REVIEW ARTICLE

Overview on Origin, Transmission, Treatment and Clinical Researches of Sars-Cov-2

Asita Elengoe[1]*, PhD; Shalini Selvam[2], BSc Student

[1]Associate Professor, Department of Biotechnology, Faculty of Science, Lincoln University College, 47301 Petaling Jaya, Selangor, Malaysia
[2]Undergraduate Student, School of Biotechnology, Manipal International University (MIU), 71800, Putra Nilai, Negeri Sembilan, Malaysia

Correspondence:
Asita Elengoe, PhD;
Associate Professor, Department of Biotechnology, Faculty of Science, Lincoln University College, 47301 Petaling Jaya, Selangor, Malaysia
Tel: +60 166506959
Email: asitaelengoe@yahoo.com
Received: 1 October 2021
Revised: 18 November 2021
Accepted: 6 December 2021

Abstract

Background: The year 2020 began with a new public health hazard. A novel coronavirus, acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was discovered in Wuhan, China on 12th December 2019. In 2020, the World Health Organization (WHO) introduced the name of the disease as 'COVID-19'. The morphology, pathogenic mechanisms, causes, transmission, symptoms, diagnosis, therapeutic potential, clinical studies on COVID-19 infection, preventive measures, and mental health care were described in this study.

Methods: A literature search was conducted using electronic databases such as PubMed, Scopus, Elsevier, Frontiers, Medline, EMBASE, Web of Science, Science Direct, and Google Scholar. The search was broadly scoped, using key terms such as SARS-CoV-2, COVID-19, etc.

Results: The genomic characterization of SARS-CoV-2, drugs, and their potential mechanisms used in humans to inhibit the SARS-CoV-2 were tabulated. Moreover, twenty-five clinical researches carried out against COVID-19 infection were also tabulated in this study. Preventive measures such as chemical disinfectants and increasing test capacity were also discussed.

Conclusion: The current study provides a snapshot of the overview of the SARS-CoV-2 and COVID-19. The findings suggested the effective preventive measures to halt the spread of SARS-CoV-2 and develop a better vaccine. The information from this review study also aids in early preparations for future pandemic outbreaks.

Please cite this article as: Elengoe A, Selvam S. Overview on Origin, Transmission, Treatment and Clinical Researches of Sars-Cov-2. J Health Sci Surveillance Sys. 2022;10(1):2-12.

Keywords: SARS-CoV-2, COVID-19, Pandemic, Infection, Vaccine

Introduction

Coronavirus disease 2019 (COVID-19) is an acute respiratory disease that was confirmed on January 12, 2020, by World Health Organization (WHO). This disease originated in Wuhan, China.[1, 2] The initial outbreak of SARS-CoV-2 was reported in December 2019 at Hunan South China Seafood Whole Sale Market. On January 7, 2020, this virus was identified as a new coronavirus with a homology similarity of more than 95% to a bat coronavirus and 70% homology similarity to the coronavirus (SARS-CoV).[3] On January 7, 2020, the Chinese scientists discovered a novel coronavirus (nCoV) that caused severe pneumonia disease; afterward, on January 12, 2020, the WHO declared the epidemic outbreak caused by the nCoV and introduced the disease as COVID-19.[4, 5]

The early quick finding showed that this SARS-CoV-2 disease was transmitted through the seafood market in Wuhan City. Other than seafood, this market has a variety of unusual delicacies such as bats, birds, and snakes, which are high potential carriers of different viruses and bacteria due to their habitats. The analyses of the collected samples from these animals found in the Hunan market identified possible virus and bacterial source that causes this pneumonia disease.[6] Once the WHO declared the outbreak, this market was closed.[1] However, the exact

origin and transmission of SARS-CoV-2 were still underdetermination.[3]

Coronaviruses are a type of virus that can cause respiratory and gastrointestinal disorders. The common colds to more severe illnesses are all examples of respiratory problems. Coronaviruses are naturally classified into four primary kinds that cause gastrointestinal and respiratory tract infections, including Beta, Gamma, Delta, and Alpha coronavirus. The first two kinds primarily infect birds, whereas the final two primarily infect mammals. Coronaviruses get their name from how they look under a microscope.[7] A protein-spiked envelope of the virus covers a core of genetic material. As a result, it has the appearance of a crown. Corona is a Latin word that means "crown."

Coronaviruses were RNA viruses with a single strand and a diameter of about 120 nanometres. Because of their sensitivity to mutation and recombination, they were highly diverse. There were approximately 40 different varieties, infecting humans, non-human species, and birds. They are found in bats and wild birds, and they can spread to other creatures, including humans.[8] Coronaviruses have a corona-like appearance due to spike glycoproteins, also known as peplomers, which are necessary for the virus to infiltrate host cells. The spike comprises two subunits: S1 binds to a receptor on the host cell's surface, and S2 fuses to the cell membrane. The SARS-CoV and SARS-CoV-2 cell membrane receptors would be a different sort of angiotensin-converting enzyme-2 (ACE-2), which would be blocked by normal ACE-1 inhibitors like enalapril and Ramipril.[8-10] The ACE-2 enzyme on the cell membrane surface interacts with the S1 subunit of the spike. Subsequently, the spike was activated and cleaved by transmembrane serine protease 2 (TMPRSS2), a host transmembrane serine protease. TMPRSS2 also interacts with the S2 subunit, allowing the virus to bind to the cell membrane. The virus makes its way into the cell. The virus was released from endosomes within the cell by acidification or the activity of cathepsin, an internal cysteine protease.[8-11]

The virus is passed from person to person by droplet transmission.[1] As a result, the virus spreads quickly in heavily populated areas. Most individuals experience only a few symptoms, such as a high body temperature and respiratory symptoms, including a sore throat, cough, and headache. However, in some instances, severe symptoms such as pneumonia and acute respiratory distress syndrome may occur.[12]

Individuals with underlying problems such as heart disease, diabetes, or chronic lung disease may also exhibit more severe symptoms. Preventive methods like masks, regular hand washing, staying home while ill, avoiding public interaction, and quarantines are being advocated to reduce the spread.[12] Because no particular antiviral therapy has been proved successful yet, infected patients must rely on symptomatic medications that demonstrated an encouraging characteristic for inhibiting the novel coronavirus in early clinical studies.[13]

On April 10, 2020, the Director-General of the WHO, Dr Tedros Adhanom Ghebreyesus, announced that SARS-CoV-2 has affected 213 countries and territories across the globe.[1] On August 16, 2021, there were 208,191,205 cases of infection by COVID-19, 4,378,718 cases of death, and 186,648,955 cases of recovery reported worldwide. The USA reported having 37,468,069 cases as the highest COVID-19 cases among other countries, 637,561death cases,and 30,153,576 recovery cases . The number of COVID-19 cases has been increased steadily for countries such as India, Russia, Iran, Thailand, and Malaysia.[14]

Few COVID-19 vaccines have been approved and administered to the public by the WHO.[15] Despite this, COVID-19 has swiftly spread worldwide, posing severe health, economic, environmental, and social problems for the entire world's population. The spread of the coronavirus is wreaking havoc on the global economy. Almost every country is battling the virus by testing and treating patients, quarantining questionable individuals through contact tracing, forbidding social gatherings, instituting total or partial lockdowns, and so on.[16] The psychological and physical health consequences from social isolation during lockdown have been correlated with adverse mental and physical health effects.

Furthermore, the COVID-19 outbreak resulted in direct revenue losses due to decreased productivity and absenteeism in the workplace, as well as a negative supply shock, with production output slowing due to global supply chain disruptions and plant closures.[17] This study discussed morphology, pathogenic mechanisms, causes, transmission, symptoms, diagnosis, therapeutic potential, clinical studies on COVID-19 infection, preventive measures, and mental health care. This information will help develop a better vaccine. Figure 1 describes the overview of SARS-CoV-2.

Methods

Literature Search

Two authors (AS and SS) searched the databases, including PubMed, Scopus, Elsevier, Frontiers, Medline, EMBASE, Web of Science, Science Direct, and Google Scholar to identify all articles on origin, transmission, treatment, and clinical researches of SARS-CoV-2. In addition, the authors carried out a manual search for related articles. We used Boolean operators like "OR" and "AND" to combine the search phrases individually and in combination. The search was broadly scoped, using search terms such as SARS-CoV-2, COVID-19, origin, transmission, mechanism, signs, symptoms, diagnosis, treatment, clinical researches, preventive measures, healthcare, etc.

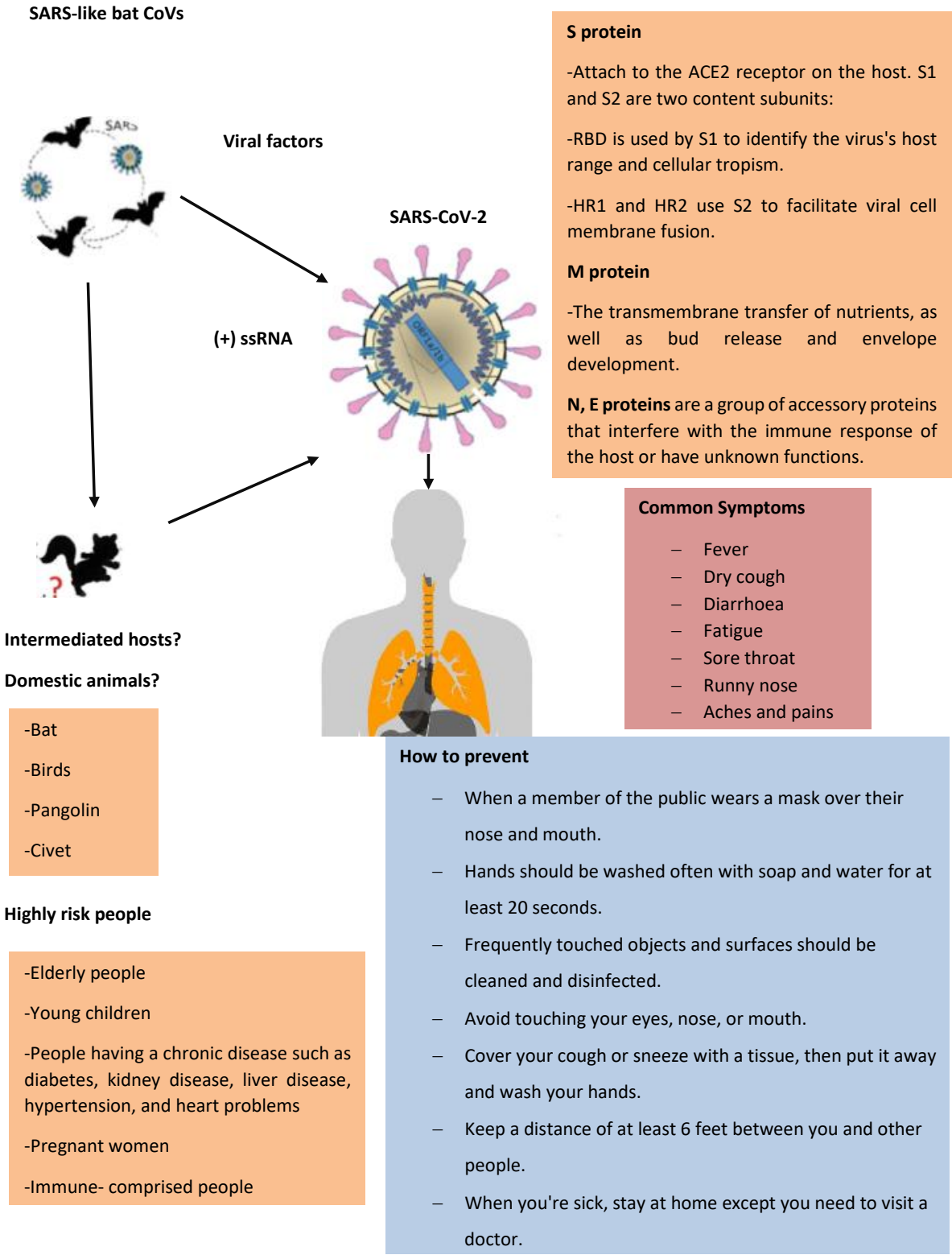

Figure 1: Overview of SARS-CoV-2

Results

SARS-CoV-2
Morphology

Coronaviruses (CoV) are classified into four genera: alpha, beta, gamma, and delta. The alpha and beta coronaviruses could infect mammals, while gamma and delta coronaviruses could infect birds. Based on sequenced viral genomes and evolutionary analysis, the SARS-CoV-2 could transmit from the bats through an unknown intermediate host to infect the humans. Therefore, the bat has been suspected of acting as a virus's natural host.[18, 19]

The SARS-CoV-2 is a beta coronavirus

genus that represents Coronaviridae family. It's a positive-sense RNA virus that's a large, spherical, encapsulated, non-segmented, single-stranded RNA virus genome of approximately 30 kb.[20, 21] Owing to the high sequencing similarity, the composition of SARS-CoV-2 is speculated to be the same as SARS-CoV. The surface viral protein spike, membrane, and coronavirus envelope are embedded in the host membrane-derived lipid bilayer that encapsulates the helical nucleocapsid of the viral RNA. Spike glycoprotein (S), a surface viral protein in SARS-CoV-2, mediates contact with cell surface receptor ACE-2. SARS-membrane CoV-2's glycoprotein (M) and envelope (E) are embedded in a lipid bilayer produced from the host membrane, encasing the viral RNA-containing helical nucleocapsid. The structure of the SARS-CoV-2 spike and protease has been determined, allowing for developing a new class of COVID-19 medicines.[22, 23] Table 1 describes the genomic characterization of SARS-CoV-2.

Pathogenic Mechanism

The complete genome of a single-stranded SARS-CoV-2 is about 30 kb and contains a variable number of open reading frames (ORFs). The remaining part of the genome encodes four vital structural proteins, including spike (S) glycoproteins, small envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein. It also encodes several accessory proteins, which disturb the innate immune response of a host.[18] The spikes on the SARS-CoV-2 were employed to block neutralizing antibodies preventing virus particles from interfacing with host cells and infecting them.[20]

The S- glycoprotein attaches to the surface of human cells through the receptor of ACE-2 that regulates both human-to-human and cross-species. S glycoprotein was divided into two subunits: S1 and S2 domains. The S1 domain controls the range of virus-host while the S2 domain facilitates the fusion of virus-cell membrane by the heptad repeats 1 (HR1) and heptad repeats 2 (HR2).[18] First, the S1 domain attaches with a specific host cell receptor, ACE-2, to induce the conformational change in S glycoprotein. Then, the S2 domain facilitates the virus membrane fusion into the host cell membrane and then enters the host cells, especially the alveolar epithelial cells found in the lower respiratory tract of humans.[20]

Etiology

SARS-CoV-2, like other coronaviruses, is disseminated by infected respiratory droplets, with viral infection occurring when respiratory particles are inhaled or deposited on mucosal surfaces such as the nasal, conjunctival, or oral mucosa. The bulk of target host receptors are available in the epithelium of the human respiratory system, which includes the oropharynx and upper airway. In addition, the conjunctiva and gastrointestinal system can potentially transmit infection, which can serve as transmission gateways.[24]

Infection risk is increased by sleeping in the same bed or marrying an infected person. In contrast, infection risk is reduced by isolating the infected person from the rest of the family. Other high-risk activities include sharing meals and participating in group activities. In enclosed locations, the danger of infection is much greater than in outdoor settings. For example, a thorough investigation of transmission clusters revealed that the majority of super-spreading occurrences occurred indoors. However, aerosol transmission can still influence

Table 1: Genomic characterization of SARS-CoV-2

Name/Gene ID	Description	Location	Aliases	Number of nucleotides (bp)
S ID: 43740568	Surface glycoprotein	NC_045512.2 (21563..25384)	GU280_gp02, spike glycoprotein	3822
ORF1ab ID: 43740578	ORF1a polyprotein;ORF1ab polyprotein	NC_045512.2 (266..21555)	GU280_gp01	21290
E ID: 43740570	Envelope protein	NC_045512.2 (26245..26472)	GU280_gp04	228
N ID: 43740575	Nucleocapsid phosphoprotein	NC_045512.2 (28274..29533)	GU280_gp10	1260
ORF8 ID: 43740577	ORF8 protein	NC_045512.2 (27894..28259)	GU280_gp09	366
ORF6 ID: 43740572	ORF6 protein	NC_045512.2 (27202..27387)	GU280_gp06	186
M ID: 43740571	Membrane glycoprotein	NC_045512.2 (26523..27191)	GU280_gp05	669
ORF7a ID: 43740573	ORF7a protein	NC_045512.2 (27394..27759)	GU280_gp07	366
ORF3a ID: 43740569	ORF3a protein	NC_045512.2 (25393..26220)	GU280_gp03	828
ORF7b ID: 43740574	ORF7b	NC_045512.2 (27756..27887)	GU280_gp08	132
ORF10 ID: 43740576	ORF10 protein	NC_045512.2 (29558..29674)	GU280_gp11	117

(meaning transmission could occur at a distance >2 m) after a long stay in congested, poorly ventilated interior situations.[9]

The role of feces shedding in SARS-CoV-2 transmission, as well as the degree of fomite transmission (through inanimate surfaces), remain unclear at this time. On flat surfaces (stainless steel, plastic, glass) and at lower temperatures and humidity, both SARS-CoV-2 and SARS-CoV may survive for several days (for example, air-conditioned workplaces). As a result, spreading illness from contaminated surfaces to the mucosa of the eyes, nose, and mouth through unwashed hands is possible. This route of transmission can lead to contamination of the environment, particularly in communal facilities. Both SARS-CoV and SARS-CoV-2 are quickly inactivated by common disinfectants, emphasizing the significance of surface cleanliness and handwashing. SARS-CoV-2 RNA was identified in stool samples, and RNA shedding generally lasts longer than in respiratory samples; nonetheless, virus isolation from the feces was rarely successful. There are no documented studies to show fecal-oral transfer. In most cases, the fecal-oral transmission was not confirmed to occur in SARS-CoV. However, one deadly outbreak was attributed to the virus's aerosolization and dissemination through an apartment building's sewage system. It should be investigated whether SARS-CoV-2 can transmit in the same way.[25]

Symptoms

Coronaviruses are dangerous organisms that affect people's lower respiratory tracts and can cause infections ranging from a simple cold to significant contamination with a 50% mortality rate. COVID-19 may be a highly infectious disease since a single infected person can infect three other people, which is higher than SARS (1.7-1.9) and MERS,[1] implying that SARS-CoV-2 has a greater risk of producing an outbreak. There are several similarities between COVID-19 and SARS, according to evidences. Approximately 79 percent of the similarities between these two illnesses' genomic arrangements have been revealed. COVID-19 has a more remarkable ability to spread within a population than MERS or SARS. Although the sickness is usually mild, it can cause respiratory failure, arrhythmias, shock, kidney failure, cardiovascular harm, or even liver failure in certain patients, particularly those with serious underlying disorders. Based on the Alimohamadi et al. study (2020), fever is the most prevalent symptom in COVID-19 patients, accounting for 81%; cough is 58%; weariness is 38%; dyspnea is 26%, and sputum is 25%.[26]

According to Viner's study (2020), COVID 19 signs and symptoms have been reported in children and adolescents.[27] The percentage of those who were asymptomatic ranged from 14% to 42%. Fever and cough were the two most common symptoms, ranging from 46% to 64% for fever and 32% to 55% for cough. All other signs or indicators were present between 10% and 20% of the time. The majority of studies showed nausea, diarrhea, and stomach pain.

Nonetheless, several studies revealed gastrointestinal problems. The percentages ranged from 7% to 17%. Fever and cough are the most common adverse effects of COVID-19, according to available data; hence, they should be included in case definitions for prospective COVID-19 cases in this age group.

Other side effects are less common. Thus they should be considered in COVID-19 case definitions. For example, Rhinorrhea and sore throat are uncommon in COVID-19, which suggests that their presence is significantly more likely to indicate sickness with viruses other than SARS-CoV-2, considering the recurrence of urinary tract infection and similar symptoms in young children.[27]

Diagnosis

RT-PCR employs nasal swab, tracheal aspirate, or bronchoalveolar lavage (BAL) specimens to diagnose COVID-19. Upper respiratory samples are extracted through nasopharyngeal and oropharyngeal swabs as the most common and recommended method for diagnosis. Bronchoscopy as a diagnostic tool for COVID-19 is not suggested because the emitted aerosol poses a substantial danger to both patients and healthcare personnel. If upper respiratory specimens are negative, bronchoscopy may be limited to intubated patients, and additional diagnostic techniques may radically alter clinical care. Bronchoscopy may be recommended when clinical and safety standards are met and when the diagnosis is ambiguous.[28]

Intubated patients can get respiratory samples from upper and lower respiratory tract specimens using tracheal aspiration or non-bronchoscopic BAL. The specificity of the RT-PCR test appears to be increasing, notwithstanding the possibility of false-positive results due to swab contamination, especially in asymptomatic individuals. The degree of sensitivity is unknown, although it is estimated to be between 66 and 80 percent. Asymptomatic individuals who have had direct contact with symptomatic individuals had poorer test validity; without verifying signs or confirming illness, the positive probability could surpass 50%.

When using a nasopharyngeal swab material in the early stages of infectiona single negative test does not rule out SARS-CoV-2 infection, especially in severely affected patients. Repeating the experiment or taking a deeper respiratory tract sample, such as BAL, may be indicated in this circumstance.[28]

Treatment

Many potential vaccines are still under research and development while a few vaccines passed the clinical trial phases and their effectiveness and safeness were confirmed.[29] In the United Kingdom (UK), the Pfizer/BioNTech had developed COVID-19 vaccines that have been approved and their results have been published in November, showing up to 95% effectiveness while two doses administered three weeks apart. That vaccine must be stored at -70°C and transported in a special box packed in dry ice. On December 2, 2020, the UK was recognized as the first country to develop and approve the Pfizer/BioNTech SARS-CoV-2 vaccine for worldwide use. According to WHO, the vaccines could be distributed in early to mid-2021 after getting approval for their safety and effectiveness.[30] Several other alternative medicines were potentially used to treat the COVID-19 patients, as stated in Table 2.

The treatment method follows (a) performing laboratory testing, (b) pneumonia diagnostic testing using diagnostic testing kits by imaging techniques such as pulmonary CT scans and chest X-rays, and (c) potential alternative medicines implement.[20]

The following criterion for a person was "suspected" for having COVID-19:[20]

- Experienced acute respiratory infection with or without fever such as breathing difficulties, dry cough, or sore throat.
- Travel history to infected areas or residing in other countries within 14 days before the disease appearance.
- Any events or gatherings that are connected to the outbreak of COVID-19.
- Having close contact in the last 14 days with an infected person before the initiation of the symptoms.

Clinical Researches for COVID-19

As a response to the COVID-19 outbreak, all the affected countries are currently conducting and supporting various research such as clinical trials and antibodies development to treat and prevent the acute respiratory illness, pneumonia. The vaccines and antibodies development is based on the research conducted through volunteers' contribution in clinical research studies to evaluate the SARS-CoV-2 patients.[33] Table 3 shows the worldwide research to find solutions against the COVID-19 infection.[34]

The clinical trial includes 5 phases: preclinical trial, phase 1, phase 2, phase 3, and approval phase. The preclinical trial phase involves testing new vaccines on cells while administered to animals to observe immune response productivity. 86 confirmed preclinical vaccines against COVID-19 in active development were reported.[32] The phase 1 trials involve vaccines administered to a small number of people to test the dosage, safety, and immune system stimulation. Phase 2 involves an expended trial in which vaccines are given to hundreds of people in divided groups such as children, adults, and the elderly to observe vaccine activity for these groups.

Then, phase 3 involves efficacy trials, where vaccines were given to thousands of people to determine vaccine production against the COVID-19. In addition, the Food and Drug Administration (FDA) announced that the vaccine makers needed to provide evidence for the produced vaccines declaring that they had at least 50% protection for those who received the vaccines in June 2020. Finally, the approval phase involved the regulation requirements. Once a vaccine is regulated and licensed, the researchers must continue to monitor vaccine safety and effectiveness.[34]

Table 2: Drugs and their potential mechanisms used in humans to inhibit the SARS-CoV-2

Drugs	Their Potential Mechanisms
Remdesivir	Act as an adenosine analogue that integrates into the growing viral ribonucleic acid (RNA) chains and terminates viral RNA-dependent RNA polymerase activity and prevents viral RNA replication.[31]
Chloroquine and Hydroxychloroquine	Blocks the viral entry into the host cells by increasing pH (acidity) of the endosome to blocks the pathways of endocytic.[10]
Favipiravir, T-705	Act as an antiviral drug that inhibits the viral RNA-dependent RNA polymerase and is known as RNA polymerase inhibitor.[31]
Lopinavir and Ritonavir	Inhibit the 20-chrymotypsin-like protease and also inhibit the translation process of RNA.[31]
Interferon-β	Naturally occurring proteins activate the innate antiviral immunity.[31]
Lopinavir and ritonavir with interferon- β	Inhibit the replication of the virus.[20]
Umifenovir (Arbidol)	Inhibit the S protein and ACE2 membrane fusion during viral envelope.[10]
Camostat mesylate	Inhibit the type II transmembrane serine protease (TMPRSS2) enzymatic activity that facilitates the entry of the virus into host cells.[20]
Ribavarin	Inhibits the capping of the viral messenger RNA (mRNA) and synthesis of viral RNA.[20]
Ribavirin with Interferon-β	Blocks the replication of viral cells.[20]
Oseltamivir	Blocks the translation process of viral RNA.[20]
Darunavir	Inhibits the replication process of viral cells.[20]
Tocilizumab and Sarilumab	Reduces the levels of the inflammatory cytokine IL-6 that reduces the viral loads.[32]
Ivermectin	Acts as an anti-parasitic drug that destabilizes viral cell-transport proteins that enter the host cell nucleus and lead to paralysis and viral cell death.[32]
Monoclonal Antibody (Bevacizumab)	Shuts down the cascade of inflammation from the endoplasmic reticulum in host cells.[32]

Table 3: The clinical researches that carried out against COVID-19 infection[34]

Types of Vaccines	Clinical Trial Phase	Research Development
Genetic based vaccines	Phase 3	1. Moderna partnership with National Institutes of Health. They studied vaccine development based on messenger RNA (mRNA) containing genetic instruction to build a SARS-CoV-2 spike protein. Once injected into cells, the vaccines induce spike protein formation and then induce immune system response. The researchrs estimated that the vaccine contains a 94.1% efficacy rate and shows no side effects when tested with the volunteers. Upon agreement on November 25, 2020, with European Commission, the 160 million doses were supplied.
	Phase 3 Approval for emergency use in the United Kingdom	2. Pfizer and BioNTech They conducted research on mRNA vaccine andreported similar findings with Moderna. The results showed that the vaccines contain over 95% effective rate and no severe side effects. Upon injection against SARS-CoV-2, the vaccines produce antibodies and T cells that respond toward the virus. The vaccines must be stored at -70°C in a deep freeze container and kept frozen at chiller temperatures. It is expected that the vaccines will be manufactured in over 1.3 billion doses worldwide by the end of 2021.
	Phase 2	3. Imperial College London partnered with Morningside Ventures They conducted research on "self-amplifying" RNA vaccines, which showed that the vaccines increase the viral protein production to induce the immune system. VacEquity Global Health company manufactured and distributed the vaccines. The researchers announced that the vaccine efficiency would be reported by the end of 2020.
	Phase 2	4. Zydus Cadila They conducted research on a DNA-based vaccine delivered by a skin patch. On August 6, 2020, they proceeded with the phase 2 trial and planned to proceed to phase 3 at the beginning of December.
	Phase 2	5. CureVac They conducted research on mRNA vaccine andreported good responses when tested on mice. On November 12, 2020, the company announced that the vaccines stored at 41°C and they can manufacture up to 300 million doses in 2021.
	Phase 2	6. AnGes partnership with Osaka University and Takara Bio The conducted research on DNA- based vaccines on June 30, 2020. The company planned to proceed to phase 3 trial by the end of 2020.
	Phase 2	7. Arcturus Therapeutics and Duke-NUS Medical School The conducted research on mRNA vaccines to self-replicate to produce greater viral protein productions. When tested with animals, it showed protection against infection. On November 9, 2020, the company announced that the vaccines could produce an immune response due to the number of recovered COVID-19 patients.
	Phase 2	8. Inovio The conducted research on DNA vaccines, and the vaccines was delivered with electric pulses into the skin through the hand-held device. There was no severe adverse effect when tested with volunteers. On September 28, 2020, the FDA partially held the vaccines because of questions about the delivery device. However, on November 16, 2020, the FDA permitted handling phase 3 clinical trial.
	Phase 1	9. Entos Pharmaceuticals They conducted research on DNA vaccine entitled Covigenix VAX-001. They chose the nucleocapsid gene, a protein found inside the virus membrane that bets to offer long-lasting immunity.
	Phase 1	10. OncoSec Immunotherapies They Experimentally developed cancer treatment which delivers the genes into the tumors producing a biological signaling molecule (IL-2), to attract immune cells to attack cancer cells. The vaccine named CORVax12 contains a loop of DNA that encodes IL-12 and the spike protein. This vaccine produces extra IL-12 inside the body and potentially enhances the immune system ability to produce antibodies to the spike protein.
Viral vector vaccines	Phase 3 Approved for limited use in China.	11. CanSino Biologics partnership with the Academy of Military Medical Sciences. Adenovirus vaccine called Ad5 produced a strong immune response during phase 2 trial in July. On June 25, 2020, the Chinese military approved the vaccine due to the urgent drug need. This vaccine proceeded to phase 3 trial at the beginning of August.
	Phase 3 Approved for early use in Russia.	12. Gamaleya Research Institute They developed vaccine, Gam-Covid-Vac, based on two adenoviruses, forming adenoviruses called Ad5 and Ad26. After getting approval for phase 3 from a Russian health care regulator, the vaccine was renamed to Sputnik V. During the phase 2 trial, this vaccine resulted in the antibodies production with mild side effects. During the phase 3 trial, the vaccine indicated effectiveness, showing a 92% efficacy rate when tested with volunteers. Based on preliminary analysis for a more extended period, volunteers showed a 95% efficacy rate, but some outside experts still questioned the findings.
	Phase 3	13. Johnson & Johnson They developed a vaccine from adenovirus 26 (Ad26) and administered a single dose during the first phase 3 trial. However, the production has been paused due to an adverse reaction in a volunteer while expecting the results by the end of 2020. Instead, they announced redo the second phase 3 trial to observe the vaccine effects with two doses.

	Phase 3	14. AstraZeneca and the University of Oxford They developed a vaccine based on chimpanzee adenovirus. On November 23, 2020, during the phase 3 trial, the vaccine showed above 90% efficiency depending on the dosage level with uncertain results. when they tested the vaccine called ChAdOx1 on monkeys, it showed protection from the disease without severe side effects. This vaccine also increases antibody production with increasing immune defenses. On September 6, 2020, the trial paused since a volunteer developed transverse myelitis. On November 23, 2020, they announced that the developed vaccines showed an excellent efficacy rate and promoted more robust immune responses.
	Phase 1	15. ReiThera with the Lazzaro Spallanzani National Institute for Infectious Diseases They developed a vaccine called GRAd-COV2, which is based on an infected gorilla's adenovirus. At the end of July 2020, they announced the end of phase 1 trial, and in November 2020, they informed that the produced vaccines can tolerate and produce antibodies. The phase 3 trial proceeded to December 2020.
	Phase 1	16. German Center for Infection Research They developed a vaccine based on Modified Vaccinia Ankara (MVA) for SARS-CoV-2, carrying a gene for spike protein produced inside the invaded cells..The registration for the phase 1 trial was proceeded on September 29, 2020. The vaccine was expected to be fully developed and receive approval by the end of 2021.
	Phase 1	17. Merck partnered with IAVI They developed vaccine based on stomatitis viruses, using the same approach in producing the first approved Ebola vaccine. In addition, they designed vaccines in tablet form for easier distribution than syringes for injections. On September 30, 2020, they received approval for the phase 1 trial.
Protein-Based Vaccines	Phase 3	18. Novavax They developed a sticking protein vaccine onto microscope particles. The preliminary studies in the phase 2 trial based on monkeys and humans showed promising safety and antibody production results. Based on the phase 3 trial in the United Kingdom, the dosages are expected to be delivered in early 2021.
	Phase 3	19. Medicago They developed a vaccine using a wild species related to tobacco, *Nicotiana benthamiana*. The plant cells create the protein shells that mimic viruses by delivering the virus's genes into leaves. In July, the phase 1 trial based on a plant-based vaccine combined with adjuvants showed an increase in the immune system's response to the viral proteins and promising antibodies level when tested with volunteers. On November 12, 2020, the phase 3 trial proceeded.
	Phase 2	20. Sanofi collaborated with GSK They developed a viral protein-based vaccine and the produced proteins and engineered virus that grows inside the insect's cells. GSK supplemented these proteins with adjuvants to induce the immune system. The phase 1 and phase 2 trials proceeded in September, and the phase 3 trial was started in December, and the vaccine safety and effectiveness was reported in the middle of 2021.
	Phase 1	21. Center for Genetic Engineering and Biotechnology of Cuba They developed a vaccine delivered through nasal spray named the Mambisa and another vaccine injected into muscle named the Abadala. The vaccines contain the receptor-binding domain, the coronavirus spike protein, along with hepatitis B protein to induce the immune system.
Inactivated or Attenuated Coronavirus Vaccines	Phase 3 Approved for Limited Use in the United Arab Emirates	22. Sinopharm collaborated with the Wuhan Institute of Biological Products Their tests were based on the two inactivated coronaviruses vaccines. The phase 1 and phase 2 trials reported that when the vaccines were tested with volunteers, the antibodies were produced and some volunteers underwent fever and some side effects. In July, in the United Arab Emirates, they proceeded with the phase 3 trial and on September 14, 2020, the United Arab Emirates government ordered an emergency approval for vaccine use on the health care workers. In China, the government permitted vaccine injection for government officials, health care workers, and other selected groups, and in November, almost a million people had received the vaccines.
	Phase 3 Approved for Limited Use in China	23. Sinovac Biotech They developed inactivated vaccines called CoronaVac without severe adverse effect with an immune response and modest antibodies when tested with volunteers during phase 1 and phase 2 trials. In July 2020, the phase 3 trial showed the vaccines' safety. In July, the Chinese government issued an emergency approval for the vaccine's limited use for medical workers, port inspectors, and public service personnel. For global distribution, the vaccines were expected to be manufactured and distributed by March 2020.
	Phase 3	24. Indian Council of Medical Research and the National Institute of Virology collaborated with the Bharat Biotech They developed an inactivated vaccine called Covaxin. It showed protection against infection ,when tested with monkeys and hamsters. . The vaccines showed an 85 to 90% efficacy rate when tested with volunteers and produced antibodies with no severe adverse effect. On October 23, 2020, the project proceeded to phase 3 trial while it was expected to distribute the vaccines on June 2021.
Repurposed Vaccines	Phase 3	25. Murdoch Children's Research Institute In the early 1900s, the Bacillus Calmette-Guerin vaccine was developed to protect against tuberculosis. The institutconducted the phase 3 trial called the BRACE to determine vaccine protection level against the coronavirus.

Prevention Measures

Since there was no approved treatment for COVID-19 infection, many preventive methods were taken to reduce the COVID-19 infection among the community populations. Therefore, the WHO announced a guideline to prevent the infection as follows:[35]

- Maintain at least 1 to 2 meters social distance
- Always wear clean masks and gloves
- Regularly wash and clean hands with sanitizer or soap.
- Avoid visiting infected, closed, and crowded areas and prevent close contact
- Avoid meeting people outside and attending any events
- Avoid touching mouth, nose, and eyes that may pick up viruses into the body.
- Avoid handshaking with people to avoid contact with SARS-CoV-2.
- Always covers the mouth and nose with a bent elbow or disposable tissues when coughing or sneezing
- Frequently clean and disinfect the surface areas that are regularly touched such as the door handles, phone screens, and faucets.
- Self-isolate if having minor symptoms such as mild fever, cough, and headache.

Ethanol and isopropanol can kill coronavirus at 70-90 percent concentrations in 30 seconds.[36] In addition to disrupting the RNA, the alcohol is thought to induce membrane damage and denaturing viral proteins. Because of their great propensity to establish hydrogen bonds and their amphoteric character, these alcohols can disrupt the tertiary structure of proteins by breaking intramolecular hydrogen bonds. Moreover, phenol-based disinfectants can also kill coronavirus at a 0.5-5% concentration range. It can occur within minutes. Furthermore, peroxide-based disinfectants, such as hydrogen peroxide and peroxyacetic acid denature proteins by oxidizing their thiol groups and disulfide linkages. At 1-3% concentrations, hydrogen peroxide is virucidal and can destroy SARS-CoV in less than a minute. In addition, both peroxy chemicals release hydroxyl radicals that target the virus's lipid membrane, proteins, and nucleic acids, among other components.[37]

Increasing the test numbers and thus identifying more cases, isolating them and tracing those who were in interaction with another essential factor in preventing the spread of infectious infection all across society. As a result, it's critical to expand laboratories' testing capabilities and develop new testing methodologies. Cases are determined using a variety of procedures around the world, including fast test kits, serological approaches, and self-collected specimen testing, which help comply with isolation guidelines.[38]

Mental Care Tips During the COVID-19 Pandemic

Al Daheri et al. (2021) demonstrated that low-income families and those who have lost their employment require moral and financial support from governments and authorities.[39] In addition, to decrease the strain on individuals during the present pandemic, working hours must be regulated. According to a KFF Health Tracking Poll from July 2020, many persons are experiencing specific adverse effects on their mental health and wellbeing due to concern and tension over the coronavirus.[40] These include difficulty sleeping (36%) and eating (32%), increasing alcohol consumption or substance use (12%), and worsening chronic conditions (12%). As the epidemic worsens, ongoing and mandatory public health measures expose an increasing number of people to scenarios linked to poor mental health outcomes, such as isolation and job loss. Dawel et al. (2020) revealed that work and social functioning impairments caused by the pandemic were closely linked to increased sadness and anxiety symptoms, and lower psychological wellbeing. Financial hardship caused by the pandemic, rather than job loss, was also a significant predictor of poor mental health.[41]

During a COVID-19 outbreak, anyone might be emotionally affected. The following are some mental health care suggestions:

- Sleep enough
- Read books
- Practice yoga or meditation
- Try to cook new dishes
- Garden or plant vegetables and fruit trees
- Dance or sing
- Listen to melody songs
- Bake cakes, biscuits, and cookies
- Have fun with family members
- Play indoor games such as chess
- Chit-chat with friends
- Watch movies
- Do exercise regularly
- Drink much water
- Take nutrient food

Conclusion

In conclusion, the current study provides a snapshot of the overview of the SARS-CoV-2 and COVID-19, including morphology, pathogenic mechanisms, causes, transmission, symptoms, diagnosis, therapeutic potential, clinical studies on COVID-19 infection, preventive measures, and mental health care. SARS-CoV-2 is a highly transmissible and deadly virus. COVID-19 is an air-borne transmission disease. SARS-CoV-2 contains a variable number of ORFs such as ORF1ab, ORF8, ORF6, ORF7a, ORF3a, ORF7b, and ORF10. The rest of the genome encodes four key structural proteins, including S, E, M and N protein, and several accessory proteins. On December 2, 2020, the UK was recognized as the first country to develop and approve the Pfizer/BioNTech SARS-CoV-2 vaccine for worldwide use. It was effectively administered

around the world. However, several other alternative medicines such as Remdesivir, Hydroxychloroquine, Lopinavir/Ritonavir, and Ribavarin or Interferon Beta were potentially used to treat the COVID-19 patients. The findings suggest to halt the spread of SARS-CoV-2 through preventive measures and develop a better vaccine. The review study also aids in early preparations for future pandemic outbreaks.

Acknowledgment

I highly appreciate the frontliners who work hard during this COVID-19 pandemic.

Conflicts of interest: None declared.

References

1 Shah AU, Safri SN, Thevadas R, Noordin NK, Abd Rahman A, Sekawi Z, Ideris A, Sultan MT. COVID-19 outbreak in Malaysia: Actions taken by the Malaysian government. International Journal of Infectious Diseases. 2020 Aug 1;97:108-16.

2 Pradhan D, Biswasroy P, Naik PK, Ghosh G, Rath G. A review of current interventions for COVID-19 prevention. Archives of Medical Research. 2020 Jul 1;51(5):363-74.

3 Singhal T. A review of coronavirus disease-2019 (COVID-19). The Indian Journal of Pediatrics. 2020 Apr;87(4):281-6.

4 World Health Organization. Coronavirus disease (COVID-2019) situation reports. 2020. Retrieved from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports (accessed on 16th November 2020).

5 COVID CD, Team R, COVID C, Team R, COVID C, Team R, Bialek S, Boundy E, Bowen V, Chow N, Cohn A. Severe outcomes among patients with coronavirus disease 2019 (COVID-19)-United States, February 12-March 16, 2020. Morbidity and mortality weekly report. 2020 Mar 27;69(12):343.

6 World Health Organization. Origin of SARS-CoV-2. 2020. Retrieved from https://apps.who.int/iris/handle/10665/332197 (accessed on 16th November 2020).

7 Fong SJ, Dey N, Chaki J. An introduction to COVID-19. In Artificial intelligence for coronavirus outbreak 2021 (pp. 1-22). Springer, Singapore.

8 Aronson JK. Coronaviruses–a general introduction. Centre for Evidence-Based Medicine, Nuffield Department of Primary Care Health Sciences, University of Oxford. 2020.

9 Kumar S, Nyodu R, Maurya VK, Saxena SK. Morphology, genome organization, replication, and pathogenesis of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronavirus Disease 2019 (COVID-19). 2020:23.

10 Ou X, Liu Y, Lei X, Li P, Mi D, Ren L, Guo L, Guo R, Chen T, Hu J, Xiang Z. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nature communications. 2020 Mar 27;11(1):1-2.

11 Cascella M, Rajnik M, Cuomo A, Dulebohn SC, Di Napoli R. Features, evaluation and treatment coronavirus (COVID-19) In StatPearls, Treasure Island (FL): StatPearls.

12 Khailany RA, Safdar M, Ozaslan M. Genomic characterization of a novel SARS- CoV-2. Gene reports. 2020 Jun 1;19:100682.

13 Vali M, Hassanzadeh J, Mirahmadizadeh A, Hoseini M, Dehghani S, Maleki Z, Méndez-Arriaga F, Ghaem H. Effect of meteorological factors and Air Quality Index on the COVID-19 epidemiological characteristics: an ecological study among 210 countries. Environmental Science and Pollution Research. 2021 May 22; 28(38):53116-53126.

14 COVID-19 Coronavirus pandemic. Worldometer. 2020. Retrieved from: https://www.worldometers.info/coronavirus/. (accessed on 16th August 2021).

15 WHO. 2021. Retrieved from: https://www.who.int/emergencies/diseases/novel- coronavirus-2019/question-and-answers-hub/q-a-detail/coronavirus-disease- covid- 19-schools (accessed on 6th July 2021).

16 Chakraborty I, Maity P. COVID-19 outbreak: Migration, effects on society, global environment and prevention. Science of the Total Environment. 2020 Aug 1;728:138882.

17 Pak A, Adegboye OA, Adekunle AI, Rahman KM, McBryde ES, Eisen DP. Economic consequences of the COVID-19 outbreak: the need for epidemic preparedness. Frontiers in public health. 2020 May 29;8:241.

18 Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research. 2020 Jul;24:91.

19 Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, Tan KS, Wang DY, Yan Y. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak-an update on the status. Military Medical Research. 2020 Dec;7(1):1-0.

20 Elengoe A. COVID-19 Outbreak in Malaysia. Osong Public Health and Research Perspectives. 2020;11(3):93-100.

21 Yousefi M, Oskoei V, Jafari AJ, Farzadkia M, Firooz MH, Abdollahinejad B, Torkashvand J. Municipal solid waste management during COVID-19 pandemic: effects and repercussions. Environmental Science and Pollution Research. 2021 May 3;28:32200-9.

22 Henderson R, Edwards RJ, Mansouri K, Janowska K, Stalls V, Gobeil SM, Kopp M, Li D, Parks R, Hsu AL, Borgnia MJ. Controlling the SARS-CoV-2 spike glycoprotein conformation. Nature Structural & Molecular Biology. 2020 Oct;27(10):925-33.

23 Elengoe A, Selvam S, Selvarajah M, Manikam H, Vijaya R. Sequence analysis and structure prediction of Malaysia SARS-CoV-2 strain's structural and accessory proteins. Biointerface Research in Applied Chemistry. 2022;12(1): 3259-3304.

24 Cevik M, Kuppalli K, Kindrachuk J, Peiris M. Virology, transmission, and pathogenesis of SARS-CoV-2. BMJ. 2020 Oct 23;371.

25 Riva L, Yuan S, Yin X, Martin-Sancho L, Matsunaga N, Pache L, Burgstaller- Muehlbacher S, De Jesus PD, Teriete P, Hull MV, Chang MW. Discovery of SARS-CoV-2 antiviral drugs through large-scale compound repurposing. Nature. 2020 Oct;586(7827):113-9.

26 Alimohamadi Y, Sepandi M, Taghdir M, Hosamirudsari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. Journal of Preventive Medicine and Hygiene. 2020 Sep;61(3):E304.

27 Viner RM, Ward JL, Hudson LD, Ashe M, Patel SV, Hargreaves D, Whittaker E. Systematic review of reviews of symptoms and signs of COVID-19 in children and adolescents. Archives of Disease in Childhood. 2021 Aug 1;106(8):802-7.

28 Rossi GA, Sacco O, Mancino E, Cristiani L, Midulla F. Differences and similarities between SARS-CoV and SARS-CoV-2: spike receptor-binding domain recognition and host cell infection with support of cellular serine proteases. Infection. 2020 Jul 31; 48(5): 665-9.

29 World Health Organization. Coronavirus disease (COVID-19): Vaccines. 2020. Retrieved from: https://www.who.int/news- room/q-a detail/coronavirus-disease-(covid-19)-vaccines. (accessed on 16th November 2020).

30 Gallagher J. BBC News. COVID vaccine update: When will others be ready? 2020. Retrieved from: https://www.bbc.com/news/health- 51665497. (accessed on 16th January 2021).

31 Trivedi A, Sharma S, Ashtey B. Investigational treatments for COVID-19. The Pharmaceutical Journal 2020; 304(7938):DOI:10.1211/PJ.2020.2020805.

32 Shaffer L. Nature medicine: 15 drugs being tested to treat COVID-19 and how they would work. 2020. Retrieved from https://www.nature.com/articles/d41591-020-00019-9#journal-info. (accessed on 16th December 2020).

33 NIH: National Institute of Allergy and Infectious Diseases. 2020. Retrieved from COVID-19 Clinical Research: https://www.niaid.nih.gov/diseases-conditions/covid-19- clinical-research. (accessed on 16th November 2020).

34 Zimmer C, Corum J, Wee S. The New York Times. Coronavirus Vaccine Tracker. 2020. Retrieved from:https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine tracker.html. (accessed on 16th January 2021).

35 Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA. 2020 May 12;323(18):1824-36.

36 Kampf G, Todt D, Pfaender S, Steinmann E. Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents. Journal of Hospital Infection. 2020 Mar 1;104(3):246-51.

37 Al-Sayah MH. Chemical disinfectants of COVID-19: an overview. Journal of Water and Health. 2020 Oct 1;18(5):843-8.

38 Guner HR, Hasanoğlu İ, Aktaş F. COVID-19: Prevention and control measures in community. Turkish Journal of Medical Sciences. 2020 Apr 21;50(SI-1):571-7.

39 Al Dhaheri AS, Bataineh MA, Mohamad MN, Ajab A, Al Marzouqi A, Jarrar AH, Habib-Mourad C, Abu Jamous DO, Ali HI, Al Sabbah H, Hasan H. Impact of COVID-19 on mental health and quality of life: Is there any effect? A cross-sectional study of the MENA region. PloS One. 2021 Mar 25;16(3):e0249107.

40 Panchal N, Kamal R, Orgera K, Cox C, Garfield R, Hamel L, Chidambaram P. The implications of COVID-19 for mental health and substance use. Kaiser family foundation. 2020 Apr 21;21.

41 Dawel A, Shou Y, Smithson M, Cherbuin N, Banfield M, Calear AL, Farrer LM, Gray D, Gulliver A, Housen T, McCallum SM. The effect of COVID-19 on mental health and wellbeing in a representative sample of Australian adults. Frontiers in Psychiatry. 2020 Oct 6;11:1026.