Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/19210
DOI URL: http://dx.doi.org/10.21474/IJAR01/19210

RESEARCH ARTICLE

DIAGNOSIS, TREATMENT AND PREVENTIONS OF COVID-19

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Manuscript Info

Manuscript History
Received: 31 May 2024
Final Accepted: 30 June 2024
Published: July 2024

Key words:-
COVID-19 Pandemic, Severe Acute Respiratory Syndrome Coronavirus 2, Natural and Synthetic Drugs Used for the Treatment of Covid-19

Abstract

The COVID-19 pandemic has resulted in outbreaks of pneumonia and multi-organ infections worldwide. The virus started in bats and was transmitted to humans through unknown creatures in Wuhan, Hubei territory, China in December 2019. The indications are fever, cough, sore throat, breathlessness, fatigue, and malaise. The disease is mild in most people; in a few (generally the old, pregnant, infant etc), it's going to get to acute respiratory distress syndrome (ARDS), pneumonia, and multi-organ dysfunction. Numerous individuals are asymptomatic. Diagnosis is by demonstration of the infection in respiratory secretions by special molecular tests. Multiple antiviral medications like remdesivir, anti-malarial medicine (Hydroxychloroquine) [11], natural herbal remedies such as Echinacea purpurea[12], oxygen therapy, dietary therapy and herbal remedies have shown activity against covid-19 or potential clinical benefits.

Introduction:-

On January 7, 2020, it was confirmed that a new strain of coronavirus known as SARS-CoV-2 (formerly called 2019-nCoV) had appeared, and the World Health Organization (WHO) identified it as a type of coronavirus disease called Wuhan Pneumonia. I performed the action. The outbreak of the novel coronavirus (COVID-19) occurred on February 11, 2019 [2]. The COVID-19 pandemic has significantly heightened the number of hospital admissions for various forms of pneumonia. As per a report from the Centers for Disease Control and Prevention (CDC), the signs of COVID-19 have shifted from symptoms to serious illness and mortality. COVID-19 symptoms consist of fever, cough, sore throat, tiredness, and difficulty breathing. 81% of COVID-19 cases are mild to moderate, while 14% are severe. Respiratory failure, septic shock, multiple organ dysfunctions, or multiple organ failure occurred in 5% of severe illnesses [5]. Due to increased comorbidities and a weakened immune system, older adults above the age of 65, pregnant women, and their infants are at a higher risk of influenza-related deaths and hospitalization [6, 7]. Due to the rapid human-to-human transmission of SARS-CoV-2, the current number of cases continues to increase, as illustrated in Figure 1. This survey compiles evidence of effectiveness related to the causes, spread, detection, and treatment of COVID-19, along with previous effective natural treatments for SARS and MERS, and research on coronavirus infection suggests potential herbal remedies for COVID-19. Infection is being alleviated with a combination of broad treatment options, including antiviral drugs like remdesivir, Hydroxychloroquine, herbal remedies like Echinacea purpurea, oxygen therapy, dietary therapy, and immune system support. Analysts are thoroughly examining authorized vaccines and treatments crucial for preventing and managing emerging global health threats [13].

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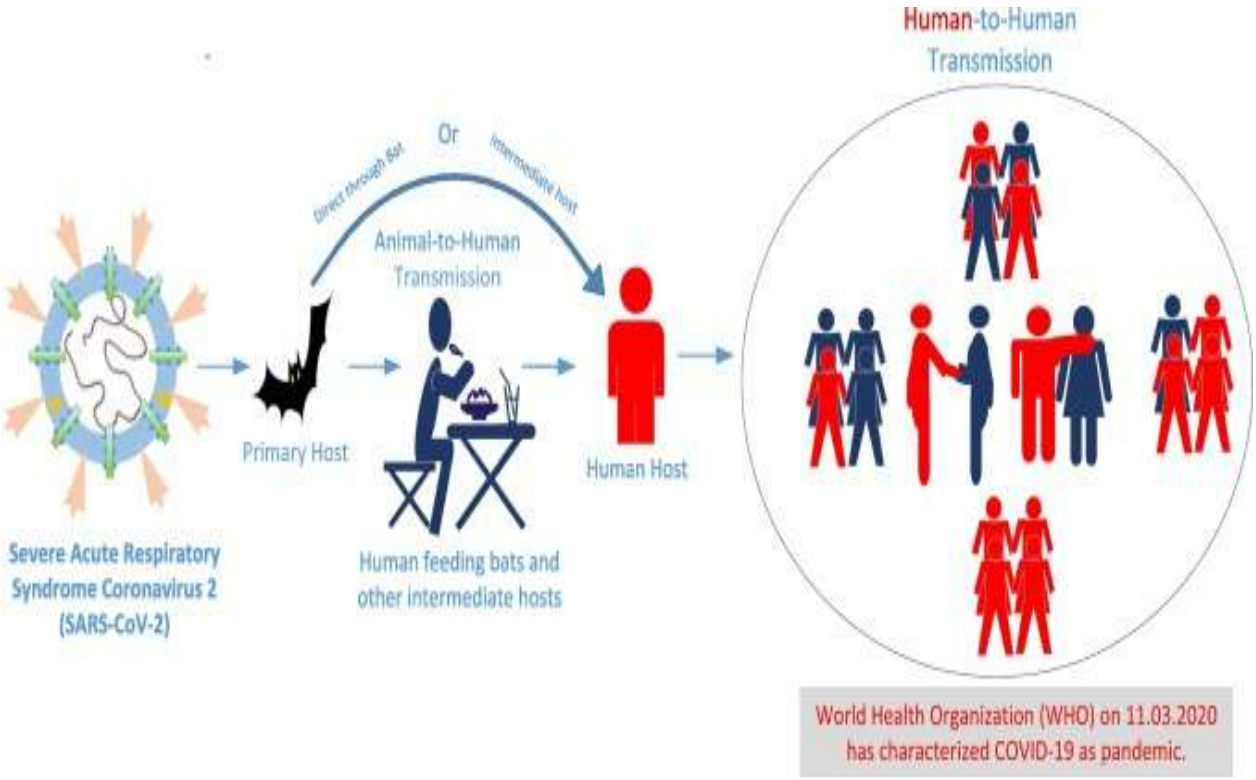

Figure 1:- Spreading of a covid-19 infection.

Origin And Spread Of Covid-19

In December 2019, adults in Wuhan, the Hubei region's capital and a major transportation hub in China, started setting up local hospitals for severe pneumonia of unknown cause. The surveillance system (established in response to the SARS outbreak) was activated, and samples of patients' respiratory specimens were sent to reference laboratories for diagnostic testing. China informed the World Health Organization (WHO) about the outbreak on December 31st, 2019, and the Huainan seafood market was closed on January 1st. On January 7th, it was confirmed that the infection was Covid and samples from the Huainan Sea food markets also tested positive, suggesting that the infection originated from there [23]. Cases started increasing rapidly, with some not linked to the live animal market, similar to how human-to-human transmission was occurring [24]. Reports have surfaced of cases in individuals who have returned from Wuhan in various regions of China and multiple nations. On January 20, 2020, a photo was taken of information being handed to a healthcare worker centered on patient care. On January 23, the 11 million inhabitants of Wuhan were put under lockdown, with restricted entry to the region. This seclusion quickly spread to different metropolitan areas across Hubei province. COVID-19 cases have been noted in countries other than China involving individuals who did not travel to China, indicating potential person-to-person transmission in those countries. Airports in multiple countries, including India, have implemented screening measures to detect and isolate suspicious individuals who have returned from China and to conduct tests for COVID-19. It quickly became evident that the illness could spread from people without symptoms before any signs were noticed. Consequently, numerous nations, such as India, repatriated their nationals from Wuhan or brought back travelers from China via dedicated flights, all of whom were either placed under suspicion or quarantine for a period of 14 days and screened for potential infection. Instances continued to rise significantly, and research has outlined the period in which the plague reproduces for a number of days [26].

Pathophysiology

Large, enveloped, single-stranded RNA viruses called coronaviruses can be found in humans and various animals like dogs, cats, chickens, cattle, pigs, and birds. Covid can lead to respiratory, gastrointestinal, and neurological infections and the most commonly known coronaviruses are 229E, OC43, NL63, and HKU1, typically causing mild cold symptoms in healthy individuals [3].

The composition of covid-19 is as follows: (SARS-CoV-2) Coronaviruses belong to the group of positive-sense

RNA viruses [30, 31] and are surrounded by an envelope that contains the viral nucleocapsid (arranged in a helical shape, showing unusual features in positive-sense RNA viruses) [34]. COVID-19 is capable of inducing clinical infection in individuals, ranging from mild cold symptoms to more serious respiratory illnesses such as SARS and MERS [32, 33]. This virus ranges in size from 60 to 140 nm in diameter, with noticeable spikes measuring 9 to 12 nm, which resembles the solar corona. COVID-19 is identified as a new betacoronavirus from the Coronavirinae family under the subgenus Sarbecovirus [35]. COVID-19's composition is categorized into four primary structural proteins as outlined below:

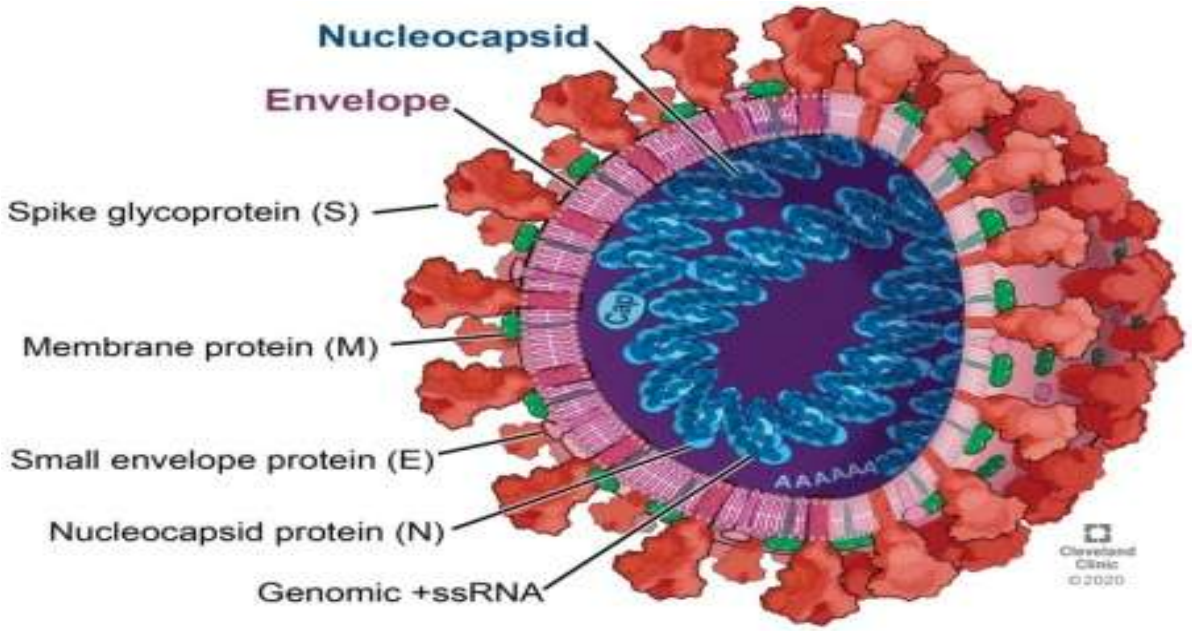

Figure 3:- Structure of COVID-19 Viru.

1. Spike glycoprotein “S”: The Covid S protein, also known as Spike glycoprotein "S", is a large multifunctional viral transmembrane protein belonging to class I. The plentiful S proteins vary in length from 1160 amino acids (IBV, poultry infectious bronchitis virus) to 1400 amino acids (FCoV, feline coronavirus). A virion's surface is shaped like a "crown" or crown-shaped. The extracellular regions of all S CoV proteins exhibit a somewhat close spatial relationship, divided into two domains [36]. S1, the former, encourages limiting host receptors while S2, the latter, encourages merging. The initial (S1) is divided into two smaller sections: the N-terminal domain (NTD) and the C-terminal domain (CTD). A recent study on the "S" protein of COVID-19 found changes in 27 amino acids. 4 out of 6 RBD substitutions in CTD S1 are RBM substitutions. It is important to mention that RBM did not show any amino acid alterations, and it interacts with the angiotensin-converting enzyme 2 (ACE2) receptor of SARS-CoV directly [16, 38]. Similarly, it has been observed that familial populations also show non-equivalent changes, indicating that viral evolution can happen through human-to-human transmission [39, 40].
2. M-proteins: M-proteins are the predominant viral proteins found in virion particles and have the ability to give a distinct shape to the viral envelope [41]. It is linked to the nucleocapsid and acts as a key organizer of COVID accumulation [42]. Covid M proteins have diverse amino acid compositions, yet they typically display fundamental similarities across different domains. The M protein contains three transmembrane domains, with a brief amino terminus located on the exterior of the virion and an extended carboxy terminus positioned within the virion [43]. Overall, interactions between monomers help support the structure of viruses. It is important to mention that there are no changes in amino acids in the M-protein when compared to SARS-CoV [37].
3. Protein E: The E Covids protein, which is the smallest of the major primary proteins, is the most mysterious. It performs various functions in the development, construction, and release of viruses [45]. This peptide is a generic membrane molecule that acts similarly to veropalene. Changes in its structure, ion inactivation, or absence have been linked to alterations in Covid toxicity. The E protein is made up of three sections: a small hydrophilic amino terminus, a big hydrophobic transmembrane domain, and a bold C-terminal domain. The amino acid structure of the SARS-CoV-2 E protein is comparable with no changes.
4. N Proteins: Coronavirus N proteins have many uses.

Transmission Of Covid-19

Epidemiological data on infections indicates that the primary way the virus spreads is through droplets released from close personal contact while speaking, coughing, and sneezing. Extended exposure to someone who is infected for at least 15 minutes within 6 feet heightens the chances of transmission, as well as brief contact with someone showing symptoms. However, short encounters with asymptomatic individuals do not lead to transmission. Another potential route of transmission involves expanding the area of contact. B. Coming into contact with a contaminated surface. It can also be transmitted through tiny droplets floating in the atmosphere. Nevertheless, it remains uncertain if this is a significant contributor to human infections beyond research facilities. Detecting aerosols or airborne nucleic acids in normal conditions doesn't imply that tiny airborne particles are contagious. There is now a belief that even low-risk mothers can be identified with COVID-19. Vertical transmission is linked. During the later stages of pregnancy, there is a low mortality rate and positive clinical outcomes for neonates when it comes to SARS-CoV-2 infection [59-61]. It is hard to describe the clinical importance of SARS-CoV-2 spreading from non-living surfaces without understanding. There seems to be a higher viral load on non-porous surfaces like stainless steel and plastic compared to porous surfaces like cardboard. The virus could be found on non-porous surfaces for 3-4 days following exposure [62].

Nevertheless, it is believed that most viruses present on surfaces are quickly eliminated in 48-72 hours [62]. Possible infected airborne transmission via fomites such as doorknobs, cutlery, and clothing contaminated with SARS-CoV-19 can spread on surfaces, highlighting the need for proper environmental hygiene. The primary method of transmission is through droplets that are passed during personal contact.

The amount of virus in the upper respiratory tract reaches its highest point when symptoms start, and the process of releasing the virus starts around 2-3 days before symptoms appear [63]. Studies have revealed that viral nucleic acids can be found in throat swabs up to six weeks after the disease starts, but it is commonly observed that viral cultures do not often detect the virus. This is corroborated by an epidemiological study on SARS-CoV-2 conducted eight days after symptoms appeared. In this research, none of the contacts reviewed developed an infection more than 5 days after the symptoms started in the cases reviewed. This indicates that being clinically better might stop people from being isolated. The Centers for Disease Control and Prevention suggest staying isolated for a minimum of 10 days once symptoms show and for a minimum of 3 days after symptoms get better. It remains uncertain if particular subgroups need a series of tests. It is appropriate for immunocompromised patients in critically ill situations who may see delayed improvement in symptoms, as well as for elderly individuals residing in smaller long-term care facilities [3]. Figure 4 illustrates the path through which the COVID-19 virus is transmitted.

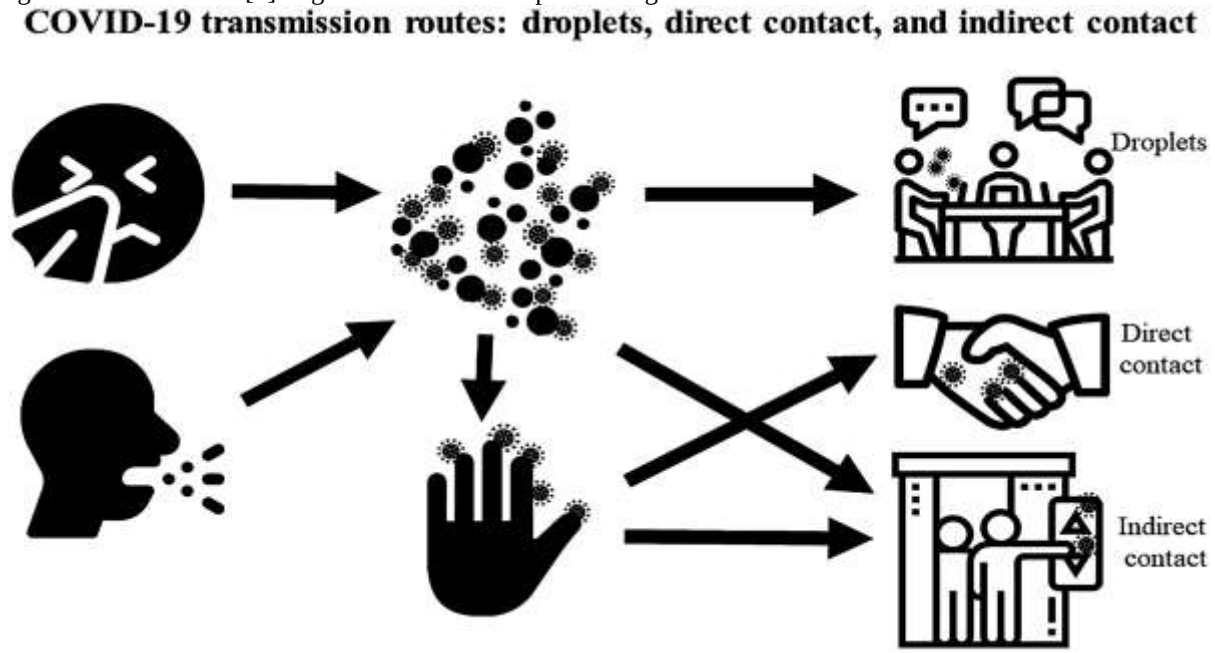

Figure 4:- Shows the mode of transmission of COVID-19.

Risk Factor

1. Infant
   2. Age 65 and older
   3. Pregnant
2. women

   Major non-communicable diseases (NCDs): diabetes, hypertension, heart disease, chronic lung disease, cerebrovascular disease, chronic kidney disease, immunosuppression, cancer [29]

Common Symptoms Of Covid-19

Most individuals who contract the COVID-19 virus experience cold and flu-like symptoms, while some do not show any symptoms at all, with approximately 80% of patients having mild symptoms. Adults are more resistant to infection, however, they have a higher chance of transmitting the infection to others. A significant number of people experience exhaustion and a dry cough with a high fever. One in three patients have symptoms of a dry cough and difficulty breathing. A study conducted in China by the CDC revealed that approximately 80% of COVID-19 cases are mild, 15% are severe, and 5% are critical. The severity of COVID-19 is worsened by the viral infection [64].

Day 1: On the day of symptom onset, there is fever, fatigue, muscle pain, and dry cough. Some people may experience nausea and diarrhea a few days before symptoms appear.

Day 5: Patients may experience side effects of breathing problems, especially if they are older or have had previous medical problems.

Day 7: Symptoms of patients requiring hospitalization, according to a study from Wuhan University.

Day 8: Patients (15%, according to the Chinese CDC) develop acute respiratory distress syndrome (ARDS), which occurs when fluid fills the lungs and is fatal in most cases, usually severe.

Day 10: Symptoms worsen as they progress. Meanwhile, the patient was transferred to the intensive care unit. Mild symptoms may be associated with increased abdominal pain and loss of appetite. Only a small percentage died. The current mortality rate is about 2%.

Day 17: Typically, patients are released after 14 days or longer once they have recovered. Yet, it is challenging to identify side effects in the period prior to the onset of infection. This typically occurs around 5 to 6 days later [64]. In 2019, symptoms of COVID-19 cases varied from mild to severe, and in some cases led to death. Immediate medical attention is necessary for emergency symptoms of COVID-19, such as ongoing chest pain or pressure. These symptoms consist of difficulty breathing, disorientation, and a bluish tint to the lips or face. Pneumonia is the result of a deteriorating illness. Due to its recent discovery, the virus does not have a known incubation period yet. Recent data indicates that signs of illness may show up within three to 13 days following infection. Based on a study that was recently released, the typical time it takes for symptoms to appear is approximately 5 days [65].

Diagnosis

Diagnostic testing for SARSCoV-2 involves detecting the virus's RNA in respiratory samples through reverse transcription-polymerase chain reaction, specifically from the nasopharynx, which is the established diagnostic standard. The variability of test results changes depending on when tests are conducted relative to disclosure. One study that was conducted measured sensitivity at 33% four days after exposure, 62% at the onset of symptom manifestation, and 80% three days after symptom onset. Contributing factors to false negative test results include the adequacy of the sample collection process, time since exposure, and source of the sample. Lower respiratory samples, such as bronchoalveolar lavage fluid, are more sensitive compared to upper respiratory samples. Gathering samples from individuals showing COVID-19 symptoms includes obtaining sputum, nasal swabs, and pharyngeal swabs, as well as possibly detecting the virus in feces but not in urine. Saliva could be a voluntary option that needs less personal protective equipment and fewer swabs, but it needs more validation. Multiple serological assay filters also aid in detecting and measuring responses to new vaccines.

Lab results: Common laboratory abnormalities in COVID-19 include increased levels of serum C-reactive protein, lactate dehydrogenase, and alanine aminotransferase. The usual blood abnormality includes low lymphocyte count, slightly decreased platelets, and increased D-dimer levels. D-dimer and lymphopenia, though to a lesser degree, seem to show the strongest prognostic correlation. Visualizing. COVID-19 demographic imaging abnormalities include spread out peripheral ground-glass opacities, unclear borders, air bronchograms, smooth or irregular interlobular or septal thickening, and pleural thickening near the affected area. A large number of individuals were hospitalized for confirmation of COVID-19 infection using a polymerase chain reaction test known as SARSCoV2 [3].

Clinical Severity:

1. The mouse was chased by the cat all over the house for many hours. At a slight level of seriousness, patients experiencing upper respiratory tract infections might exhibit mild symptoms like coughing, a sore throat, nasal congestion, malaise, and headaches.
2. Patients experiencing a moderate level of severity may develop pneumonia without exhibiting symptoms of a severe illness.
3. Reconstruct the given text with the same input language and maintain the word count. Patients experience extreme pneumonia in serious situations [66].

Treatment

To start, make sure there is enough separation to avoid the transmission of COVID-19 to other individuals such as contacts, patients, and healthcare workers. Less severe illnesses like fever, cough, sore throat, nasal congestion, malaise, and headache can be managed at home with counseling on recognizing warning signs [28]. The majority of individuals who contract COVID-19 experience a mild to moderate respiratory illness and can recover without the need for specific medical intervention. Individuals who are older or have underlying conditions like heart disease, lung disease, diabetes, or cancer are at an increased likelihood of experiencing serious infections [67].

COVID-19 Treatment Strategies

Summarizes the latest details regarding possible treatments for COVID-19. It is crucial to alert readers that updates on COVID-19 clinical features, analyses, treatment options, and outcomes are continuously being provided [65]. In this study, we examined various medications for treating COVID-19, including home remedies, natural remedies, synthetic drugs, combination drugs, plasma therapy, and vaccines [67].

General Care

Patients diagnosed with COVID-19 need proper rest in bed and continuous attention to guarantee sufficient intake of calories and fluids, as well as minimize the possibility of dehydration. Maintaining water electrolyte balance and homeostasis is essential to regulate vital functions and blood oxygen saturation. Maintain an unobstructed airway and administer oxygen in the most critical situations. Blood biochemical indicators such as blood count, creatinine protein, urine test, liver and kidney function, myocardial enzyme spectrum, and breast imaging coagulation should be regularly checked based on the patient's condition. Blood gas tests are required in specific situations.

Symptometic Treatment

Patients with elevated body temperature need to be monitored. Antipyretic therapy should be initiated when the temperature reaches 38.5 ° C or above. Warm water baths and antipyretic patches are recommended for reducing body temperature to prevent illness. The typical medication is ibuprofen, to be taken orally at a dose of 5-10 mg/kg. Oral administration of paracetamol at a dose of 10-15 mg per kilogram of body weight. Sedatives are necessary for convulsions or seizures.

Oxygen Tharepy

If the virus enters the lungs, hypoxia is more likely. A nasal cannula and oxygen mask should be provided to the patient immediately. In emergency situations, noninvasive or invasive mechanical ventilation should be provided to the patient.

Strength the Immune System

A robust immune system provides extra defense and preventative measures against illness. When the immune system is working well and maintaining an ideal figure is a challenge, the body can more effectively fight off illness. It is now important to focus on your well-being and possibly adjust your routines. In times of crisis, make sure to get sufficient rest daily and take in fresh air and sunlight. It is important for individuals to keep well-hydrated, avoid excessive processing, and ensure they consume enough micronutrients at their peak freshness in the grocery store. Various herbal remedies used in different countries to boost the immune system include items like Honey, Piper nigrum, and Curcuma longa, as well as Dried angelica root, Neem herbs, Onion, Dried ginger, Dried orange peel, and Cinnamon stick.

Home Remedy

More than 80% of individuals diagnosed with COVID-19 are required to self-manage their symptoms at home, as per data from the World Health Organization. Hence, this part provides suggestions on managing and avoiding

SARS-Cov-2 in order to decrease stress, practice self-care, and alleviate sore throats, respiratory congestion, and sinus issues.

Stress Reduction

During the COVID-19 outbreak in 2020, with rising confirmed cases and deaths, medical professionals and the general public are experiencing mental health issues like stress, anxiety, and depression. The pandemic is leading to advancements in China's emergency response, potentially enhancing its efficiency and standards in the future. The World Health Organization advises that healthy adults should do 30 minutes of exercise each day and children should aim for 1 hour daily. The World Health Organization (WHO) also suggests engaging in dancing, jumping rope, strength training, and online workouts to decrease stress and boost the immune system.

Self Help

Taking breaks and staying hydrated can lower the risk of upper respiratory infections. Consuming plenty of fluids is the initial step during this time, and specific foods like bone broth and homegrown vegetables like garlic can also be beneficial. Certain herbal teas like ginger, peppermint, eucalyptus, chamomile, and hot water with honey, lemon, and cinnamon can help hydrate and alleviate symptoms of infections.

Sore Throats

Using saltwater gargles is the initial approach for combating bacterial throat infections, as they effectively soothe mucus and offer protection. Hot teas and lozenges are great calming agents that can help alleviate throat inflammation. Peppermint and chamomile tea are highly effective in soothing a sore throat, while liquorice and marshmallow root infusions serve as great sedatives.

Synthetic Remedies

The treatment of any disease in the West is viewed as homeopathic treatment. If a patient has pneumonia and tests positive for COVID-19, they should take antivirals and consider using supplemental oxygen during emergency situations. Because of the quick transmission of COVID-19, drugs that were previously used to treat antiviral, antimalarial, and anthelmintic infections have been utilized for treatment. Conducting clinical and laboratory testing poses a difficulty for contemporary pharmaceuticals. Synthetic drugs show potential with positive outcomes [68].

1. Antiviral drugs:

a. Remdesivir is utilized to treat Ebola and Marburg virus infections by blocking RNA-dependent RNA polymerase, ultimately causing termination of RNA chains within cells. The recommended dosage is 200 mg per day, taken two times.

b. Ribavirin is prescribed for the treatment of viral hemorrhagic fever, hepatitis C, and respiratory syncytial virus (RSV) infections. It hinders RNA capping, which results in halting viral replication, with a recommended daily dosage of 500mg.

c. Umifenovir is utilized for the treatment of infections caused by influenza A and B viruses by blocking the fusion of the virus with the membrane of the host cell, ultimately hindering its entry into the host cell. The recommended amount is 200 mg per dose, taken two times daily.

d. Favipiravir is utilized to treat respiratory syncytial virus, nasal virus, and influenza virus by blocking viral RNA synthesis at the RNA binding site within the host cell. The recommended daily dose is 600 mg.

e. Lopinavir/Ritonavir is a combination that is utilized for treating immunodeficiency in individuals. When taken twice a day, a 200 mg dose of Lopinavir/50 mg dose of Ritonavir functions as a protease inhibitor and cytochrome P450 3A inhibitor [69].

Natural Treatment

Natural drugs are organic compounds obtained from organisms (such as plants, animals, fungi, bacteria, etc.) in their natural state. Highlight that naturopathic medicine plays a significant role in creating and manufacturing antiviral medications. Metabolic compounds from both plants and animals have demonstrated activity against tumors, fungi, inflammation, and viruses. In the Asian region, medicinal plants have long been utilized for a wide range of medicinal reasons.

Treatment using plasma

An additional therapy for COVID-19 involves utilizing human plasma collected post recovery from the disease. Plasma holds innate antibodies, referred to as passive antibody therapy in human serum, a crucial element in plasma treatment for COVID-19 patients in transition. After receiving the plasma transfusion, the patient experienced an

expedited recovery from COVID-19 during the recovery phase, which enabled her to reach a normal body temperature. A traditional cure has shown promising results in fighting the lethal COVID-19 virus. Serological tests will verify how well antibodies are able to neutralize COVID-19 infection before plasma is utilized. The spike proteins of coronaviruses lead to severe respiratory infections by fusing or binding with receptors on target cells. ACE2 is a carboxypeptidase that effectively changes angiotensin II to angiotensin and is viewed as a strong coronavirus binding site. This summit exhibits strong attraction to the coronavirus receptor-binding domain (RBD) and is believed to possess healing characteristics. Plasma therapy shows significant promise for severe issues, proving to be more efficient, user-friendly, and secure, enabling speedier patient recovery.

Microbial-based therapy

Microbes like algae, fungi, and bacteria contain biologically active substances that could be utilized for COVID-19 treatment. Fungi produce compounds with COVID-19 protease inhibitor activity. Paclitaxel is a fungal-derived active metabolite example. The use of H. Pestlotia and Pitomyces in treating corona virus, along with their anti-HIV properties, has been documented. Various other fungal compounds have also been mentioned. H. quercitrin from G. triplex, bergenin from D. indusiate, and dihydroartemisinin from C. stertious all block the primary proteases of COVID-19. Marine organisms assist in the growth of brown algae like Sargassum spinuligerum and Ecklonia cava by providing bioactive compounds such as 1,3,5-trihydroxy benzene, 8.8'-beckon, dieckol, and 6.6'-beckon. I possess. Furthermore, β-glucan sourced from microbes could assist the body in combatting a COVID-19 infection.

Herbal therapy

Multiple studies have found that natural herbal products may serve as potential treatments for viral infections. It is frequently stated that active metabolites are extracted from various plant parts.

1. Acacia nilotica of the Fabaceae family is a protease inhibitor of human immunodeficiency virus (HIV); antiviral and cytotoxic effects.
2. Alhagi maurorum belongs to the Fabaceae family, has an inhibitory effect on cold and flu viruses; relieve cough, chest pain, fever, vomiting and thirst, etc.
3. Allium sativum of the family Alliaceae has inhibitory effect on avian corona virus; antiviral and fungal effects.
4. Cinnamomum cassia belongs to the camphor family (Lauraceae) has antiviral, anti-inflammatory and inhibits the attachment of respiratory syncytial virus in humans.
5. Echinacea Angustifolia of the family Asteraceae exhibits antiviral activity against cold and flu viruses, inhibits viral growth, and secretes inflammatory cytokines.
6. Glycyrrhiza glabra of the Fabaceae family exhibits activity against HSV-1, Epstein-Barr virus, human cytomegalovirus and RNA viruses such as influenza A, H5N1 and H1N1.
7. Litchi chinensis belongs to the soapberry family, has an inhibitory effect on SARS-3CLpro; terpenoids inhibit HIV-1 protease.
8. Nigella sativa belongs to the ranunculus family (Ranunculaceae) with immunomodulatory, anti-inflammatory and bronchodilator effects; activity against avian influenza virus (H9N2).
9. Salvia officinalis (Lipaceae) is strongly associated with the COVID-19 proteases that inhibit the replication of SARS-CoV and HSV-1.
10. Stachys schtschegleevii (Lithuaceae) exhibits antiviral activity against SARS-CoV-2 and anti-inflammatory potential.
11. Zingiber Officinalis (Family Zingiberaceae) has antiviral activity against human respiratory syncytial virus. [71]
12. Withania somniferous of the family Solanaceae have cyclo-oxygenase-2 inhibitory properties, they have anti-inflammatory and analgesic activities.
13. Andrographis panniculitis of the Acanthaceae family has been shown to have antibacterial, antiprotozoal, anti-angiogenic, antidiabetic, anti-inflammatory, antioxidant, immunostimulating, and hepatoprotective effects.
14. Panax quinquefolius belongs to the family Araliaceae and acts as an antibacterial, antidiabetic, anti-inflammatory, anti-cardiovascular and anti-cancer antioxidant.
15. Azadirachta indica (family Meliaceae) has anti-inflammatory, antimalarial, antibacterial, antifungal, immunomodulatory, curative, hepatoprotective, antidiabetic, antitoxic, neuroprotective activities and anti-cancer properties.[72]
16. Tribulus Terrestris of the family Zygophyllaceae shows inhibition of papain-like protease (PLpro), which is a major protein target of COVID-19.
17. Curcuma longa (Zingiberaceae) is more effective against COV-19. [73]

18. Aloe barbadensis Mill. (Aloe vera) it belongs to the family Asphodelaceae which has the most important chemical constituents: aloin, emodin, aloe-emodin, barbaloin, isobarbaloin and chrysophanic acid, a rich source of quinone components; Aloe vera anthraquinones have been reported to be active against human influenza viruses.
19. Trachyspermum Ammi L. (Ajwain) belongs to the family Apiaceae used to treat sore throats in influenza, the seeds are mixed with cloves and a pinch of salt and chewed.
20. Glechoma hederacea is used to treat influenza, fever and respiratory infections. Morus alba L. (Folium Mori) (family Moraceae) is used against influenza.
21. Scutellaria baicalensis Gorgi (Baicalin) (Lithuaceae) Inhibits H1N1 influenza by cytotoxicity to infected cells.
22. Radix bupleuri (family Apiaceae) is used against influenza and upper respiratory tract infections.
23. Punica granatum L. (pomegranate) (family Punicaceae) Shows anti-influenza properties by preventing influenza A virus replication in cell culture.
24. Psidium guajava Linn (guava tea) (family Myrtaceae) Inhibits erythrocyte agglutination and viral sialidase activity, and also inhibits bacterial growth.
25. Pimpinella major (L.) Hudson (family Apiaceae) where the roots are used to treat colds, flu and fever. [74]

Sars-Cov-2/Covid-19 Vaccines

Developing and scaling up vaccine production quickly during a worldwide pandemic is difficult due to the need for coordinated preclinical and clinical studies, alongside the typical 10-year sequential process and distribution. These issues result in significant investment expenditures and substantial financial hazards. We carried out a thorough review of the literature regarding the advancement of SARS-CoV-2 vaccine creation to halt the swift transmission of COVID-19. We examined vaccines listed in the National Library of Medicine's Clinical Trials database prior to December 2020. Getting infected is a crucial stage in combatting COVID-19. The potential benefits of natural remedies are as listed:

Table 1:- Summary of active and recruiting Phase I and I/II trials registered in the Clinical Trials database

Vaccine name	Mechanism of action	Dosage regimen	Estimated study completion	Sponsor	Identifier/ clinical trials
SCB-2019 [ref. no. 75]	A recombinant protein with adjuvant AS03 or CpG/alum	2 i.m. doses	March 2021	Clover Biopharmaceuticals AUS Pty Ltd	NCT04405908/ Phase I
AdimrSC-2f [ref. no. 75]	Baculovirus vector with/ without alum	1 dose	March 2021	Adimmune Corporation	NCT04522089/ Phase I
MVC-COV1901 [ref. no. 75]	Reombinant protein with adjuvant CpG1018	2 i.m. dose	June 2021	Medigen Vaccine Biologics Corp	NCT04569383/ Phase I
COVAX-19 [ref. no. 75]	Recombinant protein with adjuvant Advax-SM	1 dose	July 2021	Vaxine Pty Ltd	NCT04487210/ Phase I
GRAd-COV2 [ref. no. 75]	Gorilla Adenovirus vector	1 i.m. dose	July 2021	ReiThera Srl	NCT04453852/ Phase I
Lipid nanoparticle encapsulated RNA. CVnCoV [ref. no. 76]		i.m	,18 June 2020	CureVac, Germany	NCT04449276/ Phase I

COVAC1 (LNP-nCoVsaRNA) [ref. no. 76]	Act on Spike protein	i.m	1 April 2020	Imperial College London, UK	ISRCTN17072692/ Phase 1
ARCT-021 [ref. no. 75]	mRNA	1 i.m. dose	January 2021	Arcturus Therapeutics, Inc.	NCT04480957/ Phase I/II
SARS-CoV-2	Inactivated virus	2 doses	September 2021	Sinovac Research and Development Co., Ltd.	NCT04551547/ Phase I/II
INO-4800	DNA (plasmid vector pGX9501)	2 i.d. doses	February, 2022	International Vaccine Institute	NCT04447781/ Phase I/II
GX-19	DNA	2 i.m. doses	June 2022	Genexine, Inc.	NCT04445389/ Phase I/II
LV-SMENP-DC	Lentivirus modified DC and antigen-specific CTLs	1 s.c. dose/1 infusion	December 2024	Shenzhen GenoImmune Medical Institute	NCT04276896/ Phase I/II
COVID-19/aAPC	Inactivated artificial APC upon lentivirus modification	3 s.c. doses	December 2024	Shenzhen GenoImmune Medical Institute	NCT04276896/ Phase I/II
Synthetic minigene transfected APCs Covid-19/aAPC [ref. no. 76]	Selected conserved structural and protease protein domains		15 February 2020	Shenzhen Geno-immune Medical Institute, China	NCT04299724/ Phase I/II

Covid-19 Prevention & Precaution

Individuals need to remain informed about the most recent updates on the COVID-19 outbreak and adhere to the guidance provided by the local health authorities in order to avoid additional infections and halt the spread of the virus from person to person. Most individuals infected by health workers and prevention efforts typically experience minor symptoms and recover quickly, but the virus can pose a more serious threat to others, including close contacts and healthcare workers, and has the potential for further global transmission. Make efforts to safeguard yourself:

• Frequently cleanse your hands with soap and water or hand sanitiser with 60% alcohol for 20 seconds, ensuring full coverage and rubbing until dry, particularly after being in public or sneezing, coughing, or blowing your nose.

- Coming into contact with various surfaces and transferring the virus onto your hands can result in transmitting the virus to your nose, eyes, or mouth. Keep your hands clean before touching this area. • Keep a distance of at least 1 meter or 3 feet from other individuals and refrain from being near someone experiencing COVID-19 symptoms like coughing or sneezing. Infected individuals can release small droplets into the air when coughing or sneezing. When a person in good health breathes in the polluted air, they can inhale it through their mouth.

• Stay away from big events and large crowds. Act to ensure the safety of others.

• If you feel unwell and don't want to see a doctor, it's best to stay at home.

• If you are feeling unwell, avoid taking public transportation.

• Make sure to use a tissue to cover both your mouth and nose when you cough or sneeze.
• Dispose of used paper towels in the garbage and cleanse your hands promptly with antiseptic soap. When feasible, separate family members and pets in a confined space and wear a mask when in the presence of others.
• Remain at your residence temporarily and adhere to the instructions given by your physician.
• Avoid sharing bedding, dishes, glasses, or other essentials while you are ill.
• Whenever feasible, it is advisable to have a dedicated bathroom and toilet space for use by individual family members.
• Apply disinfectant daily on various surfaces that are frequently touched such as desks, phones, keyboards, toilets, faucets, tables, doorknobs, light switches, countertops, handles, sinks, etc.
• Refrain from coming into direct contact with respiratory and other bodily secretions. For example, move individuals who may be contagious to isolation rooms and shut the doors.
• Limit the amount of individuals allowed into quarantine zones, such as the section for those with potential or confirmed cases of COVID-19 [65].

Conclusion:-

The global increase in hospitalized pneumonia patients due to multi-organ infections caused by SARS-CoV-2, the virus responsible for the COVID-19 pandemic, has been significant. In Wuhan, Hubei province, China, a previously unidentified animal species was discovered in December 2019, revealing SARS-CoV-2 as a member of the coronavirus family and specifically classified as β-COVID. Certain individuals have suggested viable alternative therapies for treating COVID-19 infections, and are anticipated to develop or manufacture artificial medications, organic substances, and immunizations. Numerous spices and plants from traditional systems retain beneficial biologically active compounds that show potential for modern medical therapies. Furthermore, both the organization and the entire team are dedicated to conducting extensive research for the advancement of medications and vaccines for COVID-19. Protein-based vaccines are now the primary type of vaccine being examined in early clinical trials, replacing the previously popular viral vector and genetic vaccine.

References:-

1. Burki TK. Coronavirus in China. Lancet Respir Med. 2020
2. World Health Organization. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. https://www.who.int/dg/ speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-20 19-ncov-on-11-february-2020. 2020
3. Wiersinga W. Joost, MD, Ph.D.; Rhodes Andrew, MD, Ph.D.; Cheng Allen C., MD, Ph.D.; Peacock Sharon J., Ph.D.; Prescott Hallie C., MD, MSc (2020) "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19)" Clinical Review & Education
4. Yang* Yang, Islam Md Sahidul, Wang Jin, Li Yuan and Chen Xin (2020) "Traditional Chinese Medicine in the Treatment of Patients Infected with 2019-New Coronavirus (SARS-CoV-2): A Review and Perspective" International Journal of Biological Sciences 2020; 16(10): 1708-1717. DOI: 10.7150/ijbs.45538
5. Wu, Z., & McGoogan, J. M. (2020). Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. Journal of the American Medical Association, 323, 1239.
6. Seidman JC, Richard SA, Viboud C, Miller MA. A quantitative review of antibody response to inactivated seasonal influenza vaccines. Influenza Other Respi Viruses. 2012;6(1):52-62. doi:10. 1111/j.1750-2659.2011.00268.x
7. Teo LM, Smith HE, Lwin MO, Tang WE. Attitudes and perception of influenza vaccines among older people in Singapore: a qualitative study. Vaccine. 2019;37(44):6665-6672. doi:10.1016/j. vaccine.2019.09.037
8. Fell DB, Azziz-Baumgartner E, Baker MG, et al. Influenza epidemiology and immunization during pregnancy: Final report of a World Health Organization working group. Vaccine. 2017;35(43):5738-5750. doi:10.1016/j.vaccine.2017.08.037
9. Biggerstaff M, Cohen C, Reed C, et al. A cost-effectiveness analysis of antenatal influenza vaccination among HIV-infected and HIV-uninfected pregnant women in South Africa. Vaccine. 2019;37(46):6874-6884. doi:10.1016/j.vaccine.2019.09.059
10. Liu Xue, Liu Chao, Liu2 Gang, Luo Wenxin, Xia Ningshao,(2020) "COVID-19: Progress in diagnostics, therapy and vaccination" Theranostics 2020, Vol. 10, Issue 17
11. De Clercq E. New nucleoside analogs for the treatment of hemorrhagic fever virus infections. Chem Asian J 2019; 14(22): 3962-8.

12. Nugraha Rhea Veda, Ridwansyah Hastono, Ghozali Mohammad, Khairani Astrid Feinisa, and Atik Nur "Traditional Herbal Medicine Candidates as Complementary Treatments for COVID-19: A Review of Their Mechanisms, Pros and Cons" Hindawi Evidence-Based Complementary and Alternative Medicine Volume 2020, Article ID 2560645, 12 pages https://doi.org/10.1155/2020/2560645
13. Kebede Tinsae, Kumar Dharmendra, Sharma Pramod Kumar, "Potential Drug Options for Treatment of COVID-19: A Review": https://www.researchgate.net/publication/342634827
14. Mostafa Ahmed, Kandeil Ahmed, Elshaier Yaseen A. M. M., Kutkat Omnia, Moatasim Yassmin, Rashad Adel A, Shehata Mahmoud, Gomaa Mokhtar R., Mahrous Noura, Mahmoud Sara H., GabAllah Mohamed, Abbas Hisham, Taweel Ahmed El, Kayed Ahmed E., Kamel Mina Nabil, Sayes Mohamed El, Mahmoud Dina B., El-Shesheny 1 Rabeh, Kayali Ghazi, A. Ali Mohamed, "FDA-Approved Drugs with Potent In Vitro Antiviral Activity against Severe Acute Respiratory Syndrome Coronavirus 2" Pharmaceuticals 2020, 13, 443; doi:10.3390/ph13120443
15. Chan, K.W.; Wong, V.T.; Tang, S.C.W. Covid-19: An update on the epidemiological, clinical, preventive and therapeutic evidence and guidelines of integrative Chinese-western medicine for the management of 2019 novel coronavirus disease. Am. J. Chin. Med. 2020, 48, 737–762. [CrossRef] [PubMed]
16. Wu, Y.Q.; Zou, L.; Yu, X.; Sun, D.; Li, S.B.; Tang, L.; Yang, J.R.; Chen, X.Y.; Wu, Y.G.; Fang, H. Clinical effects of integrated traditional Chinese and western medicine on COVID-19: A systematic review. Shanghai J. Tradit. Chin. Med. 2020, 1–8. [CrossRef]
17. Qi, G.; Qi, W.; Jiang, Q.; Shen, K.Q.; Zhang, X.; Zhang, L. The Efficacy of Lianhua Qingwen Combined with Western Medicine Scheme on COVID-19 General Type Patients: A Systematic Review. Clin. J. Tradit. Chin. Med. 2020, 1–9. Available online: http://kns.cnki.net/kcms/detail/34.1268.r.20200410.0909.002.html (accessed on 22 May 2020).
18. Zhan, Z.L.; Liu, J.; Yang, W.; Wang, Y.G.; Ruan, L.G.; Huang, P.; Guo, L.P.; Bian, Y.J.; Chen, S.P.; Chen, Y.; et al. Exploratory Study on Evaluation Criteria of Chinese Medicine Treatment of New Coronavirus Pneumonia Based on Case Analysis. J. Tradit. Chin. Med. 2020, 1–11. Available online: http://kns.cnki.net/kcms/detail/11.2166.R.20200312.0949.002.html (accessed on 22 May 2020).
19. Ang Lin, Song Eunhye, Won Lee Hye, Soo Lee Myeong "Herbal Medicine for the Treatment of Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-Analysis of Randomized Controlled Trials" J. Clin. Med. 2020, 9, 1583; doi:10.3390/jcm9051583
20. . Yang Y, Islam MS, Wang J, Li Y, Chen X. Traditional Chinese medicine in the treatment of patients infected with 2019-New Coronavirus (SARS-CoV-2): a review and perspective. Int J Biol Sci. 2020;16(10):1708e1717
21. Huang J, Su D, Feng Y, Liu K, Song Y. Antiviral herbs-present and future. Infect Disord - Drug Targets. 2014;14(1):61e73.
22. Panyard Suraphan, Ho Chi-Tang, Sheen Lee-Yan "Dietary therapy and herbal medicine for COVID-19 prevention: A review and perspective" Journal of Traditional and Complementary Medicine 10 (2020) 420e427
23. Xinhua. China's CDC detects a large number of new coronaviruses in the South China seafood market in Wuhan. Available at: https:// www.xinhuanet.com/2020-01/27/c_1125504355.htm. Accessed 20 Feb 2020.
24. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395: 497–506
25. Rothe C, Schunk M, Sothmann P, et al. Transmission of 2019- nCoV infection from an asymptomatic contact in Germany. N Engl J Med. 2020.https://doi.org/10.1056/NEJMc2001468.
26. Li Q, Guan X, Wu P, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020. https://doi.org/10.1056/NEJMoa2001316.
27. World Health Organization. Situation reports. Available at: https:// www.who.int/emergencies/diseases/novel-coronavirus-2019/ situation-reports/. Accessed 22 Feb 2020.
28. Singhal Tanu, "A Review of Coronavirus Disease-2019 (COVID-19)" The Indian Journal of Pediatrics https://doi.org/10.1007/s12098-020-03263-6
29. Unhale Shrikrushna Subhash, Ansar Quazi Bilal, Sanap Shubham, Thakhre Suraj, Wadatkar Shreya, Bairagi Rohit, Prof. Sagrule Suraj, and Prof. Dr. Biyani K. R. "A REVIEW ON CORONA VIRUS (COVID-19)" International Journal of Pharmaceutical and Life Sciences · April 2020: https://www.researchgate.net/publication/340362876
30. Weiss SR, Leibowitz JL. 2011. Coronavirus pathogenesis. Adv Virus Res 81:85-164. DOI: 10.1016/B978-0-12-385885-6.00009-2
31. . Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, Pan P, Wang W, Hu D, Liu X, Zhang Q, Wu J. 2020. Coronavirus infections and immune responses. J Med Virol 10.1002/jmv.25685. DOI: 10.1002/jmv.25685.

32. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N, Bi Y, Ma X, Zhan F, Wang L, Hu T, Zhou H, Hu Z, Zhou W, Zhao L, Chen J, Meng Y, Wang J, Lin Y, Yuan J, Xie Z, Ma J, Liu WJ, Wang D, Xu W, Holmes EC, Gao GF, Wu G, Chen W, Shi W, Tan W. 2020. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet pii: S0140-6736(20)30251-8. DOI: 10.1016/S0140-6736(20)30251-8.
33. Cheng VC, To KK, Tse H, Hung IF, Yuen KY. Two years after pandemic influenza A/2009/H1N1: what have we learned? Clin Microbiol Rev. 2012 Apr;25(2):223-63.
34. Fehr AR, Perlman S. 2015. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol 1282:1-23. DOI: 10.1007/978-1-4939-2438-7_1.
35. Gralinski LE, Menachery VD. 2020. Return of the Coronavirus: 2019-nCoV. Viruses 12(2): E135. DOI: 10.3390/v12020135.
36. Belouzard S, Millet JK, Licitra BN, Whittaker GR. 2012. Mechanisms of coronavirus cell entry mediated by the viral spike protein. Viruses 4(6):1011-1033. DOI: 10.3390/v4061011.
37. Kui L, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, Xiao W, Wang YN, Zhong MH, Li CH, Li GC, Liu HG. 2020. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl) 10.1097/CM9.0000000000000744. DOI: 10.1097/CM9.0000000000000744.
38. Ge XY, Li JL, Yang XL, Chmura AA, Zhu G, Epstein JH, Mazet JK, Hu B, Zhang W, Peng C, Zhang YJ, Luo CM, Tan B, Wang N, Zhu Y, Crameri G, Zhang SY, Wang LF, Daszak P, Shi ZL. 2013. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. Nature 503(7477):535-538. DOI: 10.1038/nature12711.
39. Wei X, Li X, Cui J. 2020. Evolutionary perspectives on novel Coronaviruses identified in pneumonia cases in China. National Science Review. DOI: 10.1093/nsr/nwaa009.
40. Li X, Song Y, Wong G, Cui J. 2020. Bat origin of a new human coronavirus: there and back again. Sci China Life Sci 10.1007/s11427-020-1645-7. DOI: 10.1007/s11427-020- 1645-7.
41. Neuman BW, Kiss G, Kunding AH, Bhella D, Baksh MF, Connelly S, Droese B, Klaus JP, Makino S, Sawicki SG, Siddell SG, Stamou DG, Wilson IA, Kuhn P, Buchmeier MJ. 2011. Structural analysis of M protein in coronavirus assembly and morphology. J Struct Biol 174(1):11-22. DOI: 10.1016/j.jsb.2010.11.021.
42. Nal B, Chan C, Kien F, Siu L, Tse J, Chu K, Kam J, Staropoli I, Crescenzo-Chaigne B, Escriou N, van der Werf S. 2005. Differential maturation and subcellular localization of severe acute respiratory syndrome coronavirus surface proteins S, M and E. J Gen Virol 86:1423-1434. DOI: 10.1099/vir.0.80671-0
43. Arndt AL, Larson BJ, Hogue BG. 2010. A conserved domain in the coronavirus membrane protein tail is important for virus assembly. J Virol 84(21):11418-11428. DOI: 10.1128/JVI.01131-10.
44. Schoeman D, Fielding BC. 2019. Coronavirus envelope protein: current knowledge. Virol J 16(1):69. DOI: 10.1186/s12985-019-1182-0.
45. Nieto-Torres JL, DeDiego ML, Verdia-Baguena C, Jimenez-Guardeno JM, Regla-Nava JA, Fernandez-Delgado R, Castano-Rodriguez C, Alcaraz A, Torres J, Aguilella VM, Enjuanes L. 2014. Severe acute respiratory syndrome coronavirus envelope protein ion channel activity promotes virus fitness and pathogenesis. PLoSPathog10:e1004077 doi: 10.1371/journal.ppat.1004077
46. Pervushin K, Tan E, Parthasarathy K, Lin X, Jiang FL, Yu D, Vararattanavech A, Soong TW, Liu DX, Torres J. 2009. Structure and inhibition of the SARS coronavirus envelope protein ion channel. PLoSPathog 5(7):e1000511. DOI: 10.1371/journal.ppat.1000511.
47. DeDiego ML, Alvarez E, Almazán F, Rejas MT, Lamirande E, Roberts A, Shieh WJ, Zaki SR, Subbarao K, Enjuanes L. 2007. A severe acute respiratory syndrome coronavirus that lacks the E gene is attenuated in vitro and in vivo. J Virol 81(4):1701-1713. DOI: 10.1128/JVI.01467-06.
48. Chang CK, Sue SC, Yu TH, Hsieh CM, Tsai CK, Chiang YC, Lee SJ, Hsiao HH, Wu WJ, Chang WL, Lin CH. 2006. Modular organization of SARS coronavirus nucleocapsid protein. J Biomed Sci 13:59-72. DOI: 10.1007/s11373-005-9035-9
49. Sheikh A, Al-Taher A, Al-Nazawi M, Al-Mubarak AI, Kandeel M. 2020. Analysis of preferred codon usage in the coronavirus N genes and their implications for genome evolution and vaccine design. J Virol Methods 277:113806. DOI: 10.1016/j.jviromet.2019.113806
50. McBride R, van Zyl M, Fielding BC. 2014. The coronavirus nucleocapsid is a multifunctional protein. Viruses 6(8):2991-3018. DOI: 10.3390/v6082991.
51. Fan H, Ooi A, Tan YW, Wang S, Fang S, Liu DX, Lescar J. 2005. The nucleocapsid protein of coronavirus infectious bronchitis virus: crystal structure of its N-terminal domain and multimerization properties. Structure 13(12):1859-1868. DOI: 10.1016/j.str.2005.08.021.

52. . Hurst KR, Koetzner CA, Masters PS. 2009. Identification of in vivo-interacting domains of the murine coronavirus nucleocapsid protein. J Virol 83(14):7221-7234. DOI: 10.1128/JVI.00440-09.
53. Stohlman SA, Baric RS, Nelson GN, Soe LH, Welter LM, Deans RJ. 1988. Specific interaction between coronavirus leader RNA and nucleocapsid protein. J Virol 62(11):4288-4295.
54. You J, Dove BK, Enjuanes L, DeDiego ML, Alvarez E, Howell G, Heinen P, Zambon M, Hiscox JA. 2005. Subcellular localization of the severe acute respiratory syndrome coronavirus nucleocapsid protein. J Gen Virol 86(Pt 12):3303-3310. DOI: 10.1099/vir.0.81076-0.
55. 25. Chu DK, Akl EA, Duda S, et al; COVID-19 Systematic Urgent Review Group Effort (SURGE) study authors. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. Lancet. 2020;395(10242):1973-1987. doi:10.1016/S0140- 6736(20)31142-9
56. . Bourouiba L. Turbulent gas clouds and respiratory pathogen emissions: potential implications for reducing transmission of COVID-19. JAMA. Published online March 26, 2020. doi:10.1001/ Jama.2020.4756
57. . Lewis D. Is the coronavirus airborne? experts can't agree. Nature. 2020;580(7802):175. doi:10. 1038/d41586-020-00974-w
58. Chia PY, Coleman KK, Tan YK, et al; Singapore 2019 Novel Coronavirus Outbreak Research Team. Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. Nat Commun. 2020;11(1):2800. doi:10.1038
59. Dashraath P, Wong JLJ, Lim MXK, et al. Coronavirus disease 2019 (COVID-19) pandemic, and pregnancy. Am J Obstet Gynecol. 2020;222(6): 521-531. doi:10.1016/j.ajog.2020.03.021
60. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet. 2020;395(10226):809-815. DOI: 10.1016/S0140-6736(20)30360-3
61. Zeng L, Xia S, Yuan W, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China.JAMA Pediatr. Published online March 26, 2020. doi:10.1001/jamapediatrics.2020.0878
62. 2. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. N Engl J Med. 2020; 382(16):1564-1567. doi:10.1056/NEJMc2004973
63. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med. 2020;26(5):672-675. doi:10.1038/s41591- 020-0869-5
64. Bendix A, A day-by-day breakdown of coronavirus symptoms shows how the disease, COVID-19, goes from bad to worse, Business Insider Feb 2020. https://www.businessinsider.in/science/news/a-day-by-day-breakdown-of-coronavirussymptoms-shows-how-the-disease-covid-19-goes-from-badto worse/articles how/74257460.cms
65. Hafeez Abdul, Ahmad Shmmon, Siddiqui Sameera Ali Ahmad Mumtaz, Mishra Shruti "A Review of COVID-19 (Coronavirus Disease-2019) Diagnosis, Treatments and Prevention" DOI: 10.14744/ejmo.2020.90853 EJMO 2020;4(2):116–125
66. 2Revised guidelines for Home Isolation of very mild/pre-symptomatic COVID-19 cases https://www.mohfw.gov.in/pdf/RevisedguidelinesforHomeIsolationofverymildpresymptomaticCOVID19cases10May2020.pdf
67. Barati Fatemeh, Pouresmaieli Mahdi, Ekrami Elena, Asghari Sahar, Ziarani Farzad Ramezani and Mamoudifard Matin "Potential Drugs and Remedies for the Treatment of COVID-19: a Critical Review" Barati et al. Biological Procedures Online (2020) 22:15 https://doi.org/10.1186/s12575-020-00129-1
68. Farooq Saba, Ngaini Zainab "Natural and Synthetic Drugs as Potential Treatment for Coronavirus Disease 2019 (COVID-2019)" Chemistry Africa (2021) 4:1–13 https://doi.org/10.1007/s42250-020-00203-x
69. Bhagat D S, Suryawanshi Meghraj, Suryawanshi Indranil "A Systematic Review of Antiviral Drugs for the Treatment of the COVID-19 Pandemic" Manipal Journal of Pharmaceutical Sciences | September 2020 | Volume 6 | Issue 2
70. http://www.safemedication.com/.
71. Sytar Oksana, Brestic Marian, Hajihashemi Shokoofeh, Skalicky Milan, Kubeš Jan, Lamilla-Tamayo Laura, IbrahimovaUlkar, Ibadullayeva Sayyara and Landi Marco "COVID-19 Prophylaxis Efforts Based on Natural Antiviral Plant Extracts and Their Compounds" Molecules 2021, 26, 727. https://doi.org/10.3390/molecules26030727 https://www.mdpi.com/journal/molecules
72. AK Srivastava, JP Chaurasia, R Khan, C Dhand, S Verma "Role of Medicinal Plants of Traditional Use in Recuperating Devastating COVID-19 Situation" Med Aromat Plants (Los Angeles) 9: 359. 9DOI: 10.35248/2167-0412.20.9.359.

73. Brahmbhatt Ritav Viralbhai "Herbal Medicines in Management and WđĞ|ĞŶΘŽŶ of Coronavirus Disease 2019 (COVID-19)" iMedPub Journals www.imedpub.com DOI: 10.36648/2321-2748. .1.353
74. Shahrajabian Mohamad Hesam, Sun Wenli, Cheng Qi "Traditional Herbal Medicine for the Prevention and Treatment of Cold and Flu in the Autumn of 2020, Overlapped With COVID-19" Natural Product Communications Volume 15(8): 1–10 © The Author(s) 2020 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/1934578X20951431 journals.sagepub.com/home/npx
75. Strizova Zuzana, Smetanova Jitka, Bartunkova Jirina, Milota Tomas "Principles and Challenges in anti-COVID-19 Vaccine Development" Int Arch Allergy Immunol 2021;182:339–349 DOI: 10.1159/000514225
76. Speiser Daniel E., and Bachmann Martin F "COVID-19: Mechanisms of Vaccination and Immunity" Vaccines 2020, 8, 404; doi:10.3390/vaccines8030404 www.mdpi.com/journal/vaccines.