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Early Diagnosis, Prophylaxis, Pathophysiology and Current Research on COVID-19

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ABSTRACT

In December 2019, the outbreak of the novel Corona Virus Disease (COVID-19) in China spread worldwide, becoming an emergency of major international concern. The SARS-CoV-2 infection causes a severe respiratory illness similar to severe acute respiratory syndrome coronavirus. Human-to-human transmission *via* droplets, contaminated hands or surfaces has been described, with incubation times of 2-14 days. This paper reviews the literature on all available information about the diagnosis, prophylaxis, pathophysiology and Current research on COVID-19. Current research on COVID-19 including antimalarial drugs (chloroquine and hydroxychloroquine), antiviral drugs (Ribavirin, remdesivir), antibodies, vaccines & convalescent plasma transfusion, are discussed in this article.

INTRODUCTION: -

The current worldwide outbreak of Corona Virus Disease (COVID-19), which originated from Wuhan, China and has spread all over the world, including India, Pakistan, America & Australia. COVID-19 which causes severe respiratory tract infections in humans, World Health Organization (WHO) is declared that the COVID-19 has become a global concern. The evidence indicates that Covid-19 spread to humans *via* transmission from animals in the Huanan Seafood Wholesale Market, China, and the Analysis says that the COVID-19 is a new virus of Coronaviridae family (1, 2).

The symptoms of COVID-19 are fever, fatigue, sore throat, & cough. The outbreak of COVID-19 brings about 17,106, 007confirmed cases and 6,68,910 deaths worldwide on 31st July 2020. This article aims to describe the diagnosis, prophylaxis, pathophysiology, and Current research of COVID-19.

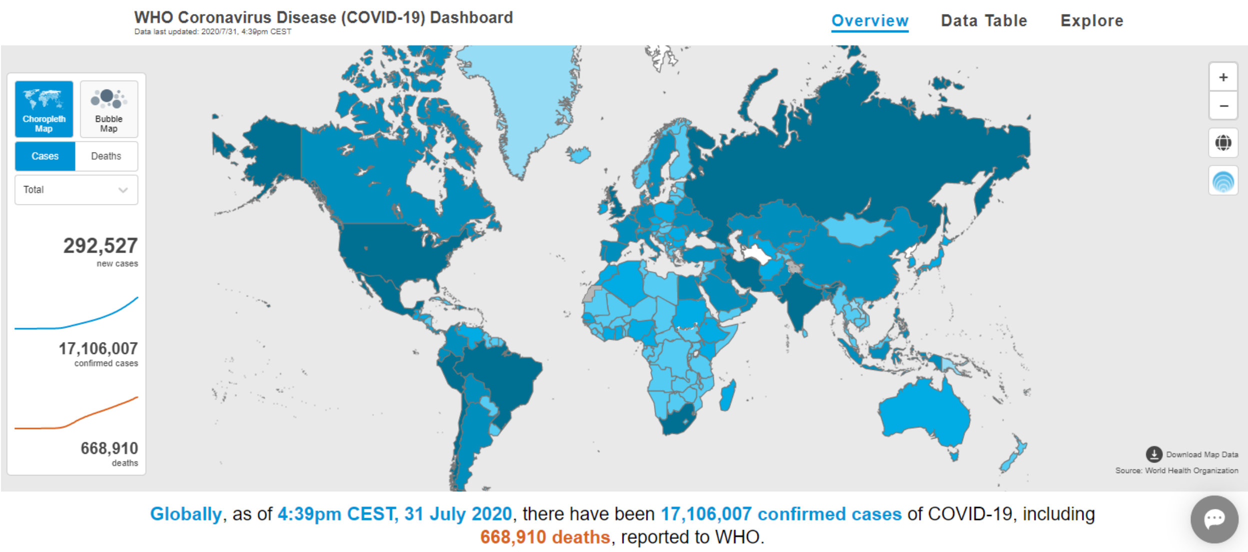

Figure No. 1: Confirmed COVID-19 cases all over the world. (3)

DIAGNOSIS: -

Current diagnostic tests for coronavirus include (Real Time-Reverse Transcription Polymerase Chain r\Reaction (RT-PCR) and Reverse Transcription Loop-Mediated Isothermal Amplification (RT-LAMP) (4, 5). RT-LAMP has a similar sensitivity to rRT-PCR and is used to detect MERS-COVID-19 (6, 7). According to the diagnostic criteria established by the China National Health Commission (CNHC), laboratory examinations, including oropharyngeal and nasopharyngeal swab tests, have become a standard assessment for diagnosis of COVID-19 infection (8). Three RT-PCR assays developed, which target the RNA-dependent RNA polymerase, spike, and nucleocapsid genes of SARS-COVID-2. Among the three novel assays, the COVID-19-RdRp (RNA Dependent RNA Polymerase) had the lowest limit of detection *in vitro*; highly sensitive and definitive assays may help to improve the laboratory diagnosis of COVID-19 (9). The RdRp gene assay combined with the one-step RT-PCR system was less sensitive than the SARS-CoV E gene assay (10).

Now the laboratory test is based on antibody and antigen detection and it is time-consuming. The patients suffering from fever, fatigue, sore throat, and coughing. COVID-19 infection should be diagnosed with typical chest Computerized Tomography (CT) (11). Chest CT scans can be used to check the severity of COVID- 19. COVID-19 also signifies with chest CT imaging abnormalities in asymptomatic patients. The diagnostic principle needs to expand to chest CT imaging for the accurate & scientific detection of the COVID-19 from laboratory examination.

PROPHYLAXIS: -

There is not a single treatment currently approved for COVID-19, and no cure for an infection, although treatments, antibodies and vaccines are currently under study. Instead of curing the disease, the treatment focuses on managing the symptoms of Covid-19. Other coronaviruses like SARS and MERS are also treated by managing symptoms. In some cases, experimental treatments are tested to see their effectiveness against Covid-19.

Examples of the therapy for the COVID-19 disease include.

- Antiviral drugs
- Antimalarial drugs
- Steroids
- Blood plasma transfusions
- Breathing support, such as mechanical ventilation

PATHOPHYSIOLOGY: -

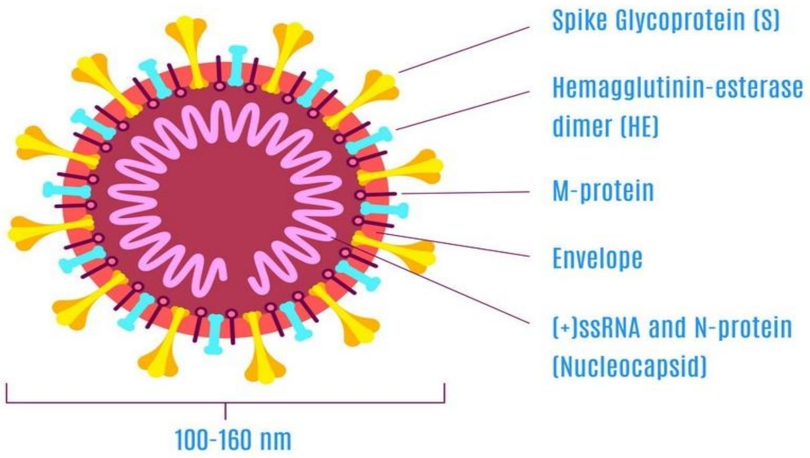

Figure No. 2: **Structure of COVID-19.**

The COVID-19 structure has various parts. The genetic encoding lies inside the virus. The virus attacks the human cells and uses the human body to develop further genetic material for its survival. The genetic material encapsulates by a protein known as the viral envelope. The S and HE proteins 12 are situated on the surface of the virion. (12). The novel SARS-COVID-2 structure is a mutated form. The replication cycle of SARS-COVID-2 is as follows.

Replication Cycle:

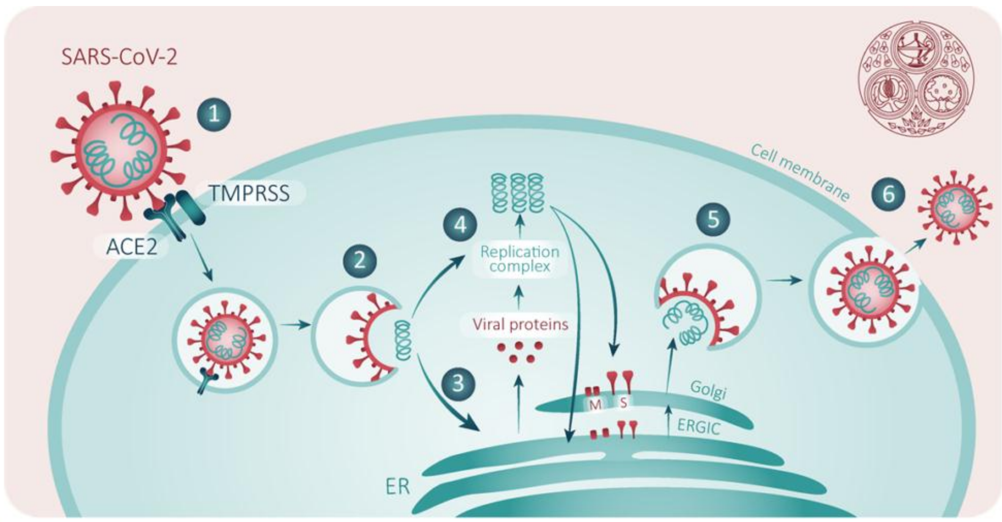

Figure No. 3: **Replication Cycle Of SARS-COVID-2 In Humans.** (13)

1) COVID-19 virus uses large S glycoprotein to get the entry into the human cells. On the cell membrane, they attach to the receptor. The exact mechanism is unknown. The process is known as endocytosis in which the human cell ingests the virus (14).

2) The endosome opens to expose the virus's genetic material, a single-stranded RNA, Once inside the cytoplasm.

3) To replicate the RNA and N protein virus hijacks the cell's machinery and forms its M protein outer layer and the all essential S protein.

4) To make more RNA, some of these proteins form a replication complex.

5) In the Golgi, the Proteins and RNA assembled into a new virion.

6) The virus is drifting out of the cell by the Golgi bodies in a process known as exocytosis so that it can infect other cells. During, the stress of viral production on the endoplasmic reticulum eventually leads to cell death (15).

CURRENT RESEARCH: -

1. Chloroquine and hydroxychloroquine: -

Chloroquine and hydroxychloroquine are an antimalarial drug which has been shown antiviral activity against COVID-19 (16-18). Chloroquine is well-known to block infection by increasing endosomal P^H required for virus or cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-COVID (19). For the prevention and treatment of COVID-19 pneumonia, chloroquine was recommended as a possible treatment (20, 21). Under the EUA issued on March 28th, 2020, the Food and Drug Administration (FDA) has allowed these drugs to be provided to certain hospitalized patients. the fewer worry about the drug-drug interactions of hydroxychloroquine as it is an analog of chloroquine (22). *In vitro,* hydroxychloroquine reported having antiviral activity against SARS-COVID-2 In the previous outbreak of SARS-COVID (23). Both drugs possess immunomodulatory responses (24, 25). Therefore, several clinical studies launched by different countries and universities (26). If the clinical trials will successfully pass then the chloroquine and hydroxychloroquine can use in the prevention and treatment of SARS-COVID-19 (27).

2. Antiviral drugs: -

From the Randomized Control Trials (RTCs) currently, there is no evidence for recommending any specific treatment for confirmed COVID-19 patients. *In vitro* and animal studies, lopinavir inhibits the protease activity of coronavirus. Based on the experience gathered from the SARS and MERS outbreaks, the protease inhibitor is an effective treatment and can use as a possible treatment (28). **Remdesivir** is an antiviral agent, which was design for the Ebola virus disease (29). Remdesivir shows antiviral activity against several RNA viruses and it may compete for RdRp (30). Remdesivir has been showing that it has a superior antiviral activity to lopinavir *in vitro.* (31). In the united states, remdesivir was used to the treat first case of COVID-19 infection; the patient's clinical condition improved after one day of treatment of remdesivir (32). In India, remdesivir are using to treat COVID-19 infection after such promising results of USA trials, remdesivir is used as a possible treatment while currently, no treatment is available. Cipla and hetero labs, The Indian pharmaceutical companies, gained approval for the generic version of remdesivir to sell it in the Indian market.

3. Antibodies: -

The development of therapeutic antibodies and vaccines which have affinity against COVID-19 has an important indication. In the SARS-COVID & SARS-COVID-2 consider the relatively high existence of the receptor-binding domain. In the continuing investigation for antibodies that could fight against SARS-COVID-2, researchers are particularly studying those individuals who already overcome the COVID-19 infection. They have two expectations, both of which have looked at the antibodies developed by a recovered patient.

Antibody taken from the SARS-COVID, called S309 & CR3022 taken from a recovered individual from SARS-COVID-2, has been shown in the lab to overcome SARS-COVID-2. Both antibodies' taken from the individual recovered from the SARS. Human monoclonal antibody CR3022 binds potently with the COVID-19 receptor-binding domain, successfully (33). For the prevention and treatment of COVID-19, alone or in combination with other neutralizing antibodies, CR3022 may be a potential therapeutic aspirant (34). Scientists Israel, Netherlands claim progress in COVID-19 antibody trials, so many trails are ongoing all over the world.

4. Vaccine: -

Currently, no vaccine developed which fight against the COVID-19 infection. SARS-COVID-2 s protein structure has revealed, this will help in the rapid development and evolution of medical treatment or vaccine development (35). The discovery provides the basis for more studies that will enhance vaccination strategies to overcome COVID-19. The development of vaccines is a long process in which so many clinical trials are performed & right now, no vaccine is available. Overall, the world So many clinical trials are ongoing, recently the Oxford University of America announced that the development of a vaccine has entered in Phase III clinical trial we hope that the vaccine against COVID-19 comes earlier as possible.

5. Convalescent plasma transfusion: -

COVID-19 is spreading all over the world rapidly, no treatment is available to overcome COVID-19 infection, not therapy is available for those who infected. Convalescent Plasma Therapy (CPT) refers to convalescent plasma which is collected from the patient after recovery from the infection and the development of antibodies. CPT may offer a short-term strategy that gives prompt immunity to the susceptible patient as an antibody administration through it. Including other outbreaks of COVID-19 infection (ex: MERS, SARS-1) various examples, where CPT has been used successfully as a treatment of infectious disease.

In India convalescent plasma therapy currently using to treat COVID-19 infected patients has delivered auspicious results, a top doctor at the facility said. In many viral illnesses such as rabies, polio, Ebola, hepatitis, and influenza convalescent plasma therapy has been used. The faster viral clearance was observed following convalescent plasma therapy when it used in MERS and SARS-1 outbreaks. Recently, In Maharashtra, India Platina project has launched, claimed to be the world's largest, trial-cum-treatment center for COVID-19 patients.

CONCLUSION: -

The origin of the Coronavirus is under investigation. Coronavirus belongs to the family Coronaviridae and classified in the β-coronavirus 2b lineage. Coronavirus can be transmitted from animals to humans and also between humans. The spread of coronavirus can be reduced by following some preventive measures. Wearing the mask, maintaining distance and washing hands can reduce the risk of infection.

The identification of the causative agent is important to select the appropriate treatment. To detect the causative agent in acute respiratory infection RT-PCR is commonly used by using throat swab. Also, the CT-SCAN is used to the screening of suspected cases and diagnosis of coronavirus.

The most common symptoms are fever, expectoration, cough, nausea, diarrhea, fatigue, headache and hemoptysis (36). All patients with COVID-19 pneumonia received antiviral drugs therapy, an antibacterial agent. Clinical trials are underway to investigate the efficacy of the vaccine and antiviral drugs. It is necessary to develop the vaccine and drug against COVID-19 infection as soon as possible.

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