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### Role of Treatment Approaches in the Treatment of Covid 19: A Review

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Abstract: The need that everyone weara mask, regular hand-washing and hand-sanitizing, remote work, social isolation, avoiding crowds, and the cancellation of public events have all been used to limit the spread of the infection and minimize death. To visualize patterns before and after the introduction of the vaccination, rates of reported COVID-19 cases, ED visits, hospitalizations, and fatalities are presented for September 6, 2020–May 1, 2021. At the Welcome Sanger Institute, where sequencing is being done, several samples have been analyzed. According to Public Health England's criteria of variations based on mutations, whole-genome sequences are assigned. SARS-CoV-2 is made up of four main structural glycoproteins: the spike (S), membrane (M), envelope (E), and nucleocapsid (N). The M, E, and N proteins are crucial for viral particle assembly and release, whereas the S protein is in charge of viral binding and entry into host cells. Both hydroxychloroquine and chloroquine affect viral replication in addition to suppressing cytokine production. It's a good idea to have a backup plan in case the backup plan doesn't work.

Keywords: SARS-CoV-2, social isolation, hydroxychloroquine, nucleocapsid.

### I. INTRODUCTION

The coronavirus disease (COVID-19), a pandemic illness, was first identified in December 2019 in the Chinese city of Wuhan. Since then, it has spread quickly throughout the globe.SARS-CoV-2 is a betacoronavirus similar to severe acute respiratory syndrome (SARS) virus and utilizes the same receptor as the angiotensin-converting enzyme 2 for cell entry. [1] SARS-CoV2 fatal outcomes are linked to an overactive immune reaction. There are numerous instances where the adult respiratory distress syndrome (ARDS) brought on by SARS illnesses is significantly influenced by inflammatory cytokines. In Wuhan, China, in December 2019, a brand-new coronavirus strain appeared.

This new coronavirus was designated a "Public Health Emergency of International Concern (PHEIC)" by the World Health Organization (WHO) on January 31, 2020. Since the outbreak of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) began, necessary steps have been taken to stop the spread of the virus and reduce mortality, including the requirement that everyone wear a mask, consistent hand-washing and hand-sanitizing, remote work, social withdrawal, avoiding crowds, and the cancellation of public events. China was the first nation to adopt a regional lockdown of cities in Hubei province as a control measure.

With a population of over 14 million, Wuhan is the largest metropolis in Hubei province and was placed under a 76-day lockdown. Later, identical lockdowns were used in Spain, Russia, India, the Philippines, Italy (provinces of Lombardy and Veneto), Turkey, and other nations. Studies have revealed that certain tactics have been successful in halting the disease's growth and lowering incidence and mortality rates.[2]After the Pfizer-BioNTech COVID-19 vaccine received Emergency Use Authorization from the Food and Drug Administration, the United States launched a national vaccination programme on December 14, 2020. The Advisory Committee on Immunization Practices (ACIP) advised giving priority to long-term care facility residents and health care employees in the early stages of the vaccination programme, then essential workers and people at risk for serious illness, including adults over 65. CDC examined the COVID-19 vaccination age spread between December 14, 2020, and May 1, 2021. Rates of reported COVID-19 cases, ED visits, hospitalisations, and deaths by age group are given for September 6, 2020–May 1, 2021, to help visualise trends before and after the introduction of the vaccine. [3] The CDC received daily information from a variety of sources about COVID-19 vaccine doses given in the United States, including partial and complete vaccination. Daily COVID-19 case data, as reported by the jurisdictional health department, were acquired from the CDC's case-based surveillance system.[4]

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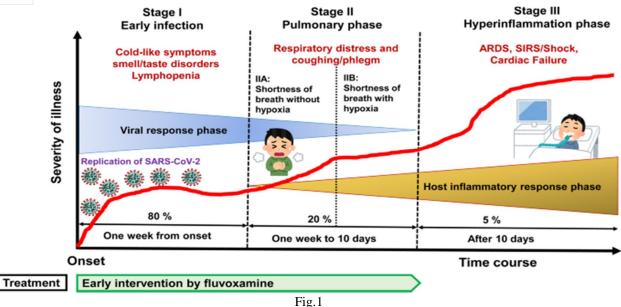
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BACKGROUND

II.

The Berlin definition for the diagnosis of ARDS was fulfilled by all patients, who were all older than 18 years of age.8 This research included all COVID-19-induced ARDS patients who met these requirements. Exclusion factors included a history of serious chronic respiratory disease, HIV infection, neoplastic diseases, inflammatory diseases, active bleeding, chronic renal and hepatic impairment, recent myocardial infraction, or coronary artery bypass transplant.[5]

### A. Identifying the Variation

The delta and alpha variations were located using whole-genome sequencing. [6] Approximately 10% of all positive samples were sequenced in February 2021, and that number rose to about 60% in May 2021. A large number of samples have been tested at the Welcome Sanger Institute, where sequencing is being done. Whole-genome sequences are allocated to Public Health England definitions of variants based on mutations.[7]

### B. Variant of Covid

The three groups of SARS-CoV-2 variants have been established by the USA government's interagency. [8] The Centers for Disease Control and Prevention (CDC) will update the variant strains in the various classes as necessary because the variant status may occasionally be escalated or deescalated based on scientific proof. [9] The classes are: variant of interest, variant of worry, and variant of significant consequence, according to the report from April 21, 2021. [10]

### C. Variant of Interest

This class contains variations with particular markers linked to alterations in receptor binding, decreased antibody neutralization against prior infection or vaccination, decreased treatment efficacy, possible diagnostic impact, or anticipated rise in disease severity transmissibility. In order to assess the disease's severity, risk of reinfection, and immunity to vaccination, this class also needs increased sequence surveillance, laboratory characterization, and epidemiological analysis. [11]

### D. Variant of Concern

This group of variants includes those that have shown high disease transmissibility, increased disease severity, such as hospitalisations and fatalities, a striking decline in antibody neutralisation, reduced treatment efficacy, and ineffective diagnostic detection. Additionally, this class necessitates greater testing kit development, vaccine efficacy research, and treatment efficacy testing to control spread. The USA currently lists the following types as being of concern: B.1.1.7, P.1, B.1.351, B.1.427, and B.1.429. The variants in this class, like the variant of interest class, share the D614G mutation (an aspartic acid to glycine shift at the amino acid position), which distributes more quickly than variants without the mutation. [12]



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### E. Variant of High Consequence

This class of variants includes those that have evidence indicating that, in comparison to previously circulating variants, preventive and medical measures are considerably less effective. This class doesn't have any variations.[13]

### III. PATHOPHYSIOLOGY OF COVID 19

Due to differences in the underlying comorbidities of the populations under study, as well as potential variations in the practise and methodologies of AKI diagnosis and reporting, determining the actual epidemiology of COVID-19 AKI is challenging. [14] In patients with COVID-19, a higher chance of AKI has repeatedly been linked to age, a history of hypertension, and diabetes mellitus. In 3,099 critically ill patients with COVID-19, chronic kidney disease (CKD) was found to be the most significant risk factor for AKI needing KRT. [16] CKD is a well-known risk factor for AKI in hospitalized patients. Indeed, a number of epidemiological studies have unequivocally shown that CKD is an independent risk factor for poorer outcomes in COVID-19 that is both pertinent and significant. [15]A case-control analysis conducted in 2021 that compared COVID-19 patients with the Danish general population, which was matched for age, gender, and comorbidities, found a link between lower estimated glomerular filtration rate (eGFR) and the rate of COVID-19 being diagnosed at the hospital and death. According to epidemiological research, low GFR and RFR levels may also promote the growth of AKI. In a Wuhan, China investigation of 4,020 consecutively hospitalized COVID-19 patients, 285 (7.09%) were found to have AKI. A higher chance of in-hospital mortality was linked to both early and late forms of AKI (i.e., AKI at presentation and AKI developing after presentation). A higher chance of late AKI was also linked to CKD, advanced age, and levels of inflammatory biomarkers.[16] The viral infiltration through its intended host cell receptors is the first stage of COVID-19 pathogenesis. In-depth descriptions of SARS-CoV-2 viral entrance can be found elsewhere (138). The four major structural glycoproteins that make up SARS-CoV-2 are the spike (S), membrane (M), envelope (E), and nucleocapsid (N). The S protein is in charge of viral binding and entrance into host cells, whereas the M, E, and N proteins are essential for viral particle assembly and release. Large respiratory droplets are the primary means of transmission for SARS-CoV-2, which also directly infects cells in the upper and lower respiratory system, particularly nasal ciliated and alveolar epithelial cell. [17]We gathered the medical data of 55 COVID-19 patients for this retrospective study's analysis. According to the coordinated plans of the local government, all of these patients were brought to Unit Z6 (a total of 64 beds) in the Cancer center of Wuhan Union Hospital on February 15, 2020 (from 13:00 to 23:00, Beijing time). Clinical traits, laboratory parameters, therapeutic modalities, and clinical results are all documented in medical documents[18].

### A. Progress in Treatment of Covid 19

The current therapy philosophies for SARS-CoV-2 infection cases focus primarily on internal organ support and protection, disease treatment at the underlying level, symptom relief, and averting complications. Patient needs include strengthening supportive treatment, giving attention to the water-electrolyte balance and preserving homeostasis. [19]

### B. Transfusion-related Treatments used in Patients with COVID-19

A multidisciplinary, comprehensive treatment strategy should be used to take into consideration the various pathogenic mechanisms because the SARS-CoV-2 pathogenic mechanism is complex. [20] Patients who survive from SARS-CoV-2 infection have stronger immune systems because the virus can trigger adaptive humoral and cellular immune responses. Little is known about the immune system's state following 2019-nCoV infection because the epidemic is still continuing strong. [21]

### C. Convalescent Plasma Therapy

There isn't presently a specific medication that works well to treat COVID-19. Clinical trials are presently being conducted on some medications that are thought to have effects that inhibit the growth of viruses. Patients who recovered from COVID-19 have convalescent plasma that includes particular antibodies that are efficient at treating SARS-CoV-2 infection. [22]

### D. Plasmapheresis

In plasmapheresis, the plasma is separated from the patient's whole blood using a blood component divider.

### E. Mesenchymal Stem cell Therapy

Mesenchymal stem cells inhibit excessive immune responses, prevent unchecked mass production of cytokines or inflammatory substances, and lessen immune-related harm to tissues and organs.



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Chloroquine, nafamostate, griffithsine, among others, can block endosome maturation, while hydroxychloroquine, apilimod, colchicine, and vinorelbine can prevent the release of viral genomes, as well as virus replication, transcription, and protein translation. (e.g., bananin, 5-hydroxychromone, remdesivir, favipiravir, ribavirin). Nucleotide analog Remdesivir, a newly developed novel antiviral drug, has demonstrated strong efficacy in treating Marburg and Ebola virus infections. [23]

### IV. FAVIPIRAVIR

Favipiravir is an antiviral medication of the pyrazine family that was primarily utilized in Japan to treat influenza. It functions by preventing the RNA-dependent RNA polymerase (RdRp) enzymes, a protein essential for the transcription and replication of virus genomes, from doing their job. [24] A small molecule medication of the aminoquinoline family called chloroquine is used to treat malaria. This drug possibly can have a broad spectrum of antiviral action on all steps of the viral entry and replication [25]

### A. Mechanism of Action of Favipiravir

Many researchers are working to understand how well-known antiviral medications work against COVID-19 in order to create an oral therapy or vaccines. [26] Favipiravir can have an effective concentration against the SARS-CoV-2 infection within a safe therapeutic dose, according to reports of in-vitro research.[27]

Within the tissue, the molecule undergoes phosphoribosylation to favipiravir-RTP, which is the active version of this drug. It works to combat viruses using the following mechanisms:

- a). The RNA-dependent RNA-polymerase (RdRp) enzyme uses this molecule as a substrate; however, the enzyme misinterprets it for a purine nucleotide, which inhibits its activity and stops the production of viral proteins.
- b)It is integrated into the viral RNA strand and prevents growth.5 The wide range of activity of this medication is explained by its mode of action and the persistence of the catalytic domain of the RdRp enzyme across different RNA viruses.
- c). Recent research has shown that the virucidal drug favipiravir causes lethal mutagenesis in vitro during influenza virus infection.6 It is unclear whether or not SARS-CoV-2 has shown a comparable activity.[28]

### B. Mechanism of Action of Chloroquine

There is a great deal of interest in the exact mechanisms by which chloroquine may act to attenuate SARS-CoV-2 infections because this knowledge may be useful for finding novel prophylactic and therapeutic candidates. In endoplasmic reticulum-Golgi intermediate compartment (ERGIC)-like structures, chloroquine may also prevent virion formation. [29]

### C. Mechanism of Action of Hydroxychloroquine

Beyond cytokine suppression, hydroxychloroquine and chloroquine have an impact on viral replication. It's a good idea to have a backup plan in case the backup plan doesn't work.[30]

Large, enveloped, single-stranded RNA viruses called coronaviruses can infect people as well as other animals like dogs, cats, chickens, cattle, pigs, and birds. [31] Coronaviruses are responsible for brain, gastrointestinal, and respiratory diseases. The most prevalent coronaviruses in clinical practice are 229E, OC43, NL63, and HKU1. In immunocompetent people, these viruses usually cause symptoms similar to the common cold. Without understanding the smallest quantity of virus particles required to cause infection, it is challenging to interpret the clinical significance of SARS-CoV-2 transmission from inanimate surfaces. Compared to permeable surfaces like cardboard, the viral load appears to persist at greater amounts on surfaces made of plastic and stainless steel, which are impermeable. [32] Numerous studies indicate that viral cultures are typically negative for SARS-CoV-2 8 days after the onset of symptoms, despite the fact that viral nucleic acid can be detected in throat swabs for up to 6 weeks after the onset of sickness. [33] The prompt diagnosis and conventional (symptomatic) therapy are still required for COVID-19 management due to the lack of an effective cure and vaccine. Therefore, effective diagnostic methods should be chosen in order to identify viruses in a timely manner. Below is a discussion of these tests' specifics as well as their clinical manifestations.[34]

A modified and/or severe presentation of an infectious disease that affects people exposed to the wild-type pathogen after having gotten a vaccine intended to prevent infection is known as vaccine-mediated enhanced disease (VMED), also known as vaccine-associated enhanced disease (VAED), or VMED.Based on observations with some experimental Middle East respiratory syndrome (MERS) and SARS-CoV-1 vaccines in specific animal models, VMED is a theoretical worry for COVID-19 vaccines. Anaphylaxis is a rare and potentially fatal systemic hypersensitivity response, and prevalence rates differed by age and gender in the studies that were conducted. Anaphylaxis-related hospitalization rates rose from 21.0 to 25.1/million from 1999 to 2009; the annual percentage shift was 2.23%. This information was obtained from hospital and emergency department (ED) records and death certificates. [35]





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COVID-19 is unusual in that patients over 60 years old have disproportionately higher case mortality rates than either young adults or children. The greatest mortality rates, at 14.8%, were observed in people over the age of 80. These results were brought out in one of the largest data analyses performed in China involving 72,314 patient records. [36] The peak viraemia of COVID-19 occurs prior to the onset of symptoms, with an incubation phase of 1 to 14 days (mean duration of 5-7 days). This emphasizes the transmission potential of patients who are silent or barely symptomatic. To the best of our understanding, this is the first fairly sizable series on the role of plasmapharesis in autoimmune encephalitis linked to COVID-19. All of the patients in this study were critically ill, had severe ARDS, and either lost consciousness during the weaning phase or displayed severe agitation. [37] Their persistently elevated inflammatory markers despite recovery from pulmonary or other organ pathologies was another characteristic they shared. On MRI, we discovered bilateral cerebral inflammation consistent with meningoencephalitis as well as elevated amounts of inflammatory acute-phase reactants like ferritin, fibrinogen, CRP, and IL-6 in the sera. No indication of a COVID-19 or other active CNS illness was found. [38] With the exception of Case 3, patients began to improve shortly after a sequential plasmapheresis was begun, and Cases 1, 2, 4, and 6 were soon transferred from the ICU to a regular ward. The goal of the current research was to determine how plasmapheresis affected the levels of cytokines and immune cells throughout the body in ARDSsevere COVID-19 patients. In severely ill COVID-19 patients, therapeutic plasmapheresis decreased levels of excess proinflammatory cytokines, liver function, and acute phase proteins, all of which could support vital organ function. [38] Additionally, plasmapheresis increased lymphocyte subset counts and oxygenation state. Furthermore, plasmapheresis was performed on every patient on NIPPV who survived. [39] These findings highlight the necessity of conducting controlled research on plasmapheresis in patients with severe COVID-19 and ARDS[40]. A wide variety of symptoms, including asymptomatic to acute respiratory failure, multi-organ failure, and death due to cytokine storm and macrophage activation, define coronavirus disease[41].

### V. MATCHING OF VACCINE IMMUNOGEN AND VARIANT TESTED

We contrasted the advancement of variant-based boosters over ancestral boosters when immunogen in the vaccine and that used in the neutralization assay were matched or unmatched in order to determine the significance of matching the variant composition of variant-based booster vaccines with the circulating variant. [42] If the variant tested was one of the variations that went into the vaccine makeup, we could say that the variant tested in vitro (v) was matched to vaccine immunogen (or vaccine makeup, m). [43] Therefore, any of the following vaccines would have been considered to be matched with the Omicron BA.1 variant when testing neutralization of that variant in vitro: (1) a monovalent BA.1 vaccine; (2) a bivalent vaccine containing BA.1 and an ancestral virus spike; or (3) a bivalent vaccine containing BA.1 and any other variant spike. (for example, Beta or Delta). However, it would be regarded as being unmatched to either a vaccine based on ancestry or one that had been changed to remove the BA.1 variant increase. [44] By a similar logic, the ancestral variant would be regarded as being matched with the ancestral-based vaccine as well as with any variant-modified vaccine that also contained the ancestral spike in its composition when evaluating the neutralizing antibody titers against the ancestor virus in vitro. [45] As a result, we were able to identify the vaccine antigen and neutralization antigen matching without regard to the vaccine valency. [46]

### VI. CONCLUSION

We conclused all that the drugs used in covid 19 were mainly antiviral drugs like Chloroquine, hydroxychloroquine, Favipiravir. For the prevention of covid 19 many of people used mask and sanitizer. After some timevaccines were discovered. Firstly, younger generation were treated with vaccines. After that below than 18 years old generation were treated. In human body respiratory tract were mainly affected by covid 19.

- A. Abbreviations
- 1) SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.
- 2) M Proteins: Myeloma protein
- 3) E Proteins: Envelope protein
- 4) N Proteins: Nucleocapsid phosphoprotein.
- 5) ARDS: Adult respiratory distress syndrome
- 6) PHEIC: Public Health Emergency of International Concern.
- 7) ACIP: Advisory Committee on Immunization Practices.
- 8) CDC:Center for disease control and prevention.
- 9) CKD: Chronic kidney disease.



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- 10) AKI: Acute kidney injury. 11) ARF: Acute renal failure.
- 12) VMED: Vaccine-mediated enhanced disease.
- 13) ERGIC: Endoplasmic reticulum-Golgi intermediate compartment.

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