a hydrophobic domain. The framework is however, hugely variable across various members of the coronavirus family (15). Ion channel development happens when they envelop protein is oligomerised. However, it is still not obvious how significant such ion channels are. Numerous other inquire about find that E-protein works in conjunction with certain cellular proteins it also helps to regulate their function (16).The virulence factor also influences the enveloping protein and envelops the protein and also plays a major role in the formation of buds and coronavirus. Envelop protein is mostly located in the endoplasmic reticulum and in golgi body. Envelop protein related ion channel tends to inhibited by hexamethylene amiloride within the mammalian cell which expresses SERSCOV protein envelop(17).

C) Membrane Protein

The key role of the membrane protein is the preservation of the structure of the viral envelope, and execution of this function by the membrane protein is performed via communicating with certain coronavirus proteins, integrating Golgi complex onto fresh virions then stabilizing the protein nucleocapsid. M protein plays a major role in intracellular viral homeostasis via numerous membrane and interaction between proteins(12). The association of M – S, M – M and M – N proteins is a particular part of viral assembly The interaction of M-S in Endoplasmic Reticulum Golgi Intermediate Compartment complex is very important for spike protein interaction, which is well known called Golgi complex,which further get incorporated to fresh or new viral progeny (10). M – N interaction is essential to the stability of the nucleocapsid – RNA complex, which constitutes the viral center, both M and N protein M protein often participates in host sensitization by the virus The SARS- CoV M protein stimulates the kappa pathway of the nuclear factor and the IFN- beta pathway by a process that is Toll-like to receptors (10,12).

D) Nucleocapsid Protein (N)

Nucleocapsid protein (N) may be a basic protein for virion, although it works in the viral multiplication in an unexplained way and serializes the complexes of viral replication. (18) The viral RNA bundled by the Nucleocapsid protein and leads to the formation of the helical N protein and Embossed throughout the budding particle (19). C-tail, N-arm, central linker (CL) are the featured intrinsically disorder regions(IDR) of N protein(19). The N-terminal domain (NTD) and the C-terminal domain (CTD) are the nucleocapsid protein's core basic protein. The vital significant role of the nucleocapsid protein N-terminal domain is to do binding RNA, and in the other hand, dimerization is the main feature of the C-terminal domain(18,20), C- terminal intrinsically disorder regions play a key role in the oligomerization of nucleocapsid proteins and in the activity of N – M proteins, The two significant roles of the nucleocapsid protein are the development and preservation of the ribonucleo protein complex. Transcription and replication are both regulated by the nucleocapsid protein, and within the host body, inhibition of translation by EF15- activity can lead to apoptosis, alteration of the host cell cycle and alteration of host cell metabolism The N-terminal domain also carries binding sites for RNA(18).

Identification tests:

Dry cough, fever, vomiting, diarrhea, pneumonia are the clinical features of COVID-19. People with

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several comorbidities are vulnerable to serious illness, and may even have acute kidney injury (AKI) and Acute respiratory distress syndrome (ARDS) characteristics. WHO and CDC are releasing recommendations for both clinical and epidemiological results evidence of COVID19 infection(20), In the case of suspected laboratory findings that must be done, Patients with high levels of C-reactive protein, erythrocyte sedimentation, lactate dehydrogenase, creatinine and a prolonged duration of prothrombin can develop (20). Full genome sequencing and phylogenetic study of bronchoalveolar lavage fluid will validate an infection with COVID-2019 (21). Investigations should also be carried out against certain respiratory pathogens.

Variety of test are available for the identification of coronavirus which are explained as below (https://www.nature.com/articles/d41587-020-00002-2?utm_source=Nature+Briefing&utm_campaign=c3e5323668-briefing-dy-20200225&utm_medium=email&utm_term=0_c9dfd39373-c3e5323668-43913957) -

1.Coronavirus nucleic acid assay: According to this study Primers and probes are assigned to detect the novel coronavirus using RT-PCR and are widely distributed in China.

2.The CDC Reverse Transcriptase PCR test screen 2019-nCoV in real time: For this diagnostic panel PCR check carried out on the applied Bio-systems 7500 Quick Dx RT-PCR instrument with the SDS 1.4 program, this study was approved by the FDA(20).

3. Transcriptase PCR Assays in Real Time: Throughout this study, Two quantitative single stage RT reverse transcription PCR sarbecovirus assays sub-genus N gene and ORF1b occur concurrently and are currently being sent to WHO and other 30 ecumenical laboratories.

4. Coronavirus gene detection kit: This kit utilizes for the detection of the coronavirus and it worked as a PCR predicated detection kit and The current status of the gene kit is that it seeks emergency approval for the administration of Chinese medical products .

5. Real-time RT-PCR fluorescent system for 2019-nCoV identification: As the BGI Group develops this kit and the test results declare within several hours withal it is now under Emergency approbation allowed by China's National Medical Products Administration.

6. The Nucleic acid detection package 2019-nCoV by the combinatorial probe-anchor synthesis process: Visual inspection of the Metagenomic Sequencing Package for the monitoring of novel coronavirus mutations is carried out in this process and is currently subject to emergency approval by the National Medical Goods Administration of China .

7. Shenzhen Shineway Science dependent molecular diagnostics program: The On-site expeditious molecular diagnostic system predicated on Shenzhen Shineway Technology, In this research Incorporated microfluidic PCR device utilizing the silicon-predicated micro-heater module for fast heating and research sample processing; and distributes device findings in 40 minutes and this framework is certified for European Coalescence CE certification .

8. Novel 2019-nCoV Coronavirus Strain: It operates on portable RT-PCR system genesig16; it provides test results in less than two hours and it was launched on 17 February and it seeks FDA EUA.

9. TaqMan 2019-nCoV Assay Kit: Throughout this process, the Lab PCR check operating on the Applied Biosystems 7500 RT-PCR system; and thus detects sequences contained in the original 44 genomes of SARS-CoV-2 and is now only for laboratory usage.

10. QIAstat-Dx Respiratory 2019-nCoV Panel: Integrated samples were prepared and 21 respiratory pathogens were identified by RT-; samples and reagents were provided in the assay cartridges and tested in the QIAstat- Analyzer desktop in an hour. It is idea plate analysis .

11. Biomeme COVID-19 Go-Strips: An integrated sample was planned, along with an RNA identification check operating on Biomeme's mobile quantitative handheld system on PCR .

12. Fortitude Kit 2.0: The key process behind this kit is the RT-PCR SARS-CoV-2 experiment, and these kit yields 100,000, results and therefore has been approved .

TREATMENT METHODS FOR COVID-19

COVID-19 is not suggested for immediate antiviral therapy, and no vaccination is currently on the

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market.The diagnosis is symptomatic, and oxygen therapy is the main medical method for seriously contaminated patients (22). Mechanical ventilation is often necessary in cases of respiratory failure refractory to oxygen therapy, whereas hemodynamic assistance is needed to treat septic shock.

But Confirmatory diagnosis, including Oxygen treatment, fluid recovery, The application of wide-spectrum antibiotics to mask secondary bacterial infections is used by many (and a number of alternatives) and several others, There are many plausible medical targets for re-use prevailing Antiviral agents or establish successful reaction to this novel coronavirus (22).

Vaccines

Active SARS-CoV-2 vaccinations are important to minimize the incidence of the disease, shedding and dissemination of infectious agents and thus help to control coronavirus outbreaks. There are many types of animal-tested SARS-CoV, MERS-CoV vaccination, live attenuated viruses, viral vectors, viruses inactivated, sub-unit vaccines, recombinant DNA and protein vaccines.

Virally targeted inhibitors

Remdesivir, an analog adenosine capable of attacking RNA-based ribonucleic acid polymerase and inhibiting viral RNA synthesis, A successful antiviral medicine has been used against a wide variety of RNA viruses (including SARS / MERS-CoV) infections in civilizing cells (22), Types with mice and non-human primates (23).

Antibody and plasma therapy

Several convalescent patients have been reported to donate plasma to SARS-CoV-2, as well as to SARS-CoV and MERS-CoV tests. Preliminary beneficial results were obtained in serious, extreme SARS-CoV-2 cases. In fact, the development of recombinant human monoclonal antibody (mAb) may be a fairly simple approach to SARS-CoV neutralization (24,25).

Protease Inhibitor

Mainly papain-like protease and CL like protease are the main two types of protease present in SARS-CoV, which facilitate cleaving the polyprotein and releasing the nonstructural protein(NSP1 - 16), in the COV life cycle it plays a very important function. Lopinavir is the best while the saquinavir least inhibitor of COV protease inhibitor. The flap closure of these SARS-COV bound inhibitors was observed in molecular dynamic studies, initially administered in combination with ritonavir and lopinavir in the treatment of oh-HIV(26).

mRNA-1273

According to the Moderna statement, the primary batch of its novel coronavirus vaccine, known as mRNA-1273, sent to the National Institute of Allergy and Infectious Diseases (NIAID), in line with the modern primary vaccine ampule. It is to be included in a phase 1 analysis in the U.S., The vaccine will be checked on a select number of eligible people beginning at the end of April, when the initial step is undoubtedly to create a vaccine that is effectively available on the market for use. Moderna has, However, to provide a tried-and-tested vaccine with its base, the RNA development tool. This attempts to produce drugs that guide cells inside the body to synthesize proteins in order to prevent or counter the disorder that allows the usage of transporter RNA an essential enzyme for the efficient processing of the body's cells.

(https://edition.cnn.com/2020/02/25/business/moderna-coronavirus-vaccine/index.html?utm_source=Nature+Briefing&utm_campaign=c3e5323668-briefing-dy-20200225&utm_medium=email&utm_term=0_c9dfd39373-c3e5323668-43913957).

Remdesivir (GS-5734)

It is an associated nucleoside analog that has been administered to many patients who are suffering from SARS-COV-2 infection in the U.S., Japan, Europe and other countries To welcome wider exposure or conscientious use of services. In preclinical studies, remdesivir is highly successful across coronavirus as well as a strong genetic resistance to tolerance. Potent antiviral activity against clinically isolated remdesivir SARS was identified in the in vitro study, and the findings show that remdesivir inhibits the activity of 2002 SARS, bat CoV strains and MERS, which has the ability to replicate in human epithelial cells and enters the CoV receptor (26).

Sofosbuvir together with ribavirin

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According to the molecular docking data experiment, by employment of SARS-CoV-2 RNA dependent RNA polymerase (RdRp) model the sofosbuvir and ribavirin have tight binding to the coronavirus RdRp, so the COVID-19 infection might get effectively cured by the therapy of sofosbuvir and ribavirin(26).

Lopinavir, ritonavir mix of ribavirin and corticosteroids

Open-label illness including incipiently treated 2002 SARS-CoV patients who are not vulnerable to acute respiratory distress syndrome (ARDS) and conjointly the primarily outcome that composed of ADR of severe hypoxaemia or death at the day 21 (26).

Interferon alfacon-1 in conjunction with corticosteroids

It is under open label trial with distinguishing the tolerability of interferon alfacon-1 plus corticosteroids and therapeutic effectiveness with the assistance of 9 patients with likely 2002 SARS-CoV therapy with corticosteroids only and since the effect of this procedure with interferon alfacon-1 resulted in a reduction in the duration of recovery of pulmonary radio-graph anomalies (medium duration, 4 days vs. 9 days, $p = 0.001$) by 50%, along with increased oxygen saturation ($p = 0.02$) and a reduced span of enhanced oxygen saturation. (a median time, 10 days vs. 16 days, $p = 0.02$) which results in a step towards faster resolution of lactate dehydrogenase. The cause of the fever and lymphopenia was the same in each event (26).

Baricitinib

Both the COV-19 and SARSCOV enters the host through the ACE2 receptor mediated invasion, which is usually located in the lungs. The receptor intervened the endocytosis handle by downstream signaling, and the associated protein kinase 1 (AAK1) of AP2 which performs a vital role in this process. Thus, the foremost vital target appeared is AAK1. According to the 2020 review 378 ligands, of which 37 have already been accepted for usage. Among these, six of them conduct high affinity inhibition among AAK1, Baricitinib also binds to another endocytosis to generate cyclic G associative kinase protein (26).

Challenges that affect the coronavirus treatment

Amid the attempts of the world to recognize COVID-19, several things stay unanswered. Primarily, some survey indicated the existence of SARS-CoV-2 in patients 'stools. Nevertheless, it remains controversial if SARS-CoV-2 may be transmitted via the fecal-oral pathway (27). Second, prior studies have already shown that SARS as well as other coronaviruses, can live on atmospheric conditions and inert artifacts. Though, any existence of SARS-CoV-2 throughout the atmosphere may not have been confirmed. Past studies show coronaviruses may be successfully denatured utilizing disinfectants using 60-80 percent ethyl alcohol, isopropyl alchol at the concentration of 20 percent do the same although there are several disinfectants like benzalkonium chloride are also used. However, there is a shortage of existing effectiveness analysis of widely employed disinfection compounds for SARS-CoV-2 (https://reynardhealth.com/using-alcohol-to-disinfect-healthcare-surfaces). Thirdly, while travel restrictions have been implemented in several nations, it is not obvious if such an action is successful. Fourth, while some event reacted well enough to remdesivir and another in vitro test indicated that remdesivir and chloroquine appeared promising for management of COVID-19, more clinical studies for potency for remdesivir and chloroquine throughout the management of SARS-CoV-2 pneumonia must be performed (27).

CONCLUSION

The emergence and progression of SARS-CoV-2 depends on the relationship between the virus and the human immune system It should be obvious that quarantine alone will not be adequate to deter the spread of COVID-19, And the global effect of this virus infection is of growing concern. Further work is certainly needed to better establish the precise process for human-to-human and animal-to-human propagation in order to promote the production of the virus-specific vaccine. The frequency and progression of SARS-CoV-2 relies on the relationship between the virus and the human immune system. Moreover, it must not be believed that surgical therapy may have a 100% curative impact. And with this pandemic explosion, it very important that we should continue developing the most promising therapeutic drug candidate to stop this global spread of COVID19.

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