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REVIEW ARTICLE: COVID – 19: INFECTION, ORIGIN, TRANSMISSION, DIAGNOSIS, TESTS AND TREATMENT OPTIONS

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ABSTRACT

The virus that causes (COV- 19 disease) , "SARS-CoV-2 disease" is to blame for the greatest epidemic since the (1918) H1N1 influenza pandemic . The World Health Organization presently recognizes coughing , the fever, exhaustion, and breathing problems as symptoms. Despite the fact that patient-reported a loss of flavor and smell has been linked to, there is not olfactory data collected empirically, testing on a group of "COV-19" infected persons with COVID-19 infection. The virus of corona , which spreads by using the same receptor as 'SARS-CoV' primarily by using the mechanism of respiration, angiotensin-converting enzyme 2. Importantly, there had been growing the proof of prolonged transmission from one person to another, as well as a large number of cases exported over the world. This article provides a critical assessment SARS CoV-2 infection and therapy options for COV - 19.

INTRODUCTION

COV-19 is the largest known RNA virus. Their nucleic acid genome is RNA that is single-stranded and has a length of 26 - 32 kb & a diameter of 65 to 125 nm. [1]Six coronaviruses have been identified since 1960 discovered to reason infections in people, following "SARS-CoV and MERS-CoV". SARS-CoV-2severest acute respiratory syndrome are the seventh virus to cause the disease.[2] While the beta corona of viruses (SARS-CoV), (MERS-CoV) respiratory disease in the Middle East , & SARS-CoV-2 cause severe to fatal pneumonia in persons, HKU1; OC43, NL63, & 229E are linked to minor signs and symptoms.[3] Pneumonia symptoms include fever, a dry cough, trouble breathing, and tiredness.[4,5] MERS-CoV, SARS-CoV, & SARS-CoV-2 had fatality rates of 9.5 percent, 2.3 percent, and 34.4 percent, one-to-one.[6]COV- 19 virus have some unknown the epidemiological, the pathogenic, & the clinical characteristics, such as its widespread and high community transmission compared to the SARS has spread to hospitals through nosocomial transmission. and MERS, as well as a lesser form of the disease and Compared to the severe phenotype, which has a greater mortality rate, the two other viruses have a lower mortality rate.[7]

SARS-ORIGIN COV-2'S AND TRANSMISSION

It is type of virus of corona , which is an enclosed positive-sense RNA virus with no segments (Orthocoronavirinae subfamily, subgenus sarbecovirus).[8] Viruses of Corona are classified into four categories genera, one of which is CoV, which can infect both humans and animals., - and -CoV, on the other hand, are more prone to infect birds. Six CoVs, including the -CoVs HCoV-229E & HCoV-NL63, had previously been discovered as human-susceptible viruses, and the -CoVs HCoV-HKU1 & HCoV-OC43, which induce minor respiratory symptoms comparable to

those of a typical cold. SARS - CoV and MERS - CoV are the other two known - CoVs.produce respiratory infections that are severe and potentially catastrophic.[9] SARS-genomic CoV-2's sequence was found 96.2 % identical to that of a bat CoV RaTG13, then only 79.5 % identical to SARS - CoV-1. Bats are considered to be the virus's native host, based on the sequencing of a virus's genome and evolutionary research, and SARSCoV-2 is a virus that can be transmitted from bats to humans intermediate hosts via unknown routes. It is now It is obvious that SARS-CoV-2 can infect people by using Angiotensin-converting enzyme 2 (ACE2) is the same receptor as SARS - CoV. [10] (upper panel, Figure. 1).

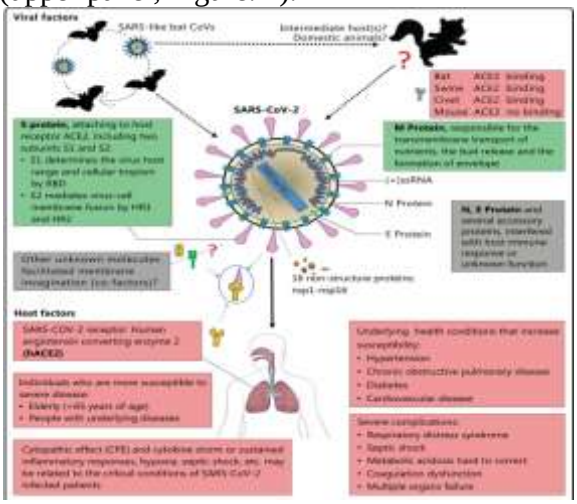

Figure. 1 The pathogenesis of SARS-CoV-2 is affected by viral and host factors. Bats carry a variety of coronaviruses, including SARS-CoV-like viruses. Before overcoming the species barrier and infecting humans, SARS-CoV-2 is assumed to have originated in bats or unknown intermediary hosts.

EPIDEMIOLOGY − RESERVOIRS & TRANSMISSION

In Wuhan, China, an outbreak of an unexplained acute respiratory tract illness has been reported, since December 12, 2019, and is thought to be linked to a seafood market. Bats have been discovered as a possible SARS - CoV- 2 reservoir in several studies.[11, 12] So yet, no evidence has been found that SARS - CoV- 2 began in the fish business. Bats, instead, serve as a SARS and MERS-like viruses, for example, have a natural of reservoir.[13–14] When the virus genome was sequenced across the genome and compared to Bat CoV RaTG13, 96.2 percent of the genome sequences were identical.[15]Despite the fact that This seafood restaurant does not sell bats market, this suggests that Human SARS - CoV- 2 and bat CoV may have shared an ancestor.[16] Furthermore, protein sequence alignment in addition to phylogenetic analysis,[17] revealed that residues on receptors that are identical were discovered in a variety of species, showing that different intermediary hosts are involved, turtles, pangolins, and nibbles, for example, may exist. Family people, such as acquaintances & relatives, who have had intimate touch with incubation carriers or patients, they are the most prevalent carriers of SARS-CoV-2,[18]that 31.3 percent of non-residents of Wuhan visited Wuhan multiple times, and 72.3 percent had interaction with Wuhan locals persons from Wuhan. According to a report released by China's , On February 14, 2020, the National Health Commission will meet, healthcare professionals infected COV-19 patients in 3.8 percent of instances. In contrast, SARS - CoV& MERS - CoV are anticipated to be Nosocomial transmission is the most common mode of transmission. Healthcare worker infections were reported in 33 – 42 percent cases of SARS, while MERS - CoV diffusion was found in 62 –79 percent of MERS-CoV cases.[19, 20]The Direct encounter with ingesting wild animals or intermediary host creatures were assumed to be the main routes of SARS-CoV-2 transmission. The CoV- 2 source(s) & transmission routine(s) for SARS are still unknown.

STRUCTURE OF SARS - COV-2

It is a single stranded, enclosed positive sense of RNA virus . The viral RNA genome comprises 10 open reading frames and includes 29,903 nucleotide bases (ORF). ORF1ab codes for the large replicase - polyprotein , which is cleaved into (non-structural proteins) 1–16 by 3-Chymotrypsin Like Protease & Papain Like Protease . ORF2-10 codes for structural proteins S, N, E, M, and auxiliary proteins.[21, 22](Figures. 1 and 2). The attachment of the Spike protein (S) to the host of ACE-2 receptor aids virus entry into the host's cells, causing alterations in conformation that cause the fusing of viral

& membranes of cell. The priming of the spike proteins by pH dependent on activation of cathepsin L inside the endocytic vesicle results in the cytoplasmic release of the viral RNA genome . "Transmembrane Protease Serine Type 2" , on the other hand, is crucial priming the cell surface for spike proteins, allowing the viral DNA to enter . Once within the cytoplasm, the viral of RNA genome's ORF1ab portion is translated into the PP1ab replicase, which is then acted on by PLpro and 3CLpro are viral enzymes (Mpro) to make nsps 1– 16, including helicase and RdRp, which are essential for virus replication. The replication-transcription complex is formed when the nsps come together. The RNA genome's positive strand is transcribed to create a negative of strand template for the creation of the novel viral genome of RNA. The structural proteins, M, E, S & N are made from the transcribed mRNAs. The viral RNA genome of Exocytosis allows it to interact with other structural proteins, & the produced virions are transferred outside of the cell. (Figure. 3)

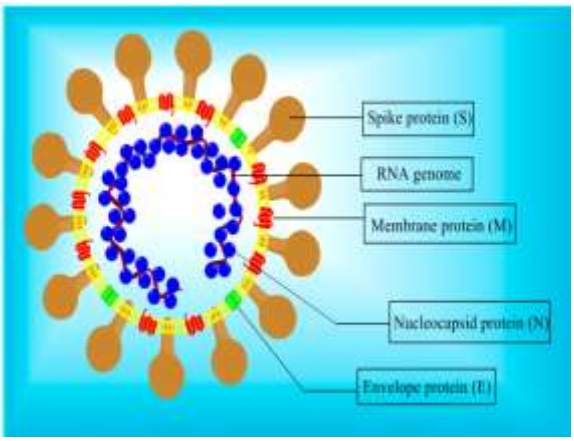

Figure. 2. Structure of SARS – CoV -2.

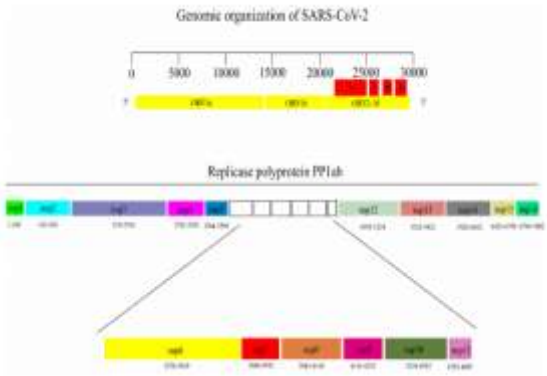

Figure. 3. (A) SARS - CoV- 2 genome arrangement. (B) non-structural proteins 1– 16.

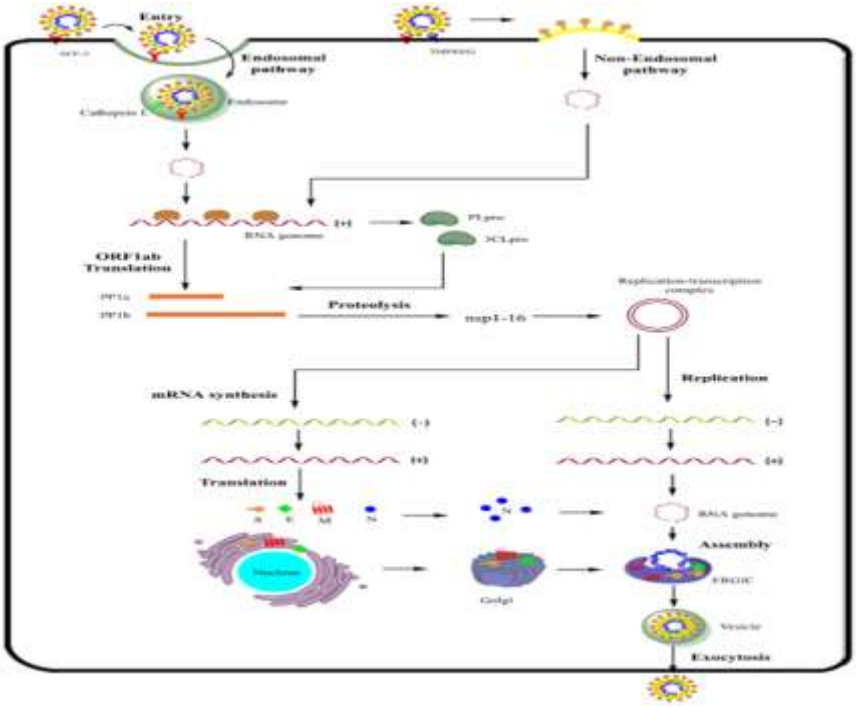

Figure. 4. SARS-life CoV-2's cycle, with (angiotensin-converting enzyme-2)

DISEASE MECHANISMS AND VIRAL PATHOGENS

It is considered that in normal olfactory loss caused by a virus, the olfactory system has been directly damaged. The olfactory epithelium is thought to be the location of injury, with biopsy tests indicating aberrant results of increased metaplasia and neuroma development in the lungs.[23-25]Animal models, on the other hand have a straight olfactory bulb is depicted injury with epithelium damage is mino.[26]Given the known ability of olfactory receptor neurons to recover after damage and the rapid improvement in smell function that occurs throughout time, the epithelial origin seems more likely. The olfactory epithelium is unknown to be affected by SARS-CoV-2 at this time due to a lack of additional data. If the vast majority of cases of olfactory resolves a loss after a few week , it is possible that virus triggered the inflammatory reaction in a nasal canal, preventing odorants from accessing the neurons of the olfactory system. To create functional connections with the olfactory bulb, olfactory neuron damage would necessitate a longer time for regeneration and renewal of axons. In addition, a recent study found that pulmonary epithelial cells exhibit larger amounts SARS-CoV-2 virus receptor, ACE2, and then olfactory epithelial cells. Cells that provide support and horizontal the cells that make up the foundation the olfactory epithelium system, but not olfactory receptor neurons, did express ACE2.[27] The virus could be transmitted by different channels and routes, causing direct damage to the olfactory bulbs. Intranasal SARS-CoV virus was injected into mice that were transgenic for human ACE2., for example, causes viral particles to spread quickly enters the bulb of the olfactory and then to other parts of the mind.[28]Without hard evidence, making assumptions, in any situation, can be disastrous during the polio epidemic, outbreak, incorrect. There were some assumptions made about how the pathogen moved to the brain via olfactory axons, resulting in intentional damage to the olfactory epithelium and irreversible smell loss.[29] It was only later that it was discovered that transmission occurred via the oral/gastrointestinal tract.

TESTS FOR SARS – COV- 2 DIAGNOSIS

Diagnosis of SARS - CoV-2 c assays were created quickly following the outbreak began, enabling for early diagnosis and the discovery of this one-of-a-kind virus. For molecular analysis, swabs from the nasopharynx are preferred specimen. If you don't have access to nasopharyngeal swabs, the CDC has deemed oropharyngeal, As of March 19, 2020, nasal swabs and mid-turbinate swabs are approved specimen types. Patients with suspected SARS - CoV-2 infection had samples taken from their “oropharyngeal and nasopharyngeal &expectorated sputum , endotracheal aspirate, or bronchoalveolar lavage”.[30] Initially, COVID19 cases were identified primarily through Isolation of viruses from swabs and identification of viral nucleic acids in respiratory samples using SARS - CoV-2 RNA detection using RT - PCR. Recently, immunosorbent related to enzymes test ELISA kits for Antibodies to N and other SARS - CoV-2 proteins were detected using IgM and IgG antibodies became available. Several more diagnostic examinations are being designed in order to detect different Genome of SARS - CoV-2 regions / to target the RdRp, Hel, E, S, & N genes.[31] Another lateral flow based on CRISPR – Cas12 test for RNA from a respiratory swab was used to detect SARS-CoV-2. extracts in less than 30 minutes is being developed.[32] For the diagnosis of COVID - 19, there are currently 628 SARS - CoV-2 tests were performed either commercially or in the works.

COMPLICATIONS AND CLINICAL OUTCOMES

The majority of patients had a positive outlook, but a minority, particularly the aged and the handicapped with persistent underlying circumstances, are in a serious situation. WHO had documented 79,968 confirmed cases in mainland China as of March 1, 2020, such as 14,475 (18.1 percent) with severe 2873 deaths and illnesses (3.5 percent).[33] ARDS arrhythmia, & shock could be among the complicationsas were acute renal acute cardiac injury, dysfunction of liver , in addition to secondary of the

infection.[34,35]The disease's seriousness was linked to the poor clinical of the outcome. The disease progresses more quickly in the elderly, with the number of median of many days between an onset of the first of the symptoms and the death being the shorter in those aged sixty five and over[36]. The older guy with ARDS and comorbidities had a greater death risk, similar to H7N9 patients.[37] In addition, over 100 children were sick, the youngest of whom was infected 30 hours after birth.[38]Because their immune systems are underdeveloped or weak, neonates and the elderly require greater attention and care.

TREATMENT FOR SARS-COV-2

The present, there aren't any vaccines or therapeutics for any of the coronaviruses that have been identified in humans have been authorized. That a fast spread of global of it has highlighted the need to novel coronavirus vaccines and medicines to combat this virus family. SARSCoV has the taxation history the worldwide economy in the range of $30 - $100 billion.[39]Treatment would be lessen an economic burden of an world. The WHO has been encouraging of the researchers all-around of the world to seek a cure for COV-19 since the outbreak began. Some of these projects, which are still within the development in its early stages, are presented here.

ANTIVIRAL DRUGS

Many antiviral medicines have been subjected to randomized controlled studies, which are now underway. Lopinavir LPV had been demonstrated to reduce In vitro action of coronavirus protease and in animal models, and it is already being used in conjunction with another antiviral drug, ritonavir medicine, to treat SARS and MERS.[40, 41] However, a recent research found that lopinavir-ritonavir provides little benefit for many infected of the patients of SARS - CoV-2.[42] Ribavirin is a homologue of guanosinethat targets the RdRp complex to treat a variety of viral diseases, including respiratory syncytial viruses and Hepatitis C are two viruses that cause hepatitis.[43] Vaccines based on messenger RNA (mRNA) are also being developed.[44]Remdesivirs are the antiviral nucleotide of analog inhibitor that may compete with RdRp and found to be effective against SARS & MERS.[45]Remdesivir has been shown to decrease SARS -CoV-2 of the proliferation in vitro, indicating that it has therapeutic potential in clinical trials.[46] Remdesivir was recently tested in a clinical trial with fifty three of patients of COV-19. Clinical improvement was seen in thirty six of the fifty three patients (sixty eight percent). So as , the medicine should be taken with caution in patients who are not undergoing invasive ventilation, as the death rate when receiving ventilation was 18% compared to five percentwhen out receiving.[47]

Chloroquine & hydroxychloroquine drugs

Chloroquine is an antimalarial & anti-autoimmune medication. It is inhibit Infection with a virus by raising pH of endosomes, cell, preventing and Fusion of virus, and encroaching on cellular receptor ACE2 of the glycosylation.[48]Hydroxychloroquine is a chloroquine analog. Both medications have an immunomodulatory effect and can reduce IL-10 & IL-6 immunological responses, which had been shown the increased as a result of SARS- CoV-2 infection. [49]Chloroquine can be found to be useful of treatment of COV-19 by lowering pneumonia exacerbation in clinical studies, and it was divided in the SARS- CoV-2 prevention and therapy recommendations.[50]

Corticosteroids

Although corticosteroids may reduce lung inflammation, evidence of clinical dose not support their use of treatment of the virus injury to the lungs still viral infection clearance is delayed and side effects are common.[51,52] Corticosteroids cannot be used Unless otherwise stated for another causes , according to the WHO.

Antibodies

Antibodies are mostly directed against the spike protein S. This protein was found to bind potently with CR3022, a monoclonal antibody against SARS- CoV., a neutralizing antibody previously obtained from a convalescent SARS patient.[53] This antibody has the potential to be used as a treatment.

Convalescent plasma transfusion (CP)

MERS, SARS, & the H1N1 pandemic of 2009 were effectively treated with Efficacy

and safety levels that are acceptable using convalescent plasma transfusion (CPT) therapy.[54–56] It entails two weeks after obtaining convalescent plasma from patients they have recovered in order to assure neutralization and a high antibody titer, and then administering it to infected individuals.[57] carried out a pilot trial in three Chinese hospitals to see if CP treatment could help 10 COV-19 patients who were severely ill. They discovered that increasing oxyhemoglobin saturation within 3 days resulted in a considerable improvement in clinical symptoms, as well as quick viremia neutralization.[58] An uncontrolled case series was the subject of yet another study of five critically ill individuals found that their clinical symptoms improved.[59] Despite the fact that CP improves the patients who are seriously infected have a higher chance of surviving, it does not allow the patient was develop Immune protection against SARS-CoV-2, and the safety of SARS- CoV-2-specific plasma globulin products warrants additional investigation.

CONCLUSION

Because the disease is so new, and the virus is likely linked to a variety of mutations and clinical patterns, there are still more questions than answers. It can create a severe, highly contagious disease that primarily affects the respiratory system, leading to misaligned immunological processes and an overactive inflammatory system, which can lead to multiple organ failure. Although the host of intermediate for SARS- CoV-2 is unknown, genetic sequence research has indicated strong similarities with bat human SARS-CoV&CoV . it is known to interact through the angiotensin-converting enzyme 2 receptor. The present understanding of SARS -CoV-2 infection pathophysiology and proliferation is extrapolated from existing SARS -CoV material. Despite intensive preventive measures, the uncontrolled spread of SARS -CoV-2 has put the health-care system under a lot of strain to find an appropriate prophylactic and treatment technique to deal with this devastating virus. The mechanisms behind the development of corona virus illness symptoms in such a distinct world population must be elucidated in future epidemiological, clinical, and basic science studies.

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