IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

The Epidemiology And Global Spread Of Severe Acute Respiratory Syndrome (SARS): Lessons Learned And Future Preparedness

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Abstract

The world was changed—in other words, a new one was created—by the COVID-19 pandemic. According to some accounts, the greatest human tragedy of the past century affected every aspect of human existence. Despite the fact that the globe is getting ready for another post-pandemic historic calamity. People won't fully understand the serious ramifications of a catastrophic nightmare for years, even while the globe is getting ready for a new post-pandemic normal.The pandemic provided a much-needed house shaking in many facets of our social and personal lives, despite the lasting and irreversible harm it caused. The education sector was one of the most severely hit initially, although it is anticipated that it would recover with time. What the epidemic taught us about professional development and instruction for second language teachers is outlined in this chapter. The volume's contributors, who were among the first to focus on the problem of language teaching during the epidemic, also take this into consideration.

Keywords: - SARS (severe acute respiratory syndrome**),SARS-CoV** (severe acute respiratory syndrome coronavirus), **nCoV** (Star Novel Coronavirus), **MERS** (Middle east respiratory syndrome) **WHO (**World Health Organisation**),RT-PCR**(Reverse-transcriptase polymerase chain reaction), **PCR**(Polymerase Chain Reaction), **R0 (**Reproduction Number**), Rt (**The effective reproduction number)

Introduction

SARS, or severe acute respiratory syndrome, is a newly discovered pneumonia-related illness in humans. (1)Three pandemics have emerged from southern China in the last 150 years, two influenza pandemics (the 1957 Asian flu and the 1968 Hong Kong flu) and the plague in the late 19th century. In China's Guangdong Province, a new "plague" was beginning to emerge in November 2002.AGuangdong doctor visited a single day in hotel "M" in Hong Kong on February 21, 2003, and while there, he infected sixteen other visitors. These in turn sparked illness epidemics in Singapore, Hong Kong, Toronto, and Vietnam. SARS spread quickly, affecting over 8,000 people in 25 countries on 5 continents.774 individuals have died worldwide by the time the pandemic ended on July 5, 2003, a very low figure when compared to the deaths caused by the past influenza and plague pandemics. However, the far more noticeable effects of SARS were largely caused by the speed at which it spread through air travel, the quick media attention that followed, and the modern globalization of economic activities. The WHO responded to these outbreaks with a travel recommendation on March 15, 2003, and a worldwide notice on March 12, 2003 (2,3). The WHO has only infrequently issued such travel advisories in reaction to the emergence and the propagation of a contagious illness. (4) The WHO used conventional public health strategies to contain a newly discovered but severe, incurable, and quickly spreading respiratory disease with an unknown cause. Increased alertness, screening at the point of entry and departure for foreign visitors, isolating affected individuals, and quarantining those in close proximity were among these measures. (5,6)

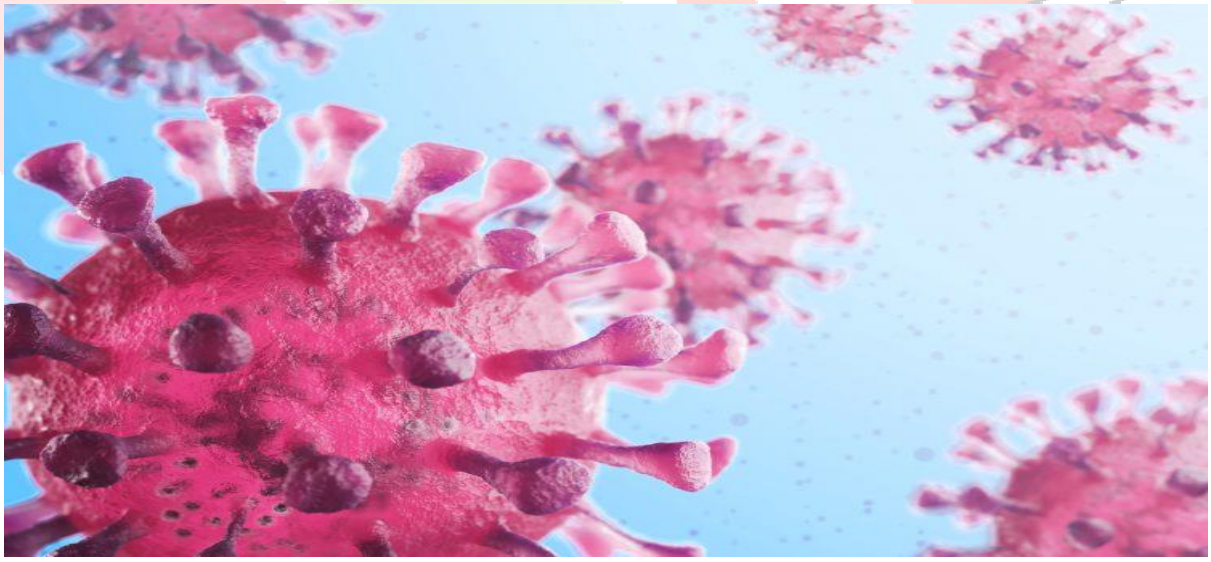


Fig no.:- 1 Severe Acute Respiratory Syndrome (7)

The National Select Agent Registry, which governs the handling and ownership of bacteria, viruses, or toxins that have the potential to seriously endanger public health and safety, now includes SARS-CoV as of October 2012. The addition of SARS-CoV allows for the upkeep of a national database and the inspection of organizations that use, possess, or transfer the virus. It also guarantees that every person who collaborates with these agents goes through a security-risk assessment conducted by the Criminal Justice Information Service and the Federal Bureau of Investigation. (8)

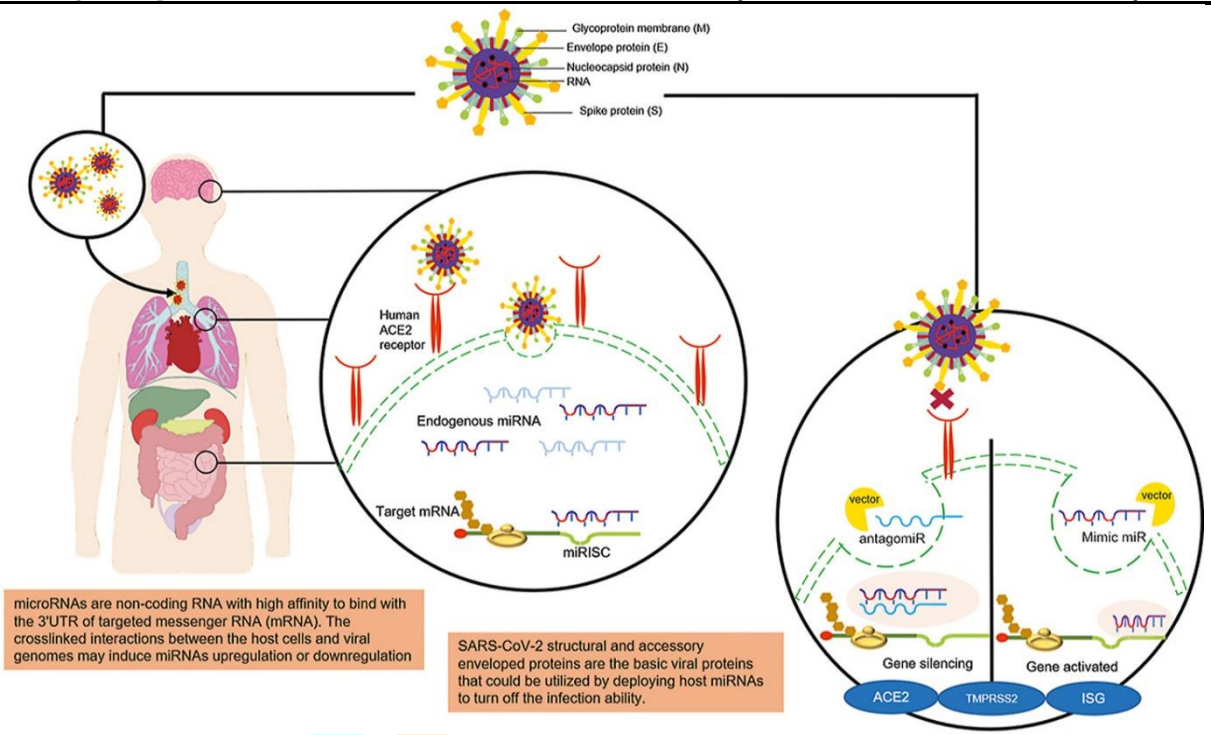


Fig no.:- 2 (9)

At the end of 2019, health experts discovered another coronavirus outbreak. This new virus, known as the Wuhan virus (or 2019-nCoV), is an RNA virus connected to the MERS and SARS coronaviruses. It most likely started as an infection in animals that were sold as food in Wuhan, China.Similar to SARS, the virus seems to travel from person to person and can cause mild to severe respiratory difficulties in humans. Within a month, the virus had spread to at least six nations, including the United States, and the majority of patients with the Wuhan virus needed hospitalization. (10, 11)

The family of enclosed, single-stranded RNA viruses known as coronaviruses affects both humans and animals, yet the common cold is the only illness caused by the other coronaviruses that are known to affect humans. Reverse-transcriptase polymerase chain reaction (RT-PCR) has been used to detect the presence of SARS-CoV, and the virus has been isolated from respiratory secretions, feces, urine, and lung biopsy tissue specimens, proving that the infection is not limited to the respiratory system. (12)

Aetiology

While the cause of SARS is still unknown, Koch's postulates have been partially satisfied for a recently identified virus belonging to the Coronaviridae family. (13)

- SARS patients' oropharyngeal tissues caused Vero E6 tissue culture cells to become cytopathic.
- Group I coronavirus polyclonal antibodies exhibited reactivity when stained with immunohistochemistry and immunofluorescence antibody. (14,15)
- With the use of consensus coronavirus primers created for reverse transcriptase-polymerase chain reaction (RT-PCR) amplification of a polymerase gene fragment, the isolate was recognized as a distinct coronavirus that is only distantly related to other coronaviruses that have been sequenced.(16)

- SARS was found in clinical samples from afflicted patients across several geographic locations using PCR techniques. (17)
- Serological data has demonstrated that the serum of SARS patients contains antibodies unique to the novel coronavirus. (18,19)

Epidemiology

- As of March 29, 2003, 1,550 cases from 13 countries had been reported, with 54 fatalities. 50–200 instances more are added to the total every day.
- There are 470 potential cases in Hong Kong alone, the majority of cases have been reported from China. Based on preliminary data from Hong Kong, the pandemic has been linked to a lone mainland Chinese traveller. In South-East Asia, the socioeconomic impact has been substantial. (20,21)
- In Singapore and Hong Kong (where the central library was once closed), school has been suspended.
- Hong Kong has begun screening its air travellers, and there have already been reports of a decline in the region's desire for vacation reservations and air travel. (22)
- The condition's understanding has grown as the epidemic has spread.
- Although the true extent of the epidemic is still unknown, the disease does not seem to be as contagious as initially thought, with the majority of secondary cases being reported in close proximity to the original case or among medical personnel providing care for a SARS patient. (23)
- One-third of the cases in Hong Kong have included healthcare personnel.
- A few of these individuals have passed away, including the WHO infectious disease specialist who was the first to discover the outbreak in Hanoi, Vietnam. (24)
- The rate of spread of an epidemic and whether it is self-sustaining depend on the **basic reproduction number (R0)**. R0 is defined as the average number of secondary cases generated by 1 primary case in a susceptible population.
- This quantity determines the potential for an infectious agent to start an outbreak, the extent of transmission in the absence of control measures, and the ability of control measures to reduce spread.
- During the course of an epidemic, **Rt, the effective reproduction number**, decreases in comparison with R0 as a result of the depletion of susceptible persons in the population, death or recovery with subsequent immunity, and the implementation of specific control measures. (25)

Pathogenesis

SARS-CoV2 belongs to the family Coronaviridae. The virus is a positive-stranded RNA that is encapsulated and has a large genome that spans 26 to 32 kilobases. (16) The virion resembles a solar crown (Latin: corona = crown) due to its spherical form, bright surface protein projections, and core shell. There are 14 open reading frames (ORFs) in the genome, encoding 27 different proteins.The transcription and replication of the SARS-CoV2 genome are carried out by 15 non-structural proteins (NSPs), which are encoded in the genome's 5′-terminus. Genes encoding the four surface structural proteins and eight additional proteins with unclear functions are found at the 3′-terminus of the genome. (26)

The four structural proteins provide the following purposes:

- The N-protein is in charge of both the virus's replication and the host's reaction to it.
- The S-protein helps the virus attach itself to vulnerable host cells. It's mainly two types s1 & s2 where s1 is responsible for bind with the host cells receptor and through s2 sub unit they are fuse and penetrate inside the cells through endocytosis. (27)
- The M-protein helps the host cell form networks that allow the virus to produce its particles
- And the E-protein helps the virus produce and release its particles into the host cell.(28, 29)

SARS-CoV2 enters the host by attaching to receptors in cells that express angiotensin-converting enzyme 2 (ACE-2). SARS-CoV2 has a higher affinity for human ACE-2 cells than it does for SARS-COV. Since ACE-2-expressing cells are present in the lungs, GI tract, medullary regions of the brain, epithelial cells, cardiovascular, and immune systems, symptoms may point to a single or multiple system compromise. (30) However, most of the pathologic findings indicate respiratory compromise. Early lung changes include pulmonary edema, protein exudation, vascular congestion, pneumocyte hyperplasia, and interstitial thickening. (31)

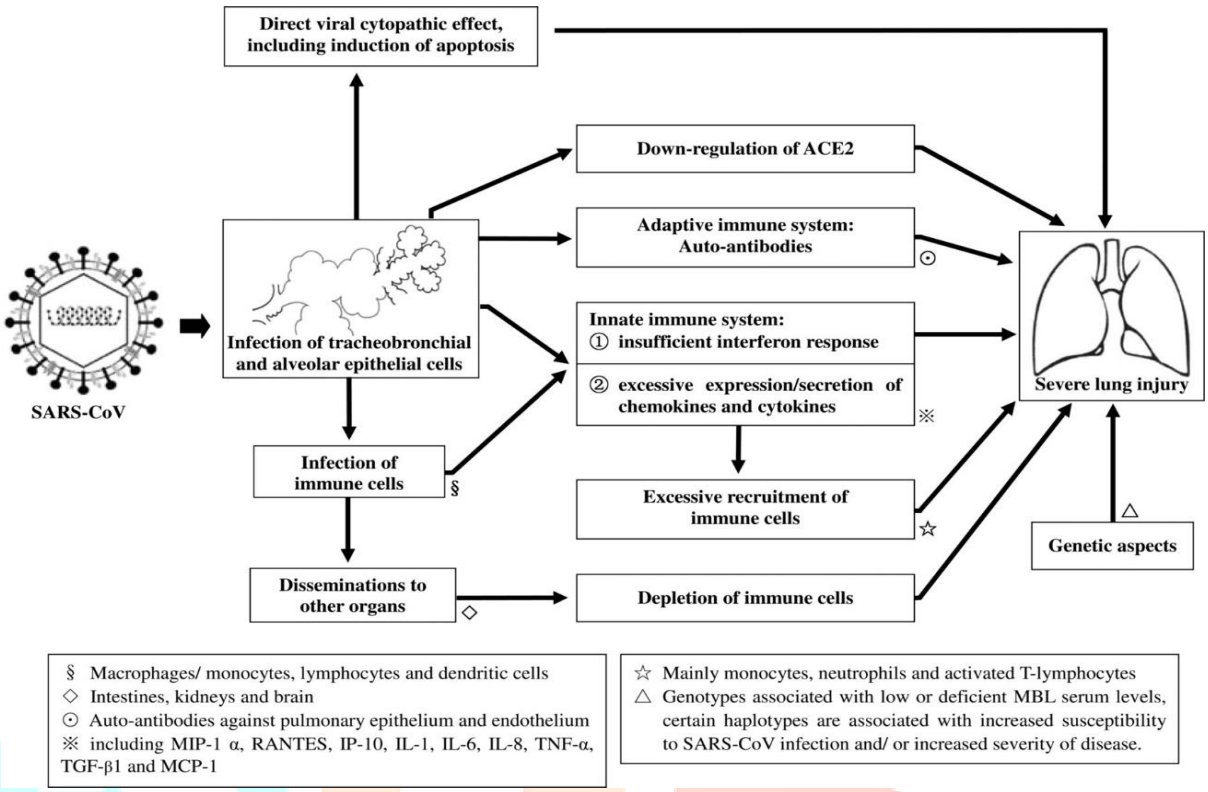
Late pulmonary changes may include injury of alveoli, formation of fibrous exudates, desquamation, and hyaline membrane formation (i.e., acute respiratory distress syndrome [ARDS]). Respiratory failure without subjective perception of dyspnea (silent hypoxemia) has been reported, and is associated with hypocapnia caused by compensatory hyperventilation. (32)

We concentrating in particular on fresh discoveries made possible by cutting-edge technologies as CRISPR screens, organoid infection models, and single-cell omics.

We demonstrate how immune responses that go awry can lead to SARS-CoV-2 infection of the lower respiratory tract and subsequent damage to alveoli.

We talk about how this could cause the endothelium and epithelium to induce a "leaky state," which would encourage coagulation and inflammation, while an inflow of immune cells would cause immunopathology and exaggerated inflammatory reactions.

Lastly, we point out how these results can help in the creation of fresh treatment approaches to combat COVID-19. (33, 34)



Pathogenesis of SARS (35)

Mechanism and Route of Transmission

Transmission of SARS-CoV-2 is believed to occur mostly through respiratory droplets and fomites, as opposed to aerosols that are transported over great distances. (36)

There are concerns regarding the potential correlation between the severity of the disease and the infectious dosage and mode of transmission of SARS-CoV-2. (37)

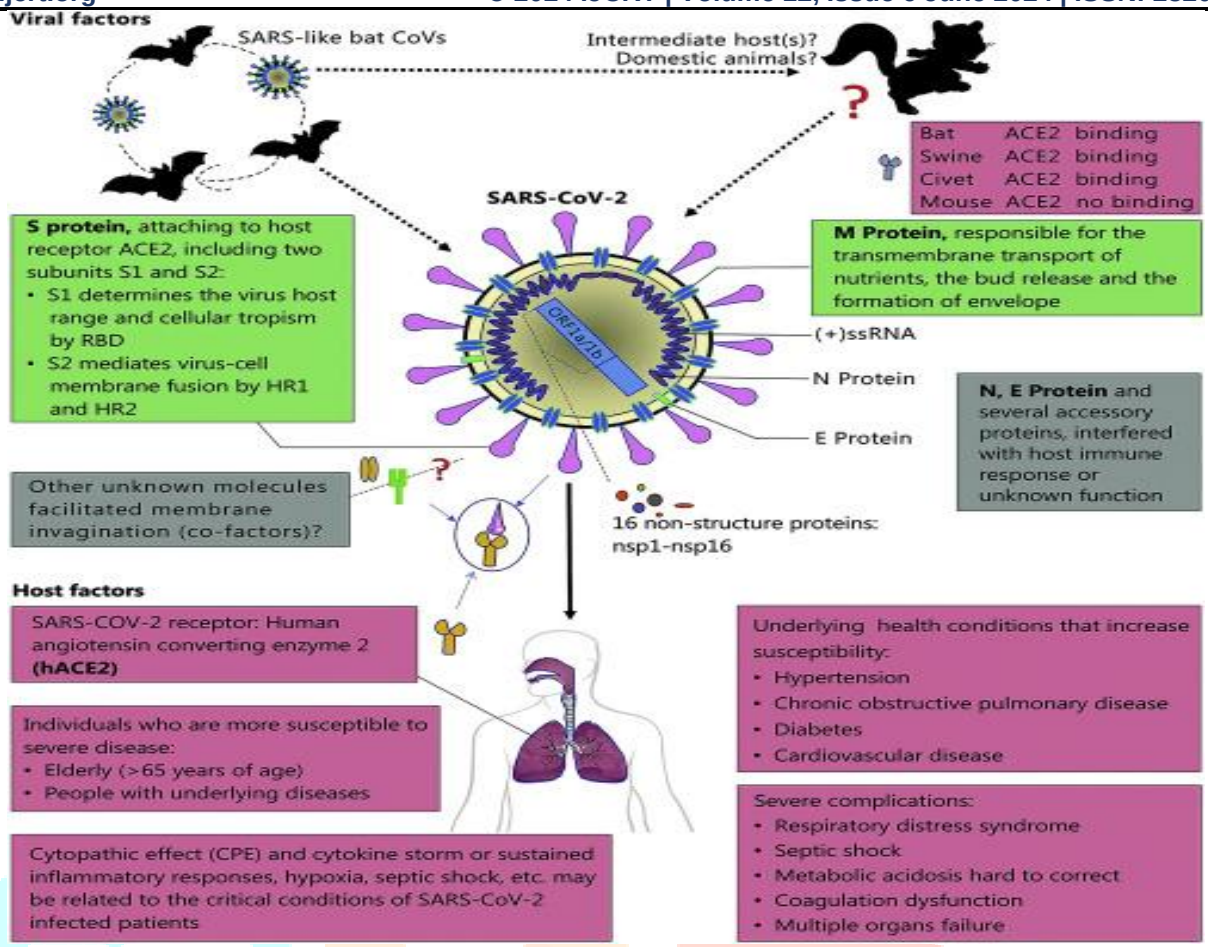
While SARS-CoV-2 is not directly known, research on other respiratory viruses and animals may offer some hints. Ferrets and cats have been shown to be susceptible to aerosol-borne SARS-CoV-2 transmission. (38)

When laboratory mice were aerosolly inoculated with the H3N2 strain of sub-lethal influenza virus, they showed increased levels of IL-6 expression in their lungs, pulmonary infiltration and inflammation, and mortality and morbidity. (39)

African green monkeys infected by the aerosol route of SARS-CoV-2 consistently displayed cytokine storms, elevated IL6, and ARDS.

Disease development was connected with higher influenza virus exposure, which was likely due to an increase in infectious dosage. (40)

Studies on laboratory-adapted mice infected with HCoV-OC43, SARS-CoV-1, and MERS-CoV revealed increased morbidity and fatality with increasing dose upon exposure in addition to studies on SARS-CoV-2 infected ferrets, rhesus macaques, and hamsters. (41)



Experimental evidences have clearly shown that SARS-CoV-2 infects humans by binding to angiotensin-converting enzyme 2 (ACE2) expressed in the respiratory tract, in a mechanism similar to that of. SARS-CoV. (42)

Diagnosis

Diagnostic criteria proposed by the World Health Organization (WHO) and Centres for Disease Control and Prevention (CDC) are predominantly epidemiologically orientated, and rely heavily on positive identification of SARS-CoV by using serology and RT-PCR. (43, 44) Thus, these criteria are not useful at the bedside, although the principle of clinical diagnosis followed by virological confirmation of SARS-CoV infection is mandatory (45).

Clinical Diagnosis

Not only will the patient benefit from clinical vigilance that leads to a suspicion or diagnosis of SARS, but healthcare personnel who are also at serious risk will also benefit from it. (46)

These characteristics are non-specific and may not be useful in differentiating between patients with non-SARS pneumonias and those with SARS, particularly those caused by the more common "atypical organisms" such Chlamydia or Mycoplasma pneumoniae. (47)

Although certain people with impaired immune systems may exhibit moderate or subclinical SARS-CoV infection, there is less indication of this type of virus spreading widely. Additionally, SARS appears to have a less severe clinical course in younger children, and oxygen therapy was not necessary for many of them (48, 49).

The primary diagnostic procedure depends on the identification of an epidemiological connection, the existence of treatment-resistant pneumonia, and the presence of SARS-like clinical characteristics. In a non-outbreak scenario, diagnosing the initial or rare cases of SARS is extremely challenging.

Although the requirements for a confirmed SARS diagnosis are likely more precise than the diagnostic standards published by the CDC and WHO. The majority of respiratory doctors who have dealt with SARS patients in the past also support tracking a patient's clinical progress. (50)

Current diagnostic tests have their own limitations including time, specificity, technician training, and cost. Here, we discuss some fast and accurate biomolecular approaches based on the latest technologies that have been suggested, developed, and even approved to be used by clinical laboratories**.**

Multiplex real-time PCR technology

Given that COVID-19 and influenza share a similar presentation, it is advantageous, economical, and time-efficient to build diagnostic techniques that can identify multiple viruses in a patient at once. The simultaneous detection of SARS-COV-2 and influenza using the multiplex reverse transcription-polymerase chain reaction (RT-PCR) technique can save time, chemicals, and the possibility of human error per sample. A multiplex RT-PCR technique was created by Norz et al. that can concurrently detect influenza A, influenza B, and SARS-CoV-2 viruses with sensitivity values of 98.1%, 97.7%, and 100% for each virus, respectively. To lessen the production of primer dimers, four sets of primer/probes for the SARS-CoV-2 E and RdRP genes, the M gene of influenza A, and the NS2 gene of influenza B were modified and adapted with 2′O-methylated RNA-bases at their penultimate (3′-end) positions. (51)

Primers for influenza viruses A and B, the SARS-CoV-2 N2 and E genes, and the human RP gene as an internal control were used in a different study by Mancini et al. to simultaneously detect the viruses in 1000 clinical samples using the multiplex RT-PCR assay. Of these, two coinfections of SARS-CoV-2 and influenzas were reported. (52)

Nano-based technology

The potential application of nano-based biosensors, such as those based on electrochemistry, optics, piezoelectricity, thermal sensing, and magnetism, for the detection of viral pathogens or antibodies has been the subject of numerous investigations. Various methods and nano-based kits have been developed to use gold nanoparticles (AuNPs) to specifically couple with different biomarkers such as antibodies or nucleic acids. These features allow AuNPs to selectively couple with SARS-CoV-2 or related antibodies. (53)

An AuNP-based colorimetric assay particularly built for the N gene and capped with thiol-modified antisense oligonucleotides (ASO) has been developed by Moitra et al. It can identify the presence of SARS-CoV-2 from the isolated RNA samples in less than 10 minutes. By using this approach, the surface plasmon resonance of the ASO capped with AuNP changes and it agglomerates selectively in the presence of the N gene. Additionally, field-effect transistor (FET)-based biosensors were created that can identify low concentrations of SARS-CoV-2

spike protein. These biosensors are essentially graphene sheets of FET covered with a particular anti-spike protein antibody. (54)

A spike protein-specific nano plasmonic resonance sensor was also proposed as a quick and direct optical way to monitor SARS-CoV-2 particles. The results can be viewed in 15 minutes on a standard microplate reader and a portable smartphone connected device, which reduces the expense and duration of viral detection. In order to improve the duration (30 min) and sensitivity of the RNA extraction. (55)

It developed an RNA extraction approach based on poly carboxyl groups-coated magnetic nanoparticles (pcMNP) that combines the virus lysis and RNA binding processes into a single step. (56)

Treatment

There are differenttreatment modalities have been used empirically with much uncertainty. The overwhelming situation of large numbers of ill patients deteriorating rapidly prevented anxious physicians from performing randomized controlled treatment trials, which were regarded as dangerous and unethical in the face of a life-threatening condition. (57)

Many treatment options, including antiviral agents, immunosuppressive agents, convalescent plasma, immunoglobulin, non-invasive positive pressure ventilation (NIPPV), and traditional Chinese medicine (TCM), have been introduced on the basis of different rationales are: -

SARS has an initial viral replicative phase, which peaks at around day 10. Response to this viral load takes the form of inflammatory cell infiltration of tissues and overproduction of cytokines, resulting in immunopathological damage. (58) Thus, there is a therapeutic window that can be exploited to prevent disease progression if a potent antiviral agent is available. Ribavirin has been chosen for use due to its wide spectrum of activity, despite being rather weak against SARS-CoV. Protease inhibitors are now under study because of the experimental evidence that they can inhibit the 3C-like (3CL) protease, which is essential for the life cycle of the SARS-CoV. (59, 60, 61)

Corticosteroids have been utilized to mitigate the tissue-damaging effects of inflammatory cells and cytokines and to treat the acute respiratory distress syndrome (ARDS), bronchiolitis obliterans organizing pneumonia (BOOP), and septic shock that may occur. (62)

Convalescent plasma has been administered in the belief that the large amount of neutralizing antibodies present can block the action of the SARS-CoV. (63)

Immunoglobulin has been employed as a salvage therapy in patients with inexorable deterioration despite usual treatment. This approach is based on the immunomodulatory effect of immunoglobulin, which includes competitive occupation of macrophage receptors, neutralization of activated complements, cytokines and superantigens, and inhibition of activated T lymphocytes. (64, 65)

Traditional Chinese Medicine has been used in China because of its known efficacy in the treatment of “fevers” throughout the ages. With the absence of a consensus on the optimal therapeutic strategy, various approaches have been devised elsewhere in the world.(66)

Novel approaches for treatment of SARS

Nano-based technology

In order to improve the specificity and efficacy of antivirals and other nanomedicines, nano-based technologies for drug encapsulation and drug delivery to the infected cells have been studied for the treatment of viral infections such as influenza, HIV, HBV (Hepatitis B virus), or HCV (Hepatitis C virus). (67, 68, 69)

It was suggested that COVID-19 patients be given dexamethasone nanomedicine, which has previously been utilized to treat multiple sclerosis, inflammatory bowel disease, and rheumatoid arthritis. (70)

Arcturus Therapeutics and Imperial College London designed and developed encapsulated self-replicating mRNA vaccines using lipid nanoparticles as delivery particles (NLPs) [85]. Using the plasma membrane of lung type II epithelia cells or human macrophages, Zhang et al. [86] created cellular nanosponges. By displaying ACE2 on their surfaces, which binds to spike protein to stop or lessen the infection of other cells, the nanosponges draw in and neutralize SARS-CoV-2. It was also suggested to use theranostic nanoparticles, which combine to deliver medicines to the targeted cells through intranasal delivery. (71, 72)

CRISPR-based technology

In addition to being a diagnostic tool, CRISPR-cas gene editing technology is recommended as a treatment strategy to combat COVID-19. Using RNA-guided endonucleases (Cas13d) and crRNA, Abbott et al. (73)

Now, recently studied the genome cleavage and destruction of SARS-CoV-2 and other coronaviruses. They created many crRNAs that target SARS-CoV-2 and a PAC-MAN system (Prophylactic Antiviral CRISPR in Human Cells). In a human lung epithelial cell line, they observed 85% and 70%, respectively, suppression of signal reporters fused to RdRP protein and N protein. A few methods for introducing the CRISPR system into the desired cells include lipofection, electroporation, nucleofection, microinjection, and viral vectors. (74)

For example, the complex of cas13-antibody specific to the S protein of SARS-CoV-2 was delivered using the antibody and CAS (ABCAS) fusion method, and it was delivered only to the infected host cell. (75)

Neutralizing-based technology

Many nations are conducting clinical trials for immunotherapy, both passive and active, to prevent SARS-CoV-2 infection. The immune response of the patient is stimulated or improved by active immunotherapy (e.g., vaccinations and direct interferon delivery). Passive immunotherapy involves the administration of immunological molecules, such as convalescent plasma and mono- or polyclonal antibodies, to patients who are unable to create them on their own. Monoclonal antibodies (mAb) can target many proteins implicated in the pathogenesis of SARS-CoV-2, including viral antigens and human immunomodulators. The majority of mAbs are full-length IgG-based monoclonal antibody format, and many are undergoing clinical studies. (76)

Spike protein epitopes that prevent spike proteins from attaching to host cell receptors are the most often targeted viral targets. (77)

The FDA has given an EUA for three laboratory-made mAbs (Immunoglobulin G1) that target the RBD of the SARS-CoV-2 spike protein thus far. For non-hospitalized COVID-19 patients aged 12 years or older with mild to moderate symptoms, as well as patients over 65 or with specific chronic medical conditions, casirivimab and imdevimab (provided by Regeneron Pharmaceutical Inc.) and bamlanivimb (provided by Eli Lilly and Company) are advised in order to prevent the progression to severe stages and hospitalization.

Moreover, a number of mAbs that target human immune responses (such as C5A, IL17, IL1β, and GM-CSF) were created or repurposed and are currently being studied in clinical trials. Levilimab (Ilsira), (by BIOCAD) and tocilizumab (Actemra) target IL-6 receptor, and itolizumab (by Biocon) targets CD6. (78, 79)

Polyclonal antibodies (pAbs) are particularly interesting because they can decrease the time, expense, and labor associated with mass manufacture and clinical evaluation of monoclonal antibodies (mAbs), as well as the possibility of the virus escaping through mutation. A small number of produced pAbs against COVID-19, such as SAB-185 (SAB Biotherapeutics), COVID-HIG, and COVID-EIG (Emergent BioSolution), which are created from immunoglobulins taken from human plasma and genetically modified cattle, respectively, are undergoing clinical testing phases [63, 68]. Recombinant anti-coronavirus immunoglobulin (rCIG), GIGA-2050 (GigaGen Inc.), is another pAb derived from B cells that, according to the manufacturer, binds to a range of viral epitopes and is currently undergoing mass manufacturing. (80)

Other neutralization platforms under preclinical or preclinical trials that target viral proteins, interleukins, or CD molecules include fusion proteins, nucleic acid-encoding mAbs, nanobodies (small single-domain antibodies), and DARPins (designed ankyrin repeat proteins). Single heavy-chain antibodies, also known as nanobodies, were initially found in camels and sharks. They are small proteins with increased permeability, stability, and solubility that are tested for a variety of viral illnesses, including poliovirus, rabies, HIV, hepatitis B, and poliovirus [Various synthetic and animal-derived (llama) nanobodies have been created and generated to target the receptor-binding domain (RBD) of SARS-CoV-2 spike proteins. (81, 82)

Conclusion

During COVID-19, the health professionals are anxious, overworked and financially unstable. Despite the challenges, they are working, planning, creating and caring for others and their families. Their heroism, dedication and selflessness offer reassurance that we will be able to overcome this virus. We need to give them all the support they need to do their jobs, be safe and stay alive. Future research should explore the fears and coping strategies of health professionals as frontline soldiers during pandemics.

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