COVID-19: Early Diagnosis, Prophylaxis, Treatment and Pharmacotherapy of Coronavirus

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Abstract: The COVID-19 pandemic is severe infectious disease in recent history. Severe acute respiratory syndrome (SARS) corona is a new emerging viral disease that has affected many countries. Its origins have been traced to a food market in Wuhan, China, in December 2019.In this review study of early diagnosis treatment prophylaxis and various pharmacotherapy has been included. Protection against corona virus by knowing the fact and taking precaution. Generally till date vaccine and medicine on corona virus are under clinical trials.

Keywords: COVID -2019, RT-PCR, SARS-Cov, corona virus, Convalescent plasma.

I. INTRODUCTION

Coronavirus disease (COVID-19) is an infectious disease Coronaviruses is zoonotic this means they first develop in animals before developing in humans. Once the virus develops in people, coronaviruses can be transmitted from person to person through respiratory droplets. The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory manners[1]. In January 2020 a new coronavirus was identified from a cluster of cases in the city of Wuhan, China. By mid-March this virus outbreak was declared a pandemic by the WHO having infected over 150,000 individuals and caused over 5000 fatalities in 123 countries around the world. Doctors are learning new things about this virus every day. So far, we know that COVID-19 may not initially cause any symptoms for some people[1]. The first case of the COVID-19 pandemic in India was reported on 30 January 2020. In India 331K are active case of corona virus and 24915 death reported till date july. You may carry the virus for 2 days or upto 2 weeks before you notice symptoms. Some common symptoms that have been specifically linked to COVID-19 include:

- shortness of breath
- having a cough that gets more severe over time
- a low-grade fever that gradually increases in temperature
- Fatigue. in some people symptoms may severe trouble breathing
- blue lips or face
- persistent pain or pressure in the chest
- confusion
- excessive drowsiness

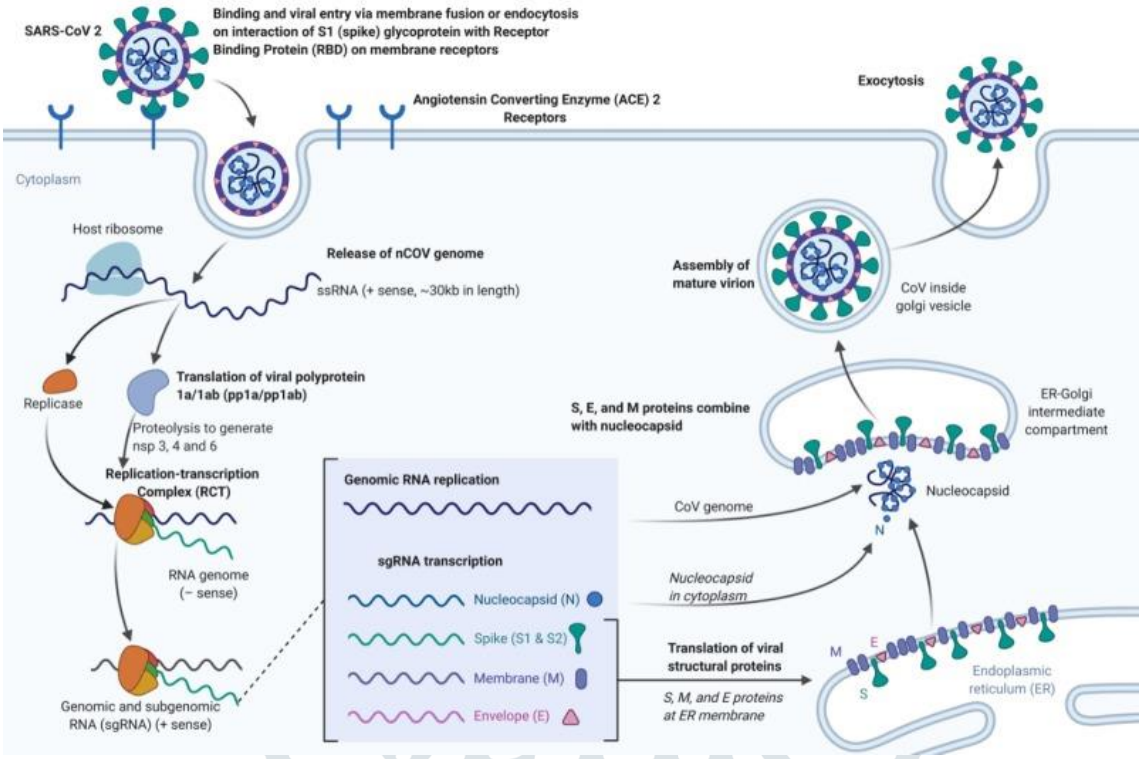

Fig. 1.1: Covid 19, Corona Replication[2]

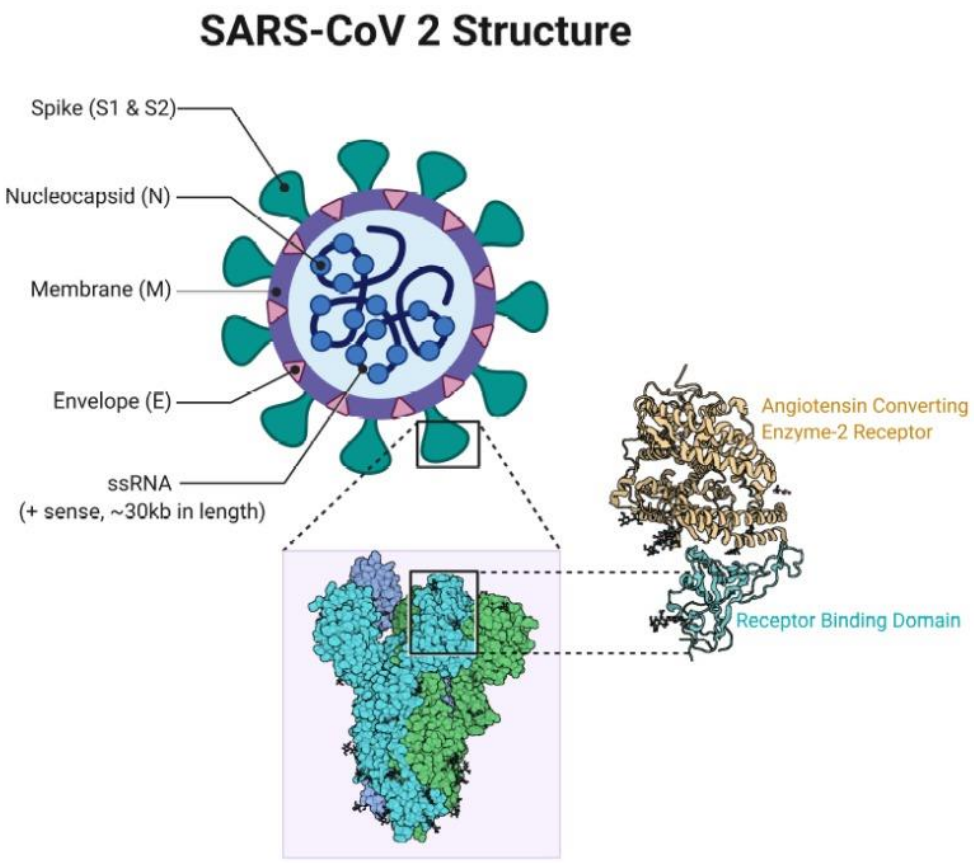

Fig. 1.2: Sars-Cov 2 structure[2]

II. EARLY DIAGNOSIS OF CORONA VIRUS

COVID-19 can be diagnosed similarly to other conditions caused by viral infections: using a blood, saliva, or tissue sample. However, most tests use a cotton swab to retrieve a sample from the inside of your nostrils[3].

RT-PCR assay for detecting SARS-CoV for diagnosis of corona virus. Covid-19 Real Time Reverse Transcription Polymerase Chain Reaction or RT-PCR test is prescribed to detect SARS-CoV-2 or corona virus in respiratory tract through a naso-pharyngeal swab collected from a patient. It detects the virus even if the viral load is less.

Real time RT–PCR is a nuclear-derived method for detecting the presence of specific genetic material in any pathogen, including a virus. Originally, the method used radioactive isotope markers to detect targeted genetic materials, but subsequent refining has led to the replacement of isotopic labelling with special markers, most frequently fluorescent dyes. This technique allows scientists to see the results almost immediately while the process is still ongoing, whereas conventional RT–PCR only provides results at the end of the process. Real time RT–PCR is one of the most widely used laboratory methods for detecting the COVID-19 virus. While many countries have used real time RT–PCR for diagnosing other diseases, such as Ebola virus and Zika virus, many need support in adapting this method for the COVID-19 virus, as well as in increasing their national testing capacities

In order for a virus like the COVID-19 virus to be detected early in the body using real time RT–PCR, scientists need to convert the RNA to DNA. This is a process called 'reverse transcription'. They do this because only DNA can be copied — or amplified — which is a key part of the real time RT–PCR process for detecting viruses.[2, 22]

A sample is collected from the parts of the body where the COVID-19 virus gathers, such as a person's nose or throat. The sample is treated with several chemical solutions that remove substances such as proteins and fats and that extract only the RNA present in the sample. This extracted RNA is a mix of the person's own genetic material and, if present, the virus's RNA. The RNA is reverse transcribed to DNA using a specific enzyme. Scientists then add additional short fragments of DNA that are complementary to specific parts of the transcribed viral DNA. If the virus is present in a sample, these fragments attach themselves to target sections of the viral DNA. Some of the added genetic fragments are used for building DNA strands during amplification, while the others are used for building the DNA and adding marker labels to the strands, which are then used to detect the virus.[22]

The mixture is then placed in an RT–PCR machine. The machine cycles through temperatures that heat and cool the mixture to trigger specific chemical reactions that create new, identical copies of the target sections of viral DNA. The cycle is repeated over and over to continue copying the target sections of viral DNA. Each cycle doubles the previous number: two copies become four, four copies become eight, and so on. A standard real time RT–PCR set-up usually goes through 35 cycles, which means that, by the end of the process, around 35 billion new copies of the sections of viral DNA are created from each strand of the virus present in the sample. As new copies of the viral DNA sections are built, the marker labels attach to the DNA strands and then release a fluorescent dye, which is measured by the machine's computer and presented in real time on the screen. The computer tracks the amount of fluorescence in the sample after each cycle. When a certain level of fluorescence is surpassed, this confirms that the virus is present.[2]

The chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease. The CT is more sensitive and specific. CT imaging generally shows infiltrates, ground glass opacities and sub segmental consolidation. It is also abnormal in asymptomatic patients/ patients with no clinical evidence of lower respiratory tract involvement. In fact, abnormal CT scans have been used to diagnose COVID-19 in suspect cases with negative molecular diagnosis; many of these patients had positive molecular tests on repeat testing[7].

II. PROPHYLAXIS OF CORONA VIRUS

Protect yourself and others around you by knowing the facts and taking appropriate precautions as follows;

- To prevent the spread of COVID-19:
- Clean your hands often. Use soap and water, or an alcohol-based hand rub.

- Maintain a safe distance from anyone who is coughing or sneezing.
- Don't touch your eyes, nose or mouth.
- Cover your nose and mouth with your bent elbow or a tissue when you cough or sneeze.
- Stay home if you feel unwell.
- If you have a fever, cough and difficulty breathing, seek medical attention. Call in advance.
- Follow the directions of your local health authority.
- Avoiding unneeded visits to medical facilities allows healthcare systems to operate more effectively, therefore protecting you and others.

In-vitro studies have shown that chloroquine is effective against several viruses, including severe acute respiratory syndrome coronavirus (SARS-CoV).[5]

Multiple mechanisms of action have been identified for chloroquine that disrupt the early stage of coronavirus replication. Moreover, chloroquine affects immune system activity by mediating an anti-inflammatory response, which might reduce damage due to the exaggerated inflammatory response.[5]

At the time of the SARS epidemic, chloroquine was suggested as a drug that could be used to treat this infection[6]

However, randomised, double-blind, controlled studies in humans to evaluate its efficacy for this use were not done, and the true clinical efficacy of chloroquine in treating coronavirus infections was not established.

The dose used might be the same as that usually administered for malaria treatment given chloroquine inhibited SARS-CoV replication at a 50% effective concentration of 8·8 μmol/L. The half-maximal inhibitory concentration (IC_{50}) of chloroquine inhibition of SARS-CoV replication in Vero E6 cells, 8·8 μmol/L, is substantially lower than the plasma concentrations that are reached in humans when the drug is prescribed to treat malaria at a dose of 25 mg/kg over 3 days.[5]

For long-term prophylaxis, even lower doses could be used. Doses of 3·6 mg/kg, similar to those generally prescribed to treat rheumatoid arthritis, lead to plasma concentrations of 1–3 μmol/L—ie, the same concentration range as the IC_{50} for SARS-CoV inhibition.[5]

The national task force for covid 2019 is constituted by medical council of medical research recommends the use of hydroxychloroquine for prophylaxis of sarscov-2 infection in India.

III. TREATMENT OF CORONA VIRUS

To date, there are no specific vaccines or medicines for COVID-19.

Self-care

Stay in a separate room from other family members, and use a dedicated bathroom if possible. Clean and disinfect frequently touched surfaces. you wear a cloth face mask that covers your mouth and nose. When worn correctly, and by large percentages of the public, these masks can help to slow the spread of SARS-CoV-2. That's because they can block the respiratory droplets of people who may be asymptomatic or people who have the virus but have gone undiagnosed.

There are some types of treatment used for these illnesses include:

- Antiviral or retroviral medications
- Breathing support, such as mechanical ventilation
- Steroids to reduce lung swelling
- Blood plasma transfusions

Special precautions are necessary during intubation of covid 19 . The procedure should be executed by an expert operator who uses personal protective equipment (PPE) such as FFP3 or N95 mask, protective goggles, disposable gown long sleeve raincoat, disposable double socks, and gloves. If possible, rapid sequence intubation (RSI) should be performed. Pre oxygenation

(100% O_2 for 5 minutes) should be performed via the continuous positive airway pressure (CPAP) method. Heat and moisture exchanger (HME) must be positioned between the mask and the circuit of the fan or between the mask and the ventilation balloon

3.1. PHARMACOTHERAPY FOR COVID 19

1. Convalescent plasma treatment

It involves injecting COVID 19 patient with convalescent sera of people who recovered from the infection. The patient cured of disease will have antibodies that drive coronavirus away. We can collect convalescent sera by two method using blood withdrawal followed by centrifuge technique. And another method is collect 180 ml to 220 ml of convalescent sera and store in -60 degree C upto one year and using apheresis machine or cell separator machine, also even collect 600 ml of convalescent sera at one time and safely store foe one year. The process of removal of abnormal substance from circulation which are either present in plasma or a tightly bound plasma proteins known as therapeutics plasma exchange. In covid-19 patients their plasma will continue enormous inflammatory mediators which cause severe lung injury. IN COVID-19 severe cases, a combination of therapeutics plasma exchange technique using convalescent sera will reduce the cytokine storm which will help recovery Figure3.1.1. shows Schematic representation of convalescent plasma components and its mechanisms of action. **A.** Main convalescent plasma components. **B.** Antiviral effects of NAbs. IgG and IgM are the main isotypes, although IgA may be also important, particularly in mucosal viral infections. Other non-NAbs may exert a protective effect. The humoral immune response is mainly directed towards spike (S) protein. **C.** Anti-inflammatory effects of CP include network of autoantibodies and control of an overactive immune system (*i.e.*, cytokine storm, Th1/Th17 ratio, complement activation and regulation of a hypercoagulable state) N: Nucleoprotein; M: Membrane; E: Envelope[9,10,11]

Thus convalescent sera treatment will be more effective therapy for COVID 19

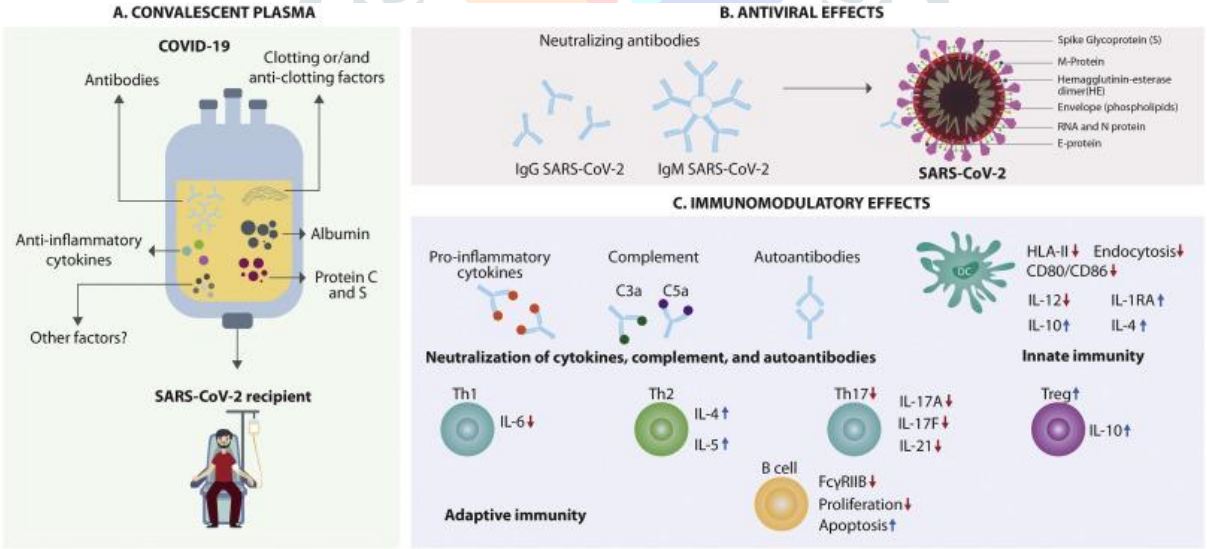

Fig. 3.1.1: convalescent plasma in covid 19: mechanism of action

2. Ribavirin

It's potential MOA is that it inhibits the replication of RNA and DNA of viruses. Based on sequencing analysis, modeling, and molecular docking, ribavirin can tightly bind to *SARS–CoV-2* RNA-dependent RNA polymerase, a crucial enzyme in the life cycle of coronavirus. Ribavirin has been recommended in combination with interferon or **Lopinavir/ritonavir** at a dose of 500 mg intravenous given twice or three times daily, not to exceed 10 days.[12]

3. **Remdesivir**

It is a broad-spectrum antiviral medication that inhibits RNA synthesis developed by the American biopharmaceutical company Gilead Sciences.[11] Remdesivir was originally developed to treat Ebola virus disease and Marburg virus disease but was ineffective for these viral infections. The proposed dosing regimen for remdesivir in clinical trials is 200 mg as a single IV dose on day 1, followed by 100 mg once daily for a total duration of 5 to 10 days. Data and results reported from a large, worldwide clinical investigation comparing remdesivir and placebo indicate it may be the first clear signal that a drug can effectively be used to treat Covid-19.[11] These early results from a large clinical trial sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) appear to position remdesivir as the standard therapy for hospitalized COVID-19 patients going forward[13,14.]

4. Intravenous immunoglobulin's (IVIG)

It offers potentially effective therapy in severe cases of COVID-19 through their role in immunomodulation. The entry of SARS-CoV-2 into host cells is mediated by the transmembrane spike (S) glycoprotein that binds to the angiotensin converting enzyme 2 (ACE2) receptor, which is highly expressed on the apical surface of many cell types, including airway epithelial cells. The S protein forms a homotrimer that protrudes from the viral surface. Receptor binding is mediated by the S_1 subunit through the receptor binding domain (RBD). After binding to the ACE2 receptor, proteolytic activation of the S_2 subunit mediates the fusion between the viral and the cellular membranes thus role of S glycoprotein in cellular infection, antibodies that bind to S_1 and S_2 can prevent infection figure3.1.2. Shows (a) Neutralizing antibodies prevent SARS-CoV2 spike protein from attaching to the ACE2 receptor, inhibiting viral entry into the cell. (b) Immune complexes consisting of viral antigens and anti-viral sub-neutralizing antibodies can activate Fcγ receptors on innate immune cells (e.g. macrophages) in the lung, triggering an exaggerated inflammatory response leading to acute lung injury via antibody dependent enhancement (ADE). Additionally, antibody-bound virus can be internalized through Fcγ receptors, enhancing viral replication. (c) Proposed mechanisms whereby IVIG exerts anti-inflammatory action include saturation of Fcγ receptor binding, anti-idiotypic binding to anti-viral antibodies, and binding of proinflammatory cytokines.[15,16,17]

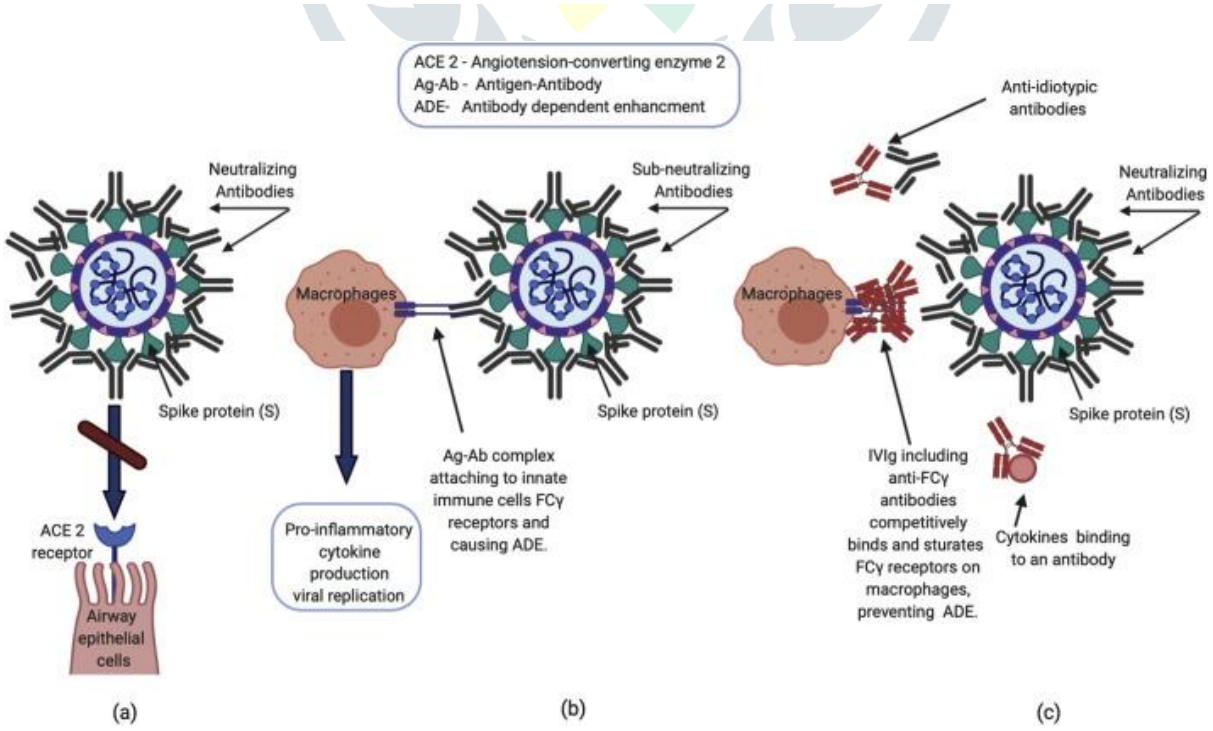

Fig.3.1.2. Mechanisms of neutralizing antibodies and IVIG in COVID-19 infection

4. Famotidine

famotidine as a COVID-19 treatment stems from observations in China that patients who were taking famotidine who were infected with COVID-19 had better outcomes.[18] In a retrospective U.S. study (n = 1,620), famotidine use (10 to 40 mg/day; n = 84) within 24 hours of admission was associated with reduced risk of death or intubation in **hospitalized** COVID-19 patients[19].

5. Hydroxychloroquine

Randomized study in hospitalized patients testing positive for SARS-CoV-2.[20] Six of 26 hydroxychloroquine patients were lost to follow-up: one due to death, three due to intensive care admission, one due to side effects (nausea), and one who left the hospital. Viral clearance at day six was 70% in the 20 remaining hydroxychloroquine patients vs 12.5% of the control patients (n = 16).[20] Six treated patients also received azithromycin 500 mg on day one, then 250 mg on days two through five to prevent bacterial infection.[20] In the combination group, viral clearance was 100% at day six vs 57.1% in the hydroxychloroquine-alone group. In china study proved that Thirty percent of hydroxychloroquine patients had adverse effects.

In US also Mortality was higher in patients who received hydroxychloroquine alone vs no hydroxychloroquine.[21]

Other therapies

Among other therapeutic strategies, systemic corticosteroids for the treatment of viral pneumonia or acute respiratory distress syndrome (ARDS) are not recommended. Moreover, unselective or inappropriate administration of antibiotics should be avoided, although some centres recommend it. Although no antiviral treatments have been approved, several approaches have been proposed such as lopinavir/ritonavir (400/100 mg every 12 hours), chloroquine (500 mg every 12 hours), and hydroxychloroquine (200 mg every 12 hours). Alpha-interferon (e.g., 5 million units by aerosol inhalation twice per day) is also used[8].

IV. CONCLUSION

This article provides information about corona virus their symptoms diagnosis prophylaxis and treatment.Till date corona virus patient is increasing day by day. research is going on to develop vaccine on covid -19

V. REFERENCE

1. WHO. Clinical management of severe acute respiratory infection when novel coronavirus [nCoV] infection is suspected
2. Marco Cascella; Michael Rajnik; Arturo Cuomo; Scott C. Dulebohn; Raffaela Di Napoli. Features, Evaluation and Treatment Coronavirus (COVID-19)
3. Drosten C, Gunther S, Preiser W, van der Werf S, Brodt HR, Becker S, Rabenau H, et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. New Engl J Med 2003;348:1967-76
4. Peiris JS, Lai ST, Poon LL, Guan Y, Yam LY, Lim W, Nicholls J, et al. Coronavirus as a possible cause of severe acute respiratory syndrome. Lancet 2003a;361:1319-25
5. Savarino ABoelaert JR Cassone A Majori G Cauda R Effects of chloroquine on viral infections: an old drug against today's diseases. *Lancet Infect Dis.* 2003; 3: 722-727
6. Al-Bari MAATargeting endosomal acidification by chloroquine analogs as a promising strategy for the treatment of emerging viral diseases. *Pharmacol Res Perspect.* 2017
7. Huang P, Liu T, Huang L, et al. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology. 2020.
8. Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. Lancet. 2020;395:473–5

9. Ministry of Health and Family Welfare. Government of India [Internet]. COVID-19 INDIA
10. Bloch E.M., Shoham S., Casadevall A. Deployment of convalescent plasma for the prevention and treatment of COVID-19. J Clin Invest. 2020 doi: 10.1172/JCI138745.
11. Shen C., Wang Z., Zhao F. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. J Am Med Assoc. 2020 doi: 10.1001/jama.2020.4783
12. COVID-19 Pharmacotherapy Treatment Guidance March 23, 2020. Livonia, Michigan:Trinity health Available at https://www.trinity-health.org/workfiles/covid-19/covid-treatment-guide.pdf. Accessed May 15, 2020
13. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res. 2020;30(3):269-271.
14. Healy M. Coronavirus treatment: Remdesivir clinical trial success may be a turning point. Los Angeles Times for The Associated Press. Apr 30, 2020
15. Long Q.X., Liu B.Z., Deng H.J., Wu G.C., Deng K., Chen Y.K. Antibody responses to SARS-CoV-2 in patients with COVID-19. Nat. Med. 2020 doi: 10.1038/s41591-020-0897-1
16. Schwab I., Nimmerjahn F. Intravenous immunoglobulin therapy: how does IgG modulate the immune system? Nat. Rev. Immunol. 2013;13(3):176–189.
17. Cao W., Liu X., Bai T., Fan H., Hong K., Song H. High-dose intravenous immunoglobulin as a therapeutic option for deteriorating patients with coronavirus disease 2019. Open Forum Infect Dis. 2020;7(3):ofaa102
18. Rogosnitzky M, Berkowitz E, Jadad AR. Delivering benefits at speed through real-world repurposing of off-patent drugs: the COVID-19 pandemic as a case point. *JMIR Public Health Surveill* .
19. Freedberg DE, Conigliaro J, Wang TC, et al. Famotidine use is associated with improved clinical outcomes in hospitalized COVID-19 patients: a propensity score matched retrospective cohort study. *Gastroenterology* 2020 May 22.
20. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label, non-randomized clinical trial. *Int J Antimicrob Agents* 2020 Mar 20:105949.
21. Magagnoli J, Narendran S, Pereira F, et al. Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19. medRxiv. 2020.04.16.20065920.
22. https://www.iaea.org/newscenter/news/how-is-the-covid-19-virus-detected-using-real-time-rt-pcr