Journal of Experimental Biology and Agricultural Sciences

<http://www.jebas.org>

ISSN No. 2320 – 8694

SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUSES AND 21ST CENTURY PANDEMIC: AN OVERVIEW OF FUNCTIONAL RECEPTORS AND CHALLENGE OF THERAPEUTIC SUCCESS

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Received – October 05, 2020; Revision – October 20, 2020; Accepted – October 28, 2020

Available Online October 30, 2020

DOI: [http://dx.doi.org/10.18006/2020.8\(Spl-1-SARS-CoV-2\).S87.S102](http://dx.doi.org/10.18006/2020.8(Spl-1-SARS-CoV-2).S87.S102)

KEYWORDS

SARS-CoV-2

ACE2

TMPPRS2

ADAM17

Plasma and Stem Cell
Therapy

ABSTRACT

Sudden prevalence of coronavirus disease-2019 (COVID-19) has badly impeded and collapsed the emerging global trend of economic development by its ongoing pandemic. The novel coronavirus also named severe acute respiratory syndrome virus – 2 (SARS-CoV-2) causes the disease COVID-19 that influences the health management of humans and the world commerce badly. It has affected the human social lives and education in underdeveloped countries and severely impeded industries, organizations, agriculture, etc. Three perceptible types of SARS-CoV-2 strains have been discovered. Each of them has specific receptors, and some of them are common in SARS and SARS-CoV-2. Among them, the ACE2 receptor is believed to be the central receptor of human infectious coronaviruses. It supports mainly to get access, enter into the cell, and causes the basic infection. Similarly, TMPPRS2 is also acting as a portal for a virus to get an approach to the cell and does not support metabolic processes like replication virus. ADAM17, which is a member of disintegrins and metalloproteases and is responsible for cell to cell and cell-array interconnections. These receptors can be important for prevention, vaccine development, and therapies. Several therapies in SARS-CoV-2 infected patients have been tried and suggested. Plasma and stem cell therapy reduce the severity of infection at certain levels in individual

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Peer review under responsibility of Journal of Experimental Biology and Agricultural Sciences.

Production and Hosting by Horizon Publisher India [HPI]
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patients. In this review, we make an effort to cover all of the said aspects of COVID-19 in a very compressive and brief way. Finally, we shed light on vaccination and therapeutic approaches like plasma therapy and stem therapy and their future perspective with the whole discussion conclusion.

1 Introduction

A newly discovered coronavirus severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which caused severe acute respiratory syndrome, appeared in Wuhan City, China Region of Hubei in December 2019 (Wakimoto, 2014; Lu et al., 2020; Xu et al., 2020). The World Health Organization (WHO) recognized the correlative agent of the pandemic as the SARS-CoV-2, developing the disease called coronavirus disease-2019 (COVID-19) that induces respiratory disease ranging from asymptomatic respiratory pathway disease to serious, moderate pneumonia, multi-organ negligence, and ultimately triggers the victim's death (Dhama et al., 2020a; Dhama et al., 2020b; Shah et al., 2020; Xu et al., 2020). SARS-CoV-2 was documented to be transmitted via contact with infected patients (Lotfi et al., 2020; Zhou et al., 2020). It has been recorded that SARS-CoV-2 infection is transferred immediately from human to human, like other pneumococcal meningitis, by intimate contact with an infected individual or by airborne droplets (aerosols) formed when an infected individual cough or sneeze (Cao & Shi, 2020). The estimated number of patients reported globally until May 6, 2020, is 3,588,773 patients and mortality rates are 247,503 deaths (Wang & Fish, 2019). According to the recent report from the World health organization (WHO), as of 11th October, 2020, the total number of cases was 37 million, with new 2.2 million new cases during the last week. While the number of deaths until has crossed the figure of 1 million with 39000 deaths during the last reported week (World health Organization 2020). While today's, the WHO report mentions 38619674 cases and 1093522 death worldwide with 225495 new cases and 5937 new death reported during the last 24 hours (World health Organization 2020).

Coronavirus cell entrance relies on attaching the viral spike (S) protein to the cell sites and after the annealing of S proteins by host cell-specific proteins. The S protein is produced in the contaminated cell secretory channel, and S protein beaters are introduced into the virus envelope (derived from the endoplasmic reticulum Golgi intermediate compartment [ERGIC]) and host cell nucleus membrane. The S protein possesses class I fused protein domain organization; it comprises an N-extreme layer section (S1) engaging the receptor, and a C-extreme trans-membrane section (S2) consisting of the membrane amalgamation machinery (Li et al., 2006).

Unraveling that cellular factors SARS-CoV-2 uses to get access to provide clues into the delivery of viruses and reveal clinical objectives (Hoffmann et al., 2020). This is used to clarify that why

SARS-S and SARS-2-S have governed entry together in the similar cellular lines. TMPRSS2 irritants were found in type I pneumocytes, while the immunofluorescence staining procedure used identified only poor coloring of the ACE2 irritants in swollen type II pneumocystis (Lucas et al., 2008; Hoffmann et al., 2020). An antibody had been used as a negative control toward SARS-CoV. We then calculated if SARS-2-S harbors nucleotide sequences that are necessary for interactions with the ACE2 SARS-S entrance receptor. There we illustrate that SARS-CoV-2 utilizes the ACE2 for intake and the TMPRSS2 serine protease for S protein annealing (D'Amico et al., 2020; Lucas et al., 2008; McKee et al., 2020). A TMPRSS2 retarder permitted restricted entry for therapeutic utilization and may represent an alternative for treatment. Our findings reveal essential similarities between outbreak with SARS-CoV-2 and SARS-CoV recognize legitimate prey for anti-viral intervention (Jia et al., 2009). ADAM17 is an active treatment of alpha tumor necrosis factor (TNF- α) on the cellular surface and inside the trans-Golgi network's intercellular membrane (Lucas et al., 2014). Necessary information about receptors is shown in table 1 & 2. Such a method, also known as 'shedding,' includes the cleavage and escape from membrane-bound pro-proteins of a soluble ectodomain (such as pro-TNF- α), and is of recognized physiological significance (Haga et al., 2008). It plays a role in releasing a diverse array of membrane-anchored growth factors, cell adhesion molecules, cytokines, metabolites, and proteins.

The "COVID-19 vaccine" is a suppositional vaccine for coronavirus diseases 2019 (Le et al., 2020). Although there are no vaccines to complete impersonal trials, there are still many struggles to develop this vaccine (Iqbal Yatoo et al., 2020). Therefore, the information source focuses on public health measures to prevent the transmission of human-related viral infections. This requires several methods. For people, this includes poor personal hygiene habits, avoiding overcrowded/crowded environments, and isolating yourself if necessary (Pittet et al., 2009). At the health center, tremendous efforts are needed to quickly diagnose, isolate causes, and provide effective supportive treatment. This will include the experimental treatment of antibiotics, antivirals, and supportive measures (Commission, 2020). Moreover, to reduce the risk of COVID-19, some used therapies like Plasma and stem therapy (Pittet et al., 2009; Cao & Shi, 2020).

In this review, we explored the role of ACE2, TMPRSS2, and ADAM17 in the entry of coronavirus to receptor cells, and tried to explain how ACE2 and TMPRSS2 help the coronavirus in its pathogenesis and increasing the infection. We also view ongoing

Table 1 Basic information about receptors

RECEPTOR	GENE ID	LOCUS	DEFINITION	ACCESSION	VERSION	FUNCTION	REFERENCE
ACE2	59272	NC_000023 107639 bp DNA linear	Homo sapiens chromosome X, GRCh38.p13 Primary Assembly	NC_000023	NC_000023.11	It participates mainly to get access to the cell and cause the basic infection.	(Ferron et al., 2018)
TMPRSS2	7113	NC_000021 43854 bp DNA linear	Homo sapiens chromosome 21, GRCh38.p13 Primary Assembly	NC_000021	NC_000021.9	It also participates in collective physiological and pathological mechanisms which include several viral and cancerous infections	(Hoffmann et al., 2020; Li et al., 2006; Lucas et al., 2008)
ADAM17	6868	NC_000002 67345 bp DNA linear	Homo sapiens chromosome 2, GRCh38.p13 Primary Assembly.	NC_000002	NC_000002.12	It performs several proteolytic activities and also actively participates in some autoimmune responses	(Boudry et al., 2019; Le et al., 2020; WHO 2020)

Table 2 Receptors and their function in the human body

Receptors	Functions in the human body	References
ACE2	It is involved in the entry of the virus in the cell to cause the final infection	(Boudry et al., 2019; Lu et al., 2020)
TMPRSS2	Transmembrane Serine Protease 2 (TMPRSS2) a protein that has recently been proven to be the basis for SARS-CoV-2 to enter cells	(Hoffmann et al., 2020)
ADAM17	It may represent a therapeutic target for human renal fibrosis	(Kefaloyianni et al., 2016)

vaccine development approaches, clinical trials, plasma therapy, future projects, prevention, and control measures. As a result, the information provided in this paper, supply important information for scholars and the public, which helped to gain knowledge about COVID-19.

2 Methodology

In this review, we are conducting PubMed information to find English language paper by October 2020. These involve SARS-CoV, SARS-CoV-2, Coronavirus, and COVID-19 in combined with diagnosis and treatments. These also involved different receptors like ACE2, TMPRSS2, and ADAM17 combined with their positive and negative impacts on the pathogen entry in the cell. We were also using different bioinformatics tools to interact with some basic species of coronavirus and understand the interaction of receptors with their respective family members. These yields are from approximately 200 papers. An analysis of cited references found additional related papers. The authors have published summary and case studies papers.

2.1 Article determination and withdrawal of data

All titles were concealed by two reviewers. Separately, a third reviewer, after many results and sorting out different problems,

finalize the abstracts and full texts. Later on, the subsequent information was withdrawal: 1. entitlement, 2. foremost writer, 3. track record, 4. Publication date, 5. first author's country, 6. order of study, 7. subject. The explanations are secured in the below diagram.

2.2 Data examination

The explanatory examination was managed by involving the compositions or literature. Resources were narrated about establish the article, date of proclamation, study order, and subject of study on COVID-19 to analyze the live spaces in groundwork.

3 Coronavirus Genetics

Viruses contain either RNA or DNA as genetic material (Almani et al., 2012; Khan et al., 2020). Coronaviruses belong to the family Coronaviridae. Because of the shortfall of proofreading occupation of viral RNA polymerase as in every single-stranded RNA viruses, it demonstrates a rapid biological mutation value (Elena & Sanjuán, 2005). SARS-COV-2 has finite abilities of proofreading in which nsp 14 permits them to increase the size of the genome of CoV other family members (Ogando et al., 2020). This character makes them slightly different from other mutated, vulnerable RNA viruses. In the process of evolution, the mechanism of

recombination also participates in a significant role, which causes numerous modifications that occurred in coronaviruses (Lau et al., 2011; Ferron et al., 2018). The viral genetic data were fetched from the NCBI database. Multiple sequence alignment was managed using MUSCLE (Multiple Sequence Comparison by Log-Expectation) (Huntley, Kalyanamoorthy et al., 2017; Wang et al., 2020; Wang et al., 2020). A whole-genome- sequence phylogenetic tree, using the maximum likelihood method and Model Finder, was erected in the IQ tree (Huntley, Lau et al., 2011; Wang et al., 2020; Wang et al., 2020). The tree was designed in such a way that it shows the branch lengths in several alternatives per site.

MEGA X conceptualizes the phylogenetic tree (MEGA). Examination of sequence exposed that SARS-CoV-2 clumps with SARS-CoV associated viruses from bats (SARSr-CoV), in that some of them use ACE2 receptor to enter in the host cell (Figure 1).

4 Receptors

4.1 ACE2

ACE2 is known as Angiotensin-Converting Enzyme 2 which is revealed as the central receiver that helps human infectious SARS-CoV, HCoV-NL63, and SARS-CoV-2 (COVID-19) to get access

in the given cell. After entering the host cell, it plays a very salient role in originating viral infection (Huntley). According to Hamming et al. 2004 and Wrapp and colleagues recently reported that bet corona viruses come up with the Cryo-EM shape of the virus S (spike) protein, which recorded that amount of ACE2 is 10-20 folds more in SARS-CoV-2 than SARS-CoV (Hamming et al., 2004; Wrapp et al., 2020).

ACE2 is chiefly present in epithelial cells of the lung, intestine, kidney, and blood vessels. These explicate increase the rate of pneumonia and bronchitis in the victims of COVID-19. Besides this, it may lead to certain cardiac symptoms (South et al., 2020; Wrapp et al., 2020; Zhang et al., 2020). Advanced studies about ACE2 reveal that it is distinctly indicated in the verbal cavity mucosa, which gives pathogen a smooth way of entrance to the latest liable (Xu et al., 2020). So it is a consequence that human infectious coronaviruses use a similar opening to get entrance in the section (Hamming et al., 2004; Xu et al., 2020). Upcoming proofs about ACE2 shows that we can use it as a knit to fight against the COVID-19 alternative as a molecular prey.

Rather than in 2014, scientists revealed that the ACE2 enzyme acts a guarding role against the influenza A (H7N9) virus, which creates severe lung injury (Hemnes et al., 2018). A higher level of this panacea gives better results in some victims. On the other hand, in

Figure 1 Genetic Analysis of CoV family with each other to check the resemblance.

mice, when we switch off the genes of ACE2, it causes severe lung destruction with H5N1, and in the same way, when these mice treated with human ACE2, they were causing irrigated lung injury here (Zhao et al., 2020). Moreover, it has been revealed that a sole dose of homogenizing human ACE2 (GSK2586881; 0.2 mg·kg⁻¹ or 0.4 mg·kg⁻¹ I.v., NCT01884051) is beneficial for pulmonic arterial hypertension has been both in the preclinical and impersonal arrangements (Zhang et al., 2018). Further research shows that the distribution of modified ACE2 amounts in the variety of folk and genetic lines has been demonstrated with some specific dissimilarity. In Asia, research about sole-cell RNA-sequencing specified that excessive expression of ACE2 tissues is present in Asian males (da Silva et al., 2017). When this research of ACE2 serum is moved towards the northeastern Chinese Han population, it shows many negative aspects related to body mass index (BMI), pulse pressure, and estrogen degrees in female EH (essential hypertension) victims (Zhang et al., 2018). The examinations about transmitting the level of ACE2 on cardiovascular shielding results and concomitantly manifest that estrogens assist in the up-regulation of ACE2 impression and task degrees (da Silva et al., 2017). These kinds of descriptions revealed that females' immunity conversely with the male in SARS-CoV-2 infection is more. These consequences indicate that males are more susceptible to this disease. This sex susceptibility also assumed the reasoning of the strange ACE plasma profile against COVID-19. The amount of ACE2 is normally more in children than adults (Guan et al., 2020). For example, after the study of 1,099 sufferers in China, only 0.9% of cases confirmed positive were under the age of 9, whereas 1.2% of cases were between 10 to 19 years. This revealed after applying the FAPGG-supported enzymatic task assay that the amount of ACE in children (from 6 months to 17 years of age) is 13–100 U/l as a contrast to adults, which is 9–67 U/l (Torres-Rosado et al., 1993).

4.2 Protein-protein interaction:

The diagram of protein-protein interaction between the following molecules are given in figure 2.

Figure 2 Protein-Protein interactions of ACE2 with other receptors of its family

4.3 TMPRSS2

The abbreviation of TMPRSS2 is 'trans-membrane serine protease 2, which contains many processes of physiology and pathology such as cancer and infections of the virus (Bugge et al., 2009). *Trans*-cleavage of SARS enables by TMPRSS2. The entry of the virus is affected by TMPRSS2. Therefore it does not affect the other phases of viral replication TMPRSS2 is an activator of SARS-CoV that does the entry into the host cell (Torres-Rosado et al., 1993). In the human lungs, TMPRSS2 is highly expressed at epithelial cells. SARS S's growth urged cell to cell merged through TMPRSS2 that revealed through the syncytium formation, which is an increase in "TMPRSS2 Positive cells affected with replication Competent SARS-CoV. On the target cells, TMPRSS2 approves effective SARS S urged virus to cell union in the occurrence of the lysosome tropic agent and the cathepsin inhibitor (Torres-Rosado et al., 1993). TMPRSS2 is affected by the S protein of the virus, which attaches towards receptors at the surface of the Cell, but it is not lately produced S proteins whichever during the transportation to the plasma membrane in the virion. TMPRSS2 is extremely expressed in local and metastatic prostate cancer 17 to 18, and its transcription process is regulated by AR (androgen receptor) (Lucas et al., 2008). This characteristic contributed to the highly express of TMPRSS2 in prostate gland 18 and the high rate of genomic reformations, including TMPRSS2 promoter and fellows of the ETS gene family, mainly ERG that placed the oncogene under the controller of the AR (Torres-Rosado et al., 1993). TMPRSS2 expresses in the lungs can describe males' improved vulnerability to grow SARS-CoV-2 infection severe infections correlate to women. AR controls TMPRSS2 show in the non-prostatic tissues, contain lungs, can describe an increase in males' weakness to grow SARS-CoV-2 severe infections (Kefaloyianni et al., 2016). These indicate that potential new therapeutic interventions for the treatment of new coronaviruses are affecting people. It is known that androgen deprivation therapy reduces the levels of "TMPRSS231 and AR antagonists" and can be used in combination with other entry or release inhibitors to reduce the degree of stiffness of COVID-19 in men. Recent and former work focus showed that TMPRSS2 is a host cell factor that is serious for transmission of numerous clinically related viruses Such as Coronaviruses as well as influenza A viruses (Elena & Sanjuán, 2005; Lucas et al., 2008). SARS-CoV infection is linked with TMPRSS2 in the lungs that protease can ably activate SARS-CoV -S protein to increase virus to cell membrane union at the surface of the Cell.

On the other hand, for improvement and homeostasis, TMPRSS2 is unessential and establishes an attractive drug target (Tomlins et al., 2005). TMPRSS2 activity is blocked through the Serine Protease inhibitor camostat mesylate used for humans in Japan, but

a dissimilar signal (Wakimoto, 2014). The related ones compound having possibly increased antiviral activity (Tomlins et al., 2005) can be considered for the off-label cure of COVID-19 patients. In normal lung tissues, the localization of TMPRSS2 expressed cells occurs, other than ACE2-expressing cells, strictly knotted to SARS-CoV-2 infection in minor wounds, signifying that TMPRSS2 might be determined viral tropism at an initial level of SARS-CoV-2 infection.

Androgen Receptor co-regulatory factors and transcription factors (e.g., ETS, SP1) can be used for down-regulate (Lucas et al., 2008). On the other hand, TMPRSS2 show which appeared in cells neighboring to virus influenced cells, not in ill cells, suggesting that TMPRSS2 might also be down regulated in unhealthy cells, as detected for ACE2. In vitro studies have shown that inhibition of TMPRSS2 may help limit SARS-CoV-2 infection (Hoffmann et al., 2020). The results in vitro and in vivo indicate that androgen administration can persuade the expression of TMPRSS2 in human lung epithelial cells, and androgen deprivation will reduce the transcription of TMPRSS2 in the rat lung (Kefaloyianni et al., 2016).

4.4 Protein-protein interaction:

The diagram of protein-protein interaction between the following molecules are given in figure 3.

Figure 3 Protein-Protein interactions of TMPRSS2 with other receptors of its family

4.5 ADAM17

ADAM17 belongs to the ADAM protein group of disintegrins and metalloprotease whose length is 70 kDa. It is metallopeptidase domain 17 (ADAM17), also known as TACE (tumor necrosis factor- α -converting enzyme) (Kefaloyianni et al., 2016). These family members' specificity is that they have anchored proteins that are structurally resembled the disintegrin of snake venom, which is then exposed in the

different biological processes including cell to cell and cell-array interconnections implantation, muscle growth and neurogenesis. Mature protease proteolytically helps to engender the encoded pre-protein. Dissolvable tumor necrosis factor-alpha burst out from the membrane-leap pioneer, which is the encoded protease functioning to get rid of tumor necrosis factor-alpha (Tomlins et al., 2005; Scharfenberg et al., 2020).

Cell adhesion proteins, cytokine, developmental factor acceptors, and epidermal development factor acceptor binders are some of the substrates on which protease can carry their functioning. The initiation of the Notch signaling pathway is also an essential function of the encoded protein. Encoded proteins give fundamental participation in autoimmune disease by hoisted the appearance of this gene distinguished in peculiar cellular varieties that arise from psoriasis, rheumatoid arthritis, multiple sclerosis, and people with Crohn's disease (Kefaloyianni et al., 2016).

ADAM17 is responsible for the mature soluble form of the membrane-leap pioneer of TNF-alpha and also conducted the proteolytical liberate the soluble JAM3 from the endothelial section plane. It also brings out the proteolytic release activity of some other cell-surface proteins, including p75 TNF-receptor, interleukin 1 receptor type II, p55 TNF-receptor, and transforming growth factor-alpha, L-selectin, growth hormone receptor, MUC1, and the amyloid progenitor protein. As it also takes action as an initiator of the Notch array by conciliating breakage of Notch and creating the membrane-relative central patch known as Notch extracellular truncation (NEXT) (Boskovski et al., 2013; Scharfenberg et al., 2020). It is also an active participant in the proteolytic clarifying of the ACE2 enzyme. Also, it helps to get rid of GP1BA and the platelet glycoprotein-Ib alpha chain. It leads to the release of LAG3 secretion and also moderates its proteolytic cleavage (Heurich et al., 2014; Kefaloyianni et al., 2016; de Queiroz et al., 2020).

Kidney fibrosis leads to kidney injury is inharmonic health factors that give rise to conspicuous morbidness and loss of life across the board (Kefaloyianni et al., 2016). In present-day research in a molecular process of kidney fibrosis, it manifested that ADAM17, TNF α , and the EGF-R ligand amphiregulin were up synchronized essential to go through the incitement of EFG-R and penetration of neutrophils and macrophages take place in fibrosis. The depletion of ADAM17 is preserved in opposition to these pathophysiologic modifications. These outcomes revealed that ADAM17 stand in for medical object in the kidney (Wakimoto, 2014; Boudry et al., 2019; Palau et al. 2020).

4.6 Protein-protein interaction

The diagram of protein-protein interaction between the following molecules are given in figure 4.

Figure 4 Protein-Protein interaction of ADAM17 with other members of its family

5 Coronavirus strains A, B and C

Researchers are mapping the actual spreading reason of SARS-CoV-2 in humans. For this purpose, they have found three distinct but closely related variants. They recreated the earliest development of all routes of this disease (virus) as we know that it extended from central China to Wuhan (China), Europe, and North America (Hussain et al., 2020). In analyzing the first 160 complete virus genome, which was compiled from human patients, researchers discovered that the variants found in bats were mostly present in patients of the United States and Australia not in Wuhan (China). Scientists believe that the known virus SAR-COV-2 is continuously evolving into different populations to overcome the resistance of the immune system of the host. They used to collect sample data from around the world between December 2019 to March 2020; then they revealed that there are three distinct but closely related variants, which are A, B, and C. Researchers found the closest type of coronavirus detected in bats (the genome of the original human virus) was found in Wuhan (China), but it was not the primary type of virus in that city. Americans living in Wuhan have reported modified versions of the type A variant, and many patients have been diagnosed with type A virus in Australia and the United States. Wigan's dominant virus was type B and it was common among patients in East Asia, but it was not extended beyond the region without a further mutation. Type C virus is the essential type of virus in Europe, which was first seemed in France, Italy, Sweden, and England by researchers. It is also observed in Singapore, Hong Kong, and South Korea but is absent from the study sample on Chinese soil. Variable A is very related to the virus, which was seen in bats and pangolin, has been cited as the root cause of the outbreak. The study concludes that the type B variant is derived from the type A variant, which was separated by mutation, yet the type C variant is known as "daughter" of the type B variant.

6 Coronavirus vaccines

Considering humans have never encountered a new coronavirus (SARS-Co-2) before, the human bodies cannot respond well to the infection they cause. The vaccine allows the body to produce an immune response against SARS-CoV-2, which can control or prevent infection. However, it needs time to produce a powerful and safe Vaccine (Le et al., 2020). The average is usually 5-10 years. Although there are global reports of the possible use of coronavirus vaccines, the development process may take 12-18 months. It's turning into faster to produce new vaccines than it turned into within the past as we can build on research from Vaccines used for different illnesses. More sources and investment may end up in the time of outbreaks, which could accelerate the project. Products may additionally be considered to be used even before being formally granted licenses to govern the disorder in seriously affected areas in emergencies (World Health Organization, 2020).

7 Vaccine Candidates and clinical trials

The globally uncontrolled situation of SARS-CoV-2 spread indicates that the vaccine will be a reliable solution to resolve this pandemic. The speed of vaccine development is many times faster than for the other infections in history due to advanced facilities and a better understanding of the nature of life (Dagotto et al., 2020). According to CEPI scientists, vaccine candidates at an initial development stage, whether in their approved effective projects or pre-symptomatic development (Li et al., 2020), phase I trials test general for protection and initial dosage for barrel healthy subjects. And Phase II trials directly after triumphing in the phase I trials compared immunogenicity, dosage level ("biomarker-based efficacy"), and candidate vaccine adverse outcomes, usually at 100 Peoples (Gouglas et al., 2018; Roback & Guarner, 2020).

WHO mentioned in a report that currently there are more than 100 candidate vaccines under investigation and specialists all over the world promising to cooperate to speed up the COVID-19 vaccine development (DiMasi et al., 2016; Le et al., 2020; World Health Organization, 2020). COVID-19 is a novel Viral target whose properties have not yet been found, it needs vaccination technology and innovative improvement techniques. That's why the development of effective vaccines at all preclinical and clinical research levels will carry a significant number of risks (Le et al., 2020). Investigation of the vaccine Development enterprise has traditionally shown 84 percent to 90 percent failure rates (Chu et al., 2004; Golchin et al., 2019).

American biotechnology company "Moderna" has developed the first vaccine for COVID-19 human trials. Several companies and institutions are using their resources for the development of the

COVID-19 vaccine, as previously mentioned in a report by WHO, more than 100 vaccine candidates are in the process of development, and several among them are at the various levels of in clinical trials " ", one of which was developed by a researchers' team at Oxford University. The candidate vaccine was confirmed in January and is currently entering clinical trials (DiMasi et al., 2016; Vaccine, 2020).

As they race to devise a vaccine, researchers are trying to ensure that their candidates do not spur a counterproductive, even dangerous, immune system reaction known as an immune enhancement. In addition to this, funding limitations may also be an important factor in the way of the cost-effective and protective vaccine development (Pereira et al., 2020). The main prospects of candidate vaccines for human testing imply high costs for vaccine developers. The average phase one trial plan is expected to be between 14 and 25 million US dollars, but can reach 70 million US dollars (Golchin et al., 2019; Golchin et al., 2019; Vaccine 2020).

Dagotto et al reported several vaccines under preparation and investigation, vaccine candidates for SARS-CoV-2, and most of the vaccines target S protein. Because of several reasons, especially the efficacy of S protein in previously reported MARS and SARS-Cov, its stabilization, and its protective in vivo response (Dagotto et al., 2020).

8 Therapies

8.1 Plasma Therapy

During 2014, the utilization of Convalescent plasma gathered from patients who had cured of Ebola infection sickness suggested by WHO as an experimental treatment during outbursts. A convention for the utilization of Convalescent plasma in the treatment of MERS-Cov was built up in 2015 (Obradović et al., 2019; Mehta et al. 2020).

In the modern pandemic, some reports discussed about the use of Convalescent plasma to deal with SARS-CoV-2 infections and for treating SARS-CoV-2 infection SARS-CoV-2 infection patients in China. Many countries are seriously considering plasma therapy as a possible treatment against COVID-19 (probably a disease caused by a new coronavirus). Plasma therapy utilizes blood Collected from cured patients to introduce antibodies to patients to be treated. Let us look at what is "Convalescent plasma therapy", the advantages and risks of possible therapies, and recent observations have revealed about that (Wakimoto, 2014). The goal of Convalescent plasma therapy is to use blood antibodies from patients cured of Covid-19 to treat people who are severely infected by the virus. The therapy can also be used to immunize people who are infected with high-risk viruses, such as healthcare professionals, patient families, and other high-risk groups (Chen et al., 2020).

This present treatment's idea is basic and depends on why the blood of a patient who has cured of COVID-19 contains antibodies with the particular capacity of battling novel coronavirus. The hypothesis is that the recouped patient's antibodies, once inoculated into someone under treatment, will start targeting and fighting the new Coronavirus in the subsequent patient (Cao & Shi, 2020). The Convalescent plasma therapy is much the same as Passive immunization, as indicated by scientists, it is not a treatment for the SARS-CoV-2 infection SARS-CoV-2 infection instead it is a preventive measure (Roback & Guarner, 2020).

8.1.1 How Convalescent plasma therapy works?

During the recovery period, plasma therapy uses antibodies produced in infected persons infected with new coronavirus (Chen et al., 2020).

The antibodies produced in patients are part of the natural immune response of the body against foreign pathogens or, in this case to new coronaviruses. These antibodies are very specific for pathogens, so they can clear new coronavirus from patients. After the patient recovers, they donate blood to utilize their antibodies in other patients' treatments. Then check the blood for other pathogens, Including hepatitis B, hepatitis C, HIV, etc. (Al Hasan et al., 2020; Fauci et al., 2020). If it is judged to be safe, the blood is drawn through the "plasma" extraction process, which is the liquid part containing antibodies. After extraction, antibody-rich plasma is ingested into the treated patient.

Immunologist John Hopkins University Arturo Casadevall commented on the plasma therapy process: "This is a simple concept". The patient was Cured of an infectious illness. Antibodies usually produce that can resist subsequent infections of the same microorganism. This immunity Force can be transferred by taking serum to patients at risk of disease (Commission, 2020) (Table:3).

8.2 Conventional therapy

In conventional therapy, the healthcare professionally (such as therapists, nurses, and pharmacists) and other medical physicians treated the diseases and symptoms by using through radiation, operation, or drugs. Other therapies are used for less danger of coronaviruses like Oxygen therapy, Antiviral Therapy, interferons, Lopinavir/ritonavir, and others drugs, antibodies, etc. (Chu et al., 2004; Rabaan et al., 2020).

8.3 Oxygen therapy

When a deficiency of oxygen occurred, effectual oxygen therapy should quickly admit rhinal catheterization, domino oxygen. Nasal consonant high-flow oxygen therapy, and non-offensive or offensive mechanically airing should take as essential (Golchin et al., 2019).

Table 3 Different therapies, their uses, and effect

Therapeutic Modality	Use	Effectiveness	reference
Mesenchymal stem cell therapy	MSC is easily accessible and can be isolated from various tissues such as Bone marrow and adipose tissue	Clinical trials do not show any adverse reactions to allogeneic MSCs.	(Golchin et al., 2019)
Convalescent Plasma therapy	CP obtained from recovered COVID-19 patients who have established humoral immunity to the virus contains many neutralizing antibodies that can neutralize SARS-CoV-2 and remove pathogens from blood circulation and pulmonary tissues.	CP therapy may be a promising treatment option for the rescue of COVID-19. Patients recovered from COVID-19 with a high titer of neutralizing antibodies can be a valuable source of CP.	(Chen et al., 2020; Rubin, 2020)

8.4 Antiviral therapies

8.4.1 Interferon- α

"Interferon- α " may reduce viral burden in the starting level of infection that may assist in easing symptoms and reduce the study of ailment (Commission, 2020). Interferon- α 2b sprayed: apply for a high-danger population with near physical contact with distrust coronavirus infected person or those in the initial stages with only higher respiratory tract symptoms. The victim may use 1 to 2 sprinkles to each side of the "Nasal cavity" and 8 to 10 showers on the oropharynx. The dosage of interferon- α 2b is 8000 IU as per inoculation, once every 1-2 hours, 8 to 10 sprays after 24 hours for seven days (Golchin et al., 2019).

8.4.2. Lopinavir/ritonavir

Attempt to use "Lopinavir / Ritonavir" to treat adult pneumonia patients with COVID-19, anyhow its safety and efficacy proved questionable, (Yang et al., 2020). However the, when used in combination with interferon beta-1b and ribavirin, was comparatively effective and reduce the viral shedding period (Hung et al., 2020).

8.4.3 Arbidol, Oseltamivir, and other anti-influenza drugs

It conducted for adulthood infecting with coronavirus; yet, its efficacy and secured remain undefined. Other anti-influenza agents like Oseltamivir may be applied to a patient's coinfect with another influenza virus (Pittet et al. 2009; Le et al., 2020).

8.4.4 Glucocorticoids

The utilization of glucocorticoids is based on the severity of the inflammatory reaction, degreed dyspneic, with or without ARDS, and the progressive position of chest image. It can be utilized just for a short time (3–5 days). The suggested dosage of methylprednisolone has not exceeded from 1 to 2 mg/kg/day. Their

clinical application has been reported to useful for COVID-19 patients in various conditions (Deng, 2020; Isidori et al., 2020; Jimenez-Britez et al., 2020; Patel et al., 2020).

Amazing innovation of dexamethasone is very encouraging that could save the thousands of lives of patients. It has given a good to hope to humanity and lighted the dark way of the COVID-19 patient's health. However, the use of the drug is limited only to the patients on ventilators, severely ill, and in critical condition, and the impact of drugs in reducing the overall mortality is hopeful. Additionally, the comparatively cost-effective and global availability of the drug will significantly reduce the troubles and could be helpful in facing challenges (Patel et al., 2020).

8.5 Mesenchymal Stem Cell Therapy

At present, cell therapy, mainly "stem cell therapy," becomes a favorable technique, and many of them see opportunities in treating irrecoverable diseases (Golchin & Farahany, 2019). Although the field of stem cell-based therapy has made considerable progress, as the main limitation of this treatment method, immunogenicity, limited cell sources, and ethical issues have not been solved. Among them, mesenchymal stem cells have received attention because of their source potential, great proliferation rate, low invasiveness, and unethical procedures. Compared with other therapies, MSC therapy has many advantages (Golchin et al., 2019). They are simple to obtain and separated from different tissues such as adipose tissue and bone marrow, involving Umbilical cord, Vestibular fat pad, Dental pulp, Fetus liver, Menstrual blood, etc.

These pluripotent stem cells; MSC could be readily expanded to clinical capacity within an appropriate period MSC can be stored for repeated treatment. Clinical trials of MSC have never shown the safety and effectiveness of MSCs with adverse reactions. It is recorded in many clinical studies (Golchin et al., 2019). As mentioned earlier, after COVID-19, it triggers excessive immune

interference in the body. In causing cytokine storms, including excessive production of immune cells and cytokines. As cited, after COVID-19, it may additionally destroy the immune system by overreaction. Patients with COVID-19 develop an immune system with high amounts of inflammatory elements that cause a squall of cytokine and the production of immune cells and cytokines beyond the optimize limits (Mehta et al., 2020). This starts the concept of MSC treatment for COVID-19 patients. Due to stem cells' repair properties, Mesenchymal Stem Cell therapy may prevent the immune system from rapidly releasing cytokines and promoting endogenous repair. After the inoculation of intravenous, a portion of the MSC trap in the lungs, that is usually considered a limitation of systemic infusion. But here, MSCs can repair the lung micro-environment, shield the alveolar epithelial cells, cut off the pulmonary fibrosis, treat lung disorder, and COVID-19 pneumonia (Leng et al., 2020).

A major restrain of this technique is the attractive source of MSCs in the clinic, so the speed of clinical preparation as a stem cell bank plays an important role here (Golchin et al., 2019). Besides, MSCs may be separated for several mature tissues, which includes ideally "Bone marrow"(BM), "Peripheral blood" (PB), and Adipose tissue (TA) (such as Abdominal fats, Infra-patellar fat pad, and Buccal fat pad) and associated with bambino birth tissues involving Placenta (PL), Umbilical cord (UC), Warton's gelatin (WJ), Amniotic fluid (AF) and Cord blood (CB), and that's why conserved for future Purposes. Consequently, it seems that MSC-primarily based treatments may be the best candidates for clinical trials or a minimum, a combination of remedies for COVID-19 patients (Leng et al., 2020) (Table 3).

9 Preventions and control

Keep a distance of at least 3 feet (1 meter) from the person who sneezes or coughs. If a person sneezes and coughs and sprays tiny droplets of liquid from the nose and mouth, these may be viral particles and may spread, which means you may breathe in the fall, including the virus COVID-19. If you are near to the person, who is affected. Avoid contracting the mouth, nostrils, and eyes because palms have touched diverse degrees and can pass on the infection.

After infection, the fingers-can transmit the disease in your eyes, nose, or mouth. World health organization (WHO) advises against closing Contact with patients as well as wild and farm animals (Ali Shah et al., 2020; Bilal et al., 2020; Chen et al., 2020).

To avoid meeting other people or avoid going to a medical institution, this will help multiple institutions more effectively and protect yourself and other people from the virus COVID-19. Regularly wash your hands thoroughly with soap and water and an alcohol cloth (Wakimoto 2014) (Table 4)

10 Future projects

In a world where we have also established guidelines for meeting strangers, this pandemic may remind us to prepare for any future challenge that may be more scaring and mortal than this. Scientific and pathological findings based on laboratory research are urgently needed to understand the viral pathogenesis and produce new therapeutic agents, such as antiviral drugs and vaccines, to impact this pandemic of the century. Some organizations are utilizing the published genomes to produce vaccine for COVID-19 (Al Hasan et al., 2020; Fauci et al., 2020). In the United States, the "Food and Drug Administration" declare their goal to use all regulatory flexibility granted by Congress to ensure the fastest Production Vaccine against COVID-19 (Pavlovic, 2020).

A hundred corporations or companies participated in the production of the vaccine. Hundreds of clinical trials have been carried out globally at diverse ranges of the development of the COVID-19 vaccine and "Therapeutic candidate drugs" that have been registered inside the WHO Clinical trial registration (Cheng et al., 2020).

Because of the vaccines and curative antibodies planned to exclude SARS-CoV-2 are also being tested, the current solution is long standing, as they need experimentation of their safety. It could be beneficial to give a telephone call to the healthcare provider instead of face to face visiting the hospital (Hollander & Carr, 2020). The airline industry does have a significant role to make epidemics and prevention of global venture of local diseases

Table 4 Preventive measures for COVID-19

		Reference
Preventions	Cleaning of hands regularly	WHO, 2020
	Do not touch eyes, nose, and mouth	
	Stay at home	
	Cleaning the surface with disinfectant.	Cao & Shi, 2020
	Use Mask for debate.	
	Self -isolation for an infected person	

conclusively. The readiness has to be from public education, steps forward in sanitation, accessibility of adequate and good quality protective equipment to stretchers, improvised hospitals, and convenience of ventilators, medication, and vaccines. Such mobility should not be un-free to COVID-19 but all the long-term authorize ideas help prepare widely distributed life standards; maybe several other pandemics could be waiting for us in the coming years.

11 Control

The vaccine is not yet prepared to treat and prevent the novel corona virus Pandemic (COVID-19). During health care control and prevention, When COVID-19 is suspected: Ensure that all infected persons when sneezing or coughing cover their mouth and nose with a medical mask or tissue paper. When the patients are in chortling rooms or waiting/public areas, Offer a medical mask to health less with the doubtful novel corona virus (Okamoto et al., 2020). After contact with respiratory secretions, wash your hands properly, or perform hand hygiene. In further, to use classic protection, including (Health Care Workers) HCWs, visitors, family members and should use droplet precautions and contact before entering the room of confirmed or suspected COVID-19 patients (Conly et al., 2011). If they are doubtful to have corona virus, their beds must be at least 1-2 meters separately placed because this distance can help reduce the Virus/Pathogens (Haga et al., 2008). Certified/suspected cases should be specifically designated to decrease the danger of infection transmission to the team of HCWs (Healthcare Workers). Health Care Workers to avoid contamination of mucous membranes, Wear face protection or eye protection. HCWs who care exclusively for confirmed cases should wear a gown, long-sleeved, clean, non-sterile, wear gloves, and medical masks (Pittet et al., 2009).

Make sure the method of disinfection and cleaning are constantly or accurate. The environment can be clean by using water and detergents. On the other hand, pesticides like sodium-hypochlorite, etc. are generally utilized in hospitals because these are powerful and adequate in their action.

Conclusion and Future Prospects

We are attending this review article for the sake of giving basic commands about SARS-CoV-2 and this pandemic. It is revealed that when the dangerous virus comes in contact with the ACE2 receptor, it conciliates the host cell's infectious effect. The break down activity of the protein in ACE2 by TMPRSS2 is not used to initiate the process. Although, TMPRSS2 enhances the ingestion of the virus. So we can conclude that the different enzymatic interest of proteases does enhancement in the introduction of the virus. While on the other hand, ADAM17 inflection does not give any participation in the virus's entry. It is also seen that the subcellular breakdown of ACE2 is only by TMPRSS2, not by ADAM17.

More studies and observations showed that ADAM17 can be used as a disinfectant against ACE2 to prevent the virus's entry. The cause of the distinct falling of ACE2 by ADAM17 and TMPRSS2 is still not known. We are also sum up some of the recent practicable, under-observation and used in near future therapeutic therapies for this disease. Some of them are described earlier at the initial level of the outbreak and apply to the victim on a large scale. Some of the examples which may be used recently are *favipiravir*, *hydroxychloroquine* and some others. These drugs make scuffles in the action of the entry of the virus in the cell.

There are two major ways to manage essential precautions. Firstly, we should be aware of the surroundings and the effects of COVID-19 on it. Secondly, if a person will catch the disease, what are the precautionary measures should it take and how this person will make itself in self-quarantine mode to avoid it, from spreading among others. The staff working with this outbreak should be highly trained to handle any situation moderately and come with blows with every pandemic in the future. Moreover, we should train our children so well that they should be adequate knowledge about the epidemic so they can protect themselves completely. According to the present situation, there is not a specific way to get rid of that pandemic. It may possible that the vaccine will be in progress but at that time we have two situations. Either virus infects a lot of people in the world or we may get immunity against it.

Conflict Of Interest

Authors would hereby like to declare that there is no conflict of interests that could possibly arise.

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