Communication

An Overview on SARS-CoV-2 Variants from Alpha to Omicron: Epidemiology, Treatment Plans and Preventive Strategies for Future Pandemic

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Abstract: SARS-CoV-2 is severe acute respiratory syndrome coronavirus 2 which induces severe pneumonia that has considerable death rate. In this article, we summarised the evolution of SARS CoV-2 from alpha to omicron variant. The origin, transmission capability, and innate immunity potential of the Omicron variety remain unknown in the aftermath of its appearance. It's also unclear whether further varieties based on Omicron may emerge in the future. However, there is no question that the Omicron version of SARS-CoV-2 would not be the last. The COVID-19 pandemic has become more difficult to control due to the constant appearance of new SARS-CoV-2 mutations. We have discussed about the epidemiology, treatment plans for SARS CoV-2 and preventive strategies for future pandemic.

Keywords: SARS CoV-2, Variants, Epidemiology, Treatment Plans and Preventive Strategies

1.Introduction:

The seventh human coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS CoV- 2), was found in Wuhan, Hubei Province, China in January 2020 [1,2]. SARS CoV-2 induces severe pneumonia, with death rate of 2.9 percent [3–5]. Since the discovery of SARS CoV-2, its origin has been questioned by scientists [6]. It's been a while, SARS-CoV-2 is thought to be a laboratory-created virus. However, genetic evidence contradicts this [7]. SARS-CoV-2 is closely related to bat SARS-like coronaviruses [2], suggesting that bats could be the reservoir host. RaGT13 is bat corona virus which is nearly identical to

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SARS-CoV-2, except for certain variations in the spike receptor binding domain (RBD), which may explain the discrepancies in ACE2 affinity between SARS-CoV-2 and SARS-like coronaviruses. [6].

WHO has divided SARS-CoV-2 variants into three groups in order to prioritise monitoring and research: variants of concern (VOCs), variants of interest (VOIs), and variants under monitoring (VUMs). Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), and Delta (D.1) are the previous four VOCs (B.1.617.2) [8]. They all evolved into a new epidemic with countless deaths in multiple countries and areas, if not the entire planet. WHO identified a novel variation dubbed Omicron (B.1.1.529) as the fifth VOC on November 26, 2021, prompting widespread worry [9].In this article, we summarise the evolution of SARS CoV-2 from alpha to omicron variant. Furthermore, we have discussed about the epidemiology, treatment plans for SARS CoV-2 and preventive strategies for future pandemic. Figure 1 elucidates the timeline of SARS-CoV-2 variants

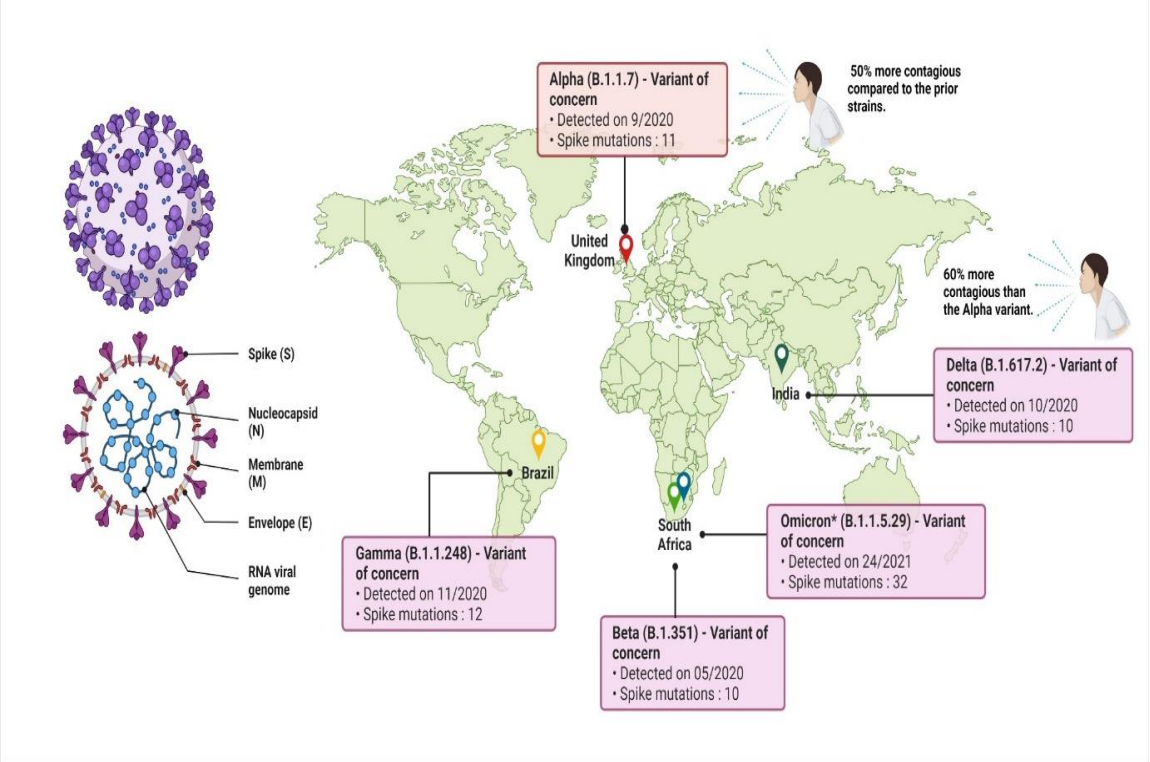

Figure 1: Timeline of SARS-CoV-2 variants

2.Materials and Methods:

Search engines like PubMed, Medline, Web of Science, Science Direct, Scopus, Wiley Online Library, Google Scholar were used for reviewing literature and to get the information regarding the research. The various information and ideas have been identified and modified based on this research to make it authentic one.

3. Symptoms of SARS-CoV-2:

Patients with SARS-CoV-2 infection can have mild to severe symptoms, and a considerable section of the population is asymptomatic carriers. 83 % of patients experience fever which is the most common reported symptoms, 82 % patients experience Cough, and 31

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% patients has loss of breath [10]. Chest X-rays in pneumonia patients generally show numerous mottling and ground glass opacity [11]. 2–10% of cases has pain in the abdomen [12], and 10% of COVID-19 patients has diarrhoea and nausea that occur before the onset of the disease [10].

COVID-19 patients typically had lower lymphocyte and eosinophil counts, lower median haemoglobin values, and higher WBC, neutrophil counts, and CRP, LDH, AST, and ALT serum levels [13]. Furthermore, early CRP serum levels have been shown to be a reliable predictor of the severity of COVID-19 infection [14,15].

Although the lung is the primary target of coronavirus infection, the widespread presence of ACE2 receptors in organs [16] can cause harm to the cardiovascular, gastrointestinal, renal, liver, central nervous system, and eyes, which must be continuously monitored [17]. Myocardial damage, myocarditis, acute myocardial infarction, heart failure, dysrhythmias, and venous thromboembolic events are all common consequences, and monitoring with high-sensitivity cardiac troponin may be helpful [18].

The so-called "cytokine storm" can cause patients with acute respiratory distress syndrome to rapidly deteriorate and multiple organ failure [12]. Increased interleukin (IL)-2, IL-7, granulocyte colony stimulating factor, interferon-c inducible protein-10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-a, and tumour necrosis factor-a have been described in severe COVID-19 cases and are characterised by increased interleukin (IL)-2, IL-7, monocyte chemoattractant protein 1, granulocyte colony stimulating factor. Furthermore, higher ferritin and IL-6 levels are predictors of death, and death is most likely owing to virus-induced hyperinflammation [19]. Tocilizumab (IL-6 receptor blockage) is given to individuals with COVID-19 pneumonia and increased serum IL-6 to minimise lung inflammation based on this evidence. [20]

The course of COVID-19 disease in children is often asymptomatic or moderate compared to that seen in adults. Nonetheless, serious and deadly cases in youngsters have been observed. Clinical laboratory data in children differs significantly from that in adults [21], which indicated inconsistent changes in the leukocyte index; nonetheless, CRP, procalcitonin, and LDH levels were also elevated in children with severe disease. Recent study reported [22], creatine kinase-MB was high in one-third of patients, raising the hypothesis of cardiac involvement in COVID-19 paediatric patients.

4. Phases of SARS-CoV-2 infection:

i. Early Phase of infection:

SARS-CoV-2 infiltrates the lung parenchyma and begins to multiply in the early stages of illness. Similar to SARS-CoV-2, ACE2 and TMPRSS2 perform critical roles in cellular entrance. SARS-CoV is an infectious disease caused by the coronavirus SARS. The spike protein's S1 subunit binds to the host cell surface cellular ligand ACE2. TMPRSS2 priming of cellular proteases enhances S1/S2 subunit cleavage of spike protein, and the S2 subunit allows virus fusion through host cell membranes. After the entry of cell, the genome of the Coronavirus is replicated, and transcription occurs at the cytoplasmic membrane. The replicase complex is responsible for the continual and irregular synthesis of RNA, as well as the production of 16 viral subunits and a large number of cellular proteins.[23]

ii. Pulmonary Phase:

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The existence of an inflammation, tissue damage, and respiratory failure characterise the pulmonary phase. In most cases, viral penetration into human lung tissues resulted in mild upper respiratory tract dysfunction. Similar to SARS-CoV, scientists believe that viral replication and budding causes type 2 alveolar cells to undertake apoptosis and epithelial regeneration. COVID-19-induced respiratory failure has distinct characteristics from normal ARDS. Non-cardiogenic pulmonary oedema causes ARDS, a complex clinical syndrome of acute respiratory failure. The most frequent clinical diseases linked to the development of ARDS are bacterial and viral pneumonia. When the lungs are harmed by infection or inflammatory diseases, inflammatory pathway gets triggered [24].

iii. Hyperinflammation Phase

As a consequence of the greater host inflammatory response and hypercoagulable state, the hyperinflammation phase is characterised by the presence of systemic inflammation and damage to distant organs, resulting in multiorgan failure (MOF).In COVID-19 patients with severe disease, higher levels of IL-2, IL-6, IL-7, IL-10, C-reactive protein (CRP), granulocyte-colony stimulating factor (G-CSF), interferon-gamma inducible protein (IP) 10, monocyte chemoattractant protein (MCP) 1, macrophage inflammatory protein (MIP) 1, and tumour necrosis factor (TNF) were found, as well as higher levels of the inflammatory-induced lung injury caused by this 'Cytokine storm' has life-threatening consequences such as MOF, ARDS, septic shock, hemorrhage/coagulopathy, acute heart/liver/kidney injury, and secondary bacterial infections. This is comparable to what happens in SARS-CoV and MERS-CoV infection [24].

5.Transmission of SARS-CoV-2:

SARS-CoV-2, like other respiratory viruses, spreads primarily through the respiratory tract with great efficiency and infectivity. Droplet transmission is the most well-known method, while aerosols may play a role as well [25,26]. The oral-faecal pathway, like SARS-CoV, could be another way for the virus to spread. SARS-CoV-2 RNA was found in the stool of a COVID-19 pneumonia patient [27]. As a result, sewage could play a role in SARS-CoV-2 transmission. Technical treatments, such as bio sorbents capable of retaining and inactivating the virus, should be studied in light of this [28].

SARS-CoV-2 has been found in infected people's saliva [29], which can be linked to the presence of ACE2 receptors in salivary gland duct epithelial cells [30]. Patient urine has been screened for SARS-CoV-2 virus RNA in various studies. The pooled rate of RNA positive in these trials was around 5–6%; however, the length of viral shedding in urine samples, as well as the infectivity of urine, have yet to be determined [31]. In the homes of patients with confirmed COVID-19, SARS-CoV-2 RNA has been found on surfaces like door handles and the cell phones. As a result, those who came in contact with diseased surfaces may become infected if they touch their eyes, mouth, or nose [26]. Figure 2 shows the transmission of SARS-CoV-2 during the initial days.

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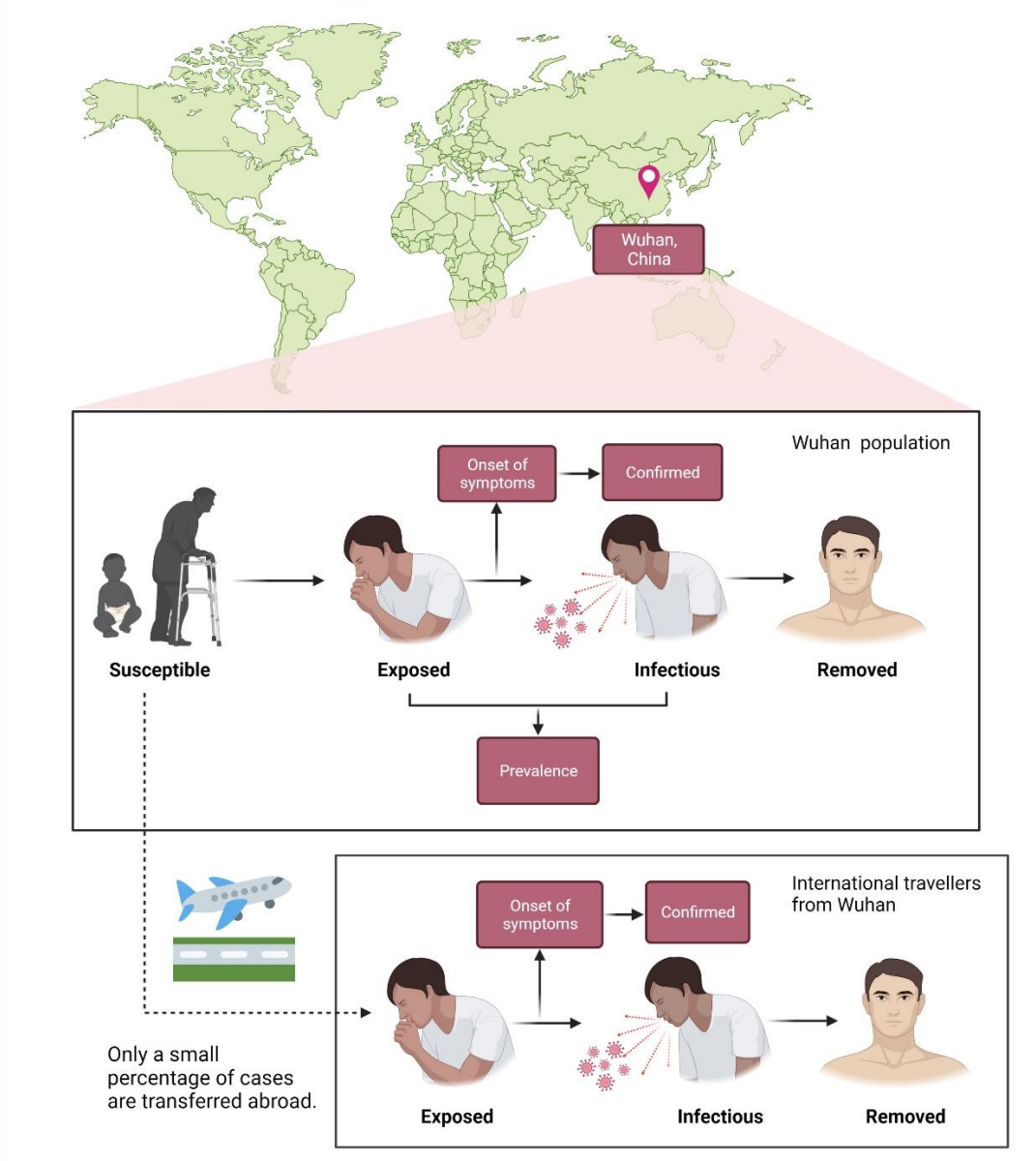

Figure 2: Transmission of SARS-CoV-2

SARS-CoV-2 could be transmitted through the eyes. SARS-CoV-2 RNA was found in ocular swabs of a patient having COVID-19. Surprisingly, an ocular swab virus was propagated in Vero E6 cells, implying that ocular secretions may be infectious [32]. When assessing individuals with suspected or confirmed COVID-19, eyewear should be worn notwithstanding the lack of conclusive data [33].

6.Evolution of SARS CoV-2:

i. Alpha:

The World Health Organization classifies alpha as a variety of concern, and it was first discovered in Kent, England, in September 2020, sparking the UK's second wave. While it was once considered that this variation was roughly 70% higher transmittable than the initial (wild-type) SARS-CoV-2 coronavirus, new research suggests that it is just 30-40% more transmissible. [34] Oxford-AstraZeneca vaccine efficacy (two doses) against the alpha variant was 74.5 percent, 93.7 percent with the Pfizer-BioNTech vaccine,[35] 85.6 percent with the Novavax vaccine,[36] and 100 percent with the Moderna vaccine, according to research. [37]. According to Thailand's Public Health Ministry, two doses of the Sinovac

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vaccination are 71-91 percent effective against the alpha version, according to a study that looked at the Sputnik V vaccine. [38]

ii. Beta:

Beta was first discovered in South Africa in May 2020, and the World Health Organization has classified it as a variety of concern. Beta has been linked to a 50 percent increase in transmission by Centre for Disease Control and Prevention (CDC),[39] but the real concern is that it appears to be able to dodge several existing vaccines. Early investigations suggest that the Pfizer vaccine is slightly less efficient (72-75% against beta) than the wild-type SARS-CoV-2 vaccine, however both Pfizer and Moderna claim that both vaccines are still 95% efficient against severe sickness and mortality. Johnson and Johnson (57%) and Novavax (60%) perform slightly worse. While early investigations of the Oxford-Astra-Zeneca vaccine appeared to demonstrate modest efficiency against beta, real-world data published on July 23 showed that a single vaccination dosage was successful in preventing severe sickness and death from covid [40]. Although, the producer of Sputnik V says that it is "very effective" against beta, at least one research has revealed that neutralising efficacy against this variation has decreased [41]. Although studies from Hong Kong observed that the level of prevention against beta was 70% lower than against wild-type, data on the effectiveness of Sinovac's CoronaVac are lacking [42].

iii. Gama:

Gamma was first discovered in November 2020 in Manaus, Brazil, and is another variety of concern for WHO. It is still the most common variation in South America. [43]. Gamma SARS-CoV-2 is 1.7-2.4 times more transmissible than wild-type SARS-CoV-2 [44]. Few trials have been done to see if covid vaccinations are effective against the gamma version. However, a report on a gamma outbreak between workers of a goldmine in French Guiana found a "strikingly high attack rate" among people fully immunised with the Pfizer vaccine, with 60% of fully vaccinated people becoming infected, compared to 75% of unvaccinated miners with no history of infection. [45]. Sputnik V's maker claim it's "very effective" against variants like gamma, but a research of antibody responses published in July indicated lower neutralising efficacy against gamma as well as other variants. [46]

iv. Delta:

Delta continues to drive a significant surge of cases throughout of Asia, including Bangladesh, Malaysia, Japan, Myanmar, Iran, Pakistan and Iraq, Japan, Thailand, Kazakhstan, Vietnam, and South Korea [47], as well as in India, where it was first diagnosed in October 2020.According to a study, the delta variation of SARS-CoV-2 is the most transmissible, up to 60% more so than the alpha variant. It's been dubbed an "enhanced" version of the alpha variety, which is ineffective in airways due to the mutation, according to researchers. This means that the infected person has more virus in their body, allowing them to discharge excess virus into the air, and one preliminary study found that infected patients had viral loads up to 1260 times more than infected people with wild-type SARS-CoV-2. [48] Another issue was if the delta form is more effective at infecting human airway cells, people could become infected even after receiving less exposure. [49] In terms of existing vaccinations, research reveals that the Oxford-AstraZeneca vaccine has a 67 percent efficacy against delta and the Pfizer-BioNTech vaccine has an 88 percent efficacy over delta, while the producers of Sputnik V say that it is 90 percent efficient against it.

Further advancement is the advent of delta plus, which is delta with a K417N spike protein mutation. In England the delta plus instances had mostly been in younger people, according to Colin Angus, a public health policy modeller and analyser, but preliminary data revealed that antibodies from immunized persons were still efficient against this version. [50]

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v. Eta:

The eta variation has been discovered in 72 nations, including Nigeria and the United Kingdom, where it was originally discovered in December 2020.Although the CDC stated that eta has the potential to impair the neutralising efficacy of different monoclonal antibody therapies and convalescent plasma, little is known about it. It has been classified as a "variant of interest" by the WHO, which is the second highest level of alert [51].

vi. Iota:

Like eta, very little documented about the iota variation, which was discovered in November 2020 in New York City, USA. It has been recorded in 53 countries thus far, and according to the CDC, it has a decreased susceptibility to the monoclonal antibody treatment combination bamlanivimab-etesevimab. WHO deemed it a variation of interest [51].

vii. Kappa:

Kappa was first identified in India in October 2020, and WHO considers it to be a variation of interest. According to the CDC, this variation may impair the ability of certain monoclonal antibody therapy to neutralise the virus. There have been reports from 55 different nations [51].

viii. Lambda:

Lambda was discovered in Peru in December 2020 and quickly became the prevalent variety, accounting for 80% of all cases within three months. It is a variant of interest to WHO because of its rapidity and the existence of mutations that might alter transmissibility and antibody efficacy. It's been found in 41 nations, but it hasn't yet beaten out any of the most common types [51].

ix. Omicron:

According to WHO documents, the first confirmed Omicron infection was discovered in a specimen gathered on November 9, 2021. [52] However, the very first Omicron sequence was discovered in a specimen obtained in Botswana on November 11, 2021. Since the discovery of Omicron, the strain appeared to have spread swiftly. A new genomic-sequence analysis of 77 viral samples collected in South Africa's Gauteng province between November 12 and 20 revealed that all of the studied variants were really B.1.1.529, suggesting that Omicron had become prevalent in Gauteng. Furthermore, Omicron's discovery coincides with a recent rise in the amount of reported COVID-19 infections in South Africa. After the Omicron variant was confirmed, the overall number of COVID-19 cases per day climbed from 280 to 800. [53] On November 26, 2021, this number surpassed 2000, and on December 3, 2021, it surpassed 10,000. [54] Furthermore, investigating the origins of COVID-19 cases demonstrated that B.1.1.529 had most likely spread throughout western Europe when the first cases were discovered in southern Africa [55]. Three large COVID-19 outbreaks have been documented in South Africa since early 2020. The Beta and Delta variations are responsible for two of them. Within 100 days of the outbreak, the number of persons infected with the Beta variation grew to 50% of total daily infections, according to epidemiological data. During the same time frame, however, the Delta variant's infection rate increased to 80%, indicating that the Delta version is more transmissible among people than the Beta variant. In South Africa, on the other hand, the proportion of Omicron infection attained 90% in about 25 days. The Beta, Delta, and Omicron types' early doubling times were calculated to be 1.7, 1.5, and 1.2 days, correspondingly. [53] According to these findings, the Omicron form is more contagious than the Delta and Beta variants. It's also worth noting that a retrospective study was based on community

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epidemiologic study in South Africa found a link between Omicron and a greater risk of SARS-CoV-2 re infection. [56] The likelihood of a fresh COVID-19 outbreak in South Africa, and possibly the rest of the world, should not be discounted.

7. Treatment for SARS-CoV-2:

- *Antiviral therapy:*

Chloroquine:

Chloroquine is a medication used to treat autoimmune and antimalarial conditions. According to Wang et al., chloroquine is a possible medication for successfully suppressing COVID-19 in vitro [57].

Many viruses, like coronaviruses and dengue virus, have been discovered to be resistant to chloroquine. It can cause phospholipidosis, which results in the accumulation of bis (monoacylglycero)phosphate, and elevate endosomal pH, which hinders virus or cell fusion and so blocks viral infection (BMP). Due to the combined effect of chloroquine on endosomal pH and the BMP cause impaired SARS-CoV -2 endosomal: lysosomal trafficking [58]. Furthermore, chloroquine has been demonstrated to interfere with the glycosylation of cellular receptors in SARS-CoV by inhibiting the acidic proteases involved in developing viral fusion protein. It has both antiviral and immune-modulating properties, which work together to boost the antiviral action synergistically [59]. When compared to the control treatment, Gao et al. found that chloroquine therapies is superior in preventing pneumonia exacerbations, enhancing lung imaging, and reducing the illness course [60].

Type 1 interferons (IFN–I):

Type 1 interferons (IFN–I) are a class of cytokines released by a variety of cell types in response to the identification of viral components by pattern recognition receptors (PRR). The cytokines IFN-I are the ones that are produced first during a viral infection. IFNARs (interferon Alpha/Beta receptors) on the plasma membrane identify IFN-I and cause phosphorylation of transcription factors including STAT1. If factors re-localize to the nucleus, interferon-stimulated genes (ISG) will be activated. Signalling, inflammation, and immunological regulation are among processes that ISG play a part in. As a result, they will obstruct virus replication and spread through a variety of processes.

Cell metabolism will be slowed, or immunity will be triggered by cytokine secretion. ISGs encode PRRs, which increase the cell's sensitivity to pathogens and reduce membrane fluidity, preventing viral egress or membrane fusion. IFN-I is responsible for most of the antiviral immunity [61]. IFN-1 is effective in the short term after infection. However, it is unable to prevent virus multiplication and has some negative effects when used later.

Lopinavir/ritonavir:

The mixture of protease inhibitors lopinavir/ritonavir (LPV/RTV) is used to prevent the replication and manufacturing of the human immunodeficiency virus (HIV). Under the influence of LPV/RTV, only immature and non-infectious viruses can be generated. Despite the fact that coronaviruses encode a different enzymatic class of protease, it was proposed to be utilised to block the viral protein synthesis of SARS-CoV-2 in COVID-19 patients. In a case described by Lim et al., the viral load of SARS-CoV-2 was dramatically reduced, and clinical symptoms improved during treatment with the use of LPV/RTV [62].

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Cao et al. observed no obvious treatment benefits above basic treatment when LPV/RTV was used alone in another randomised, controlled, open-label trial in people hospitalised with severe COVID-19 [63].

Remdesivir:

Remdesivir is a broad-spectrum antiviral medication that has been shown in vitro and in vivo to inhibit SARS-CoV-2. It is one of the potential direct antiviral medications for SARS-CoV-2 that has been authorized by a number of regulatory bodies throughout the world. Subjects were randomly allocated to receive either remdesivir (200 mg on day 1, followed by 100 mg daily for up to 9 further days) or placebo for up to 10 days in a double-blind, randomised, placebo-controlled trial involving 1,062 patients hospitalised with COVID-19. Remdesivir was found to be superior to placebo in terms of recovery time. In a trial, patients who took remdesivir had a median recovery time of 10 days (95 percent confidence interval: 9 to 11 days), compared to 15 days (95 percent confidence interval: 13 to 18 days) for those who received placebo [64]. Several investigations, however, have shown that remdesivir is best suited for viral prophylaxis or beginning before to peak viral replication. Remdesivir administration after peak virus replication would have little effect on disease severity or fatality [65–67].

- *Immunotherapy:*

Convalescent plasma therapy:

Several antiviral antibodies are seen in convalescent plasma (CP) obtained from healed individuals. CP has been widely utilised to treat infectious diseases like Ebola [68]. CP treatment is a neutralising antibody-based passive immunotherapy. Supplement activation and phagocytosis can be aided by CP-derived antibodies to limit virus replication [69].

Wong et al. discovered in prior SARS studies that having CP transfusion after 24 hours lowered the viral load in plasma from 105 copies/mL to undetectable levels during the early stages of the disease [70]. So that the neutralising antibody levels remains high enough for treatment, convalescent plasma from treated individuals should be obtained within 2 weeks of recovery. Obtaining appropriate plasma during convalescence is a problem. As a result, more research and design efficacy, and safety CP, are required [71]. Figure 3. illustrate the principle of convalescent plasma therapy for SARS-CoV-2 patients.

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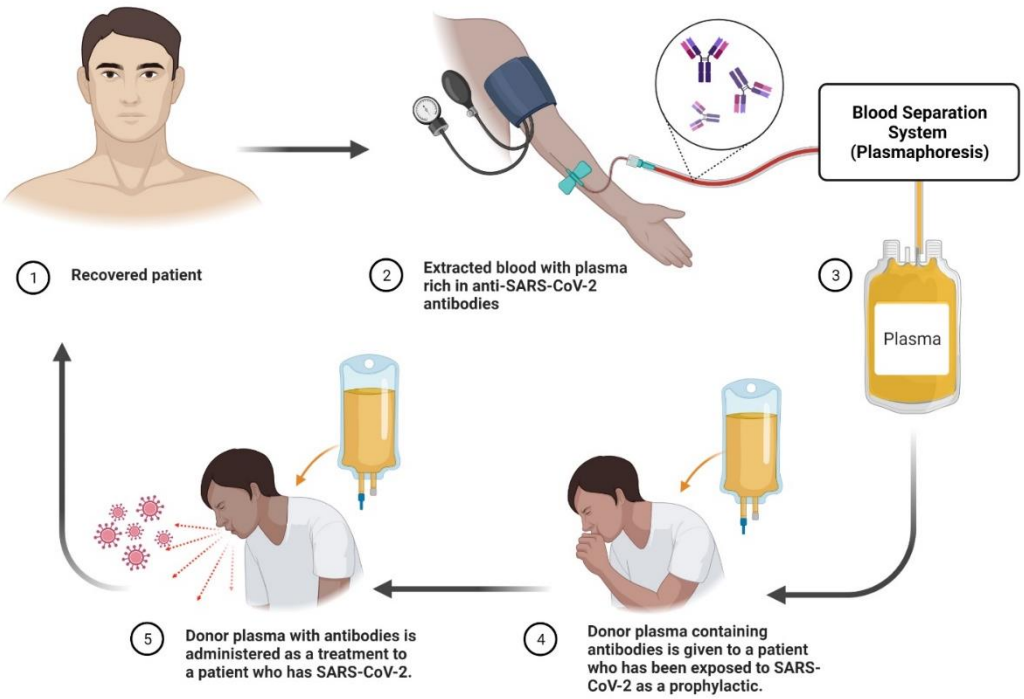

Figure 3. Principle of convalescent plasma therapy for SARS-CoV-2 patients.

- *Anti-Inflammatory agents:*

Glucocorticoids:

COVID-19 is linked to inflammation that is dysregulated and excessive, leading to diffuse lung injury. SARS, Middle East respiratory disease (MERS), severe influenza, and community-acquired pneumonia have all been treated with glucocorticoids, which are identical to COVID-19. The use of glucocorticoids, either systemically or locally, may help to minimise inflammation-induced lung injury and the development to respiratory failure and death. Dexamethasone reduced 28-day mortality in patients receiving respiratory assistance, either invasive mechanical ventilation or oxygen, in a controlled, open-label trial involving 9,355 patients hospitalised with COVID-19. However, there was no indication that dexamethasone alone, without respiratory support, could help COVID-19 patients [72].

Tocilizumab:

COVID-19 is caused by SARS-CoV-2 infection, which causes excessive cytokine release followed by lung damage. In COVID-19 patients, a higher level of serum interleukin-6 (IL-6) is linked to a worse result. Tocilizumab is a recombinant-humanized monoclonal antibody that targets the IL-6 receptor in both soluble and membrane-bound forms. Tocilizumab is used to treat severe rheumatoid arthritis, giant cell arthritis, systemic juvenile idiopathic arthritis, and cytokine release syndrome, which can be fatal. Because of its anti-IL-6 properties, tocilizumab therapy is thought to have a therapeutic benefit. Patients treated with tocilizumab, both intravenously or subcutaneously, had a lower risk of intrusive mechanical ventilation or death in a multicentre retrospective trial [73].Figure 4 to shows the summary of therapies for SARS-CoV-2.

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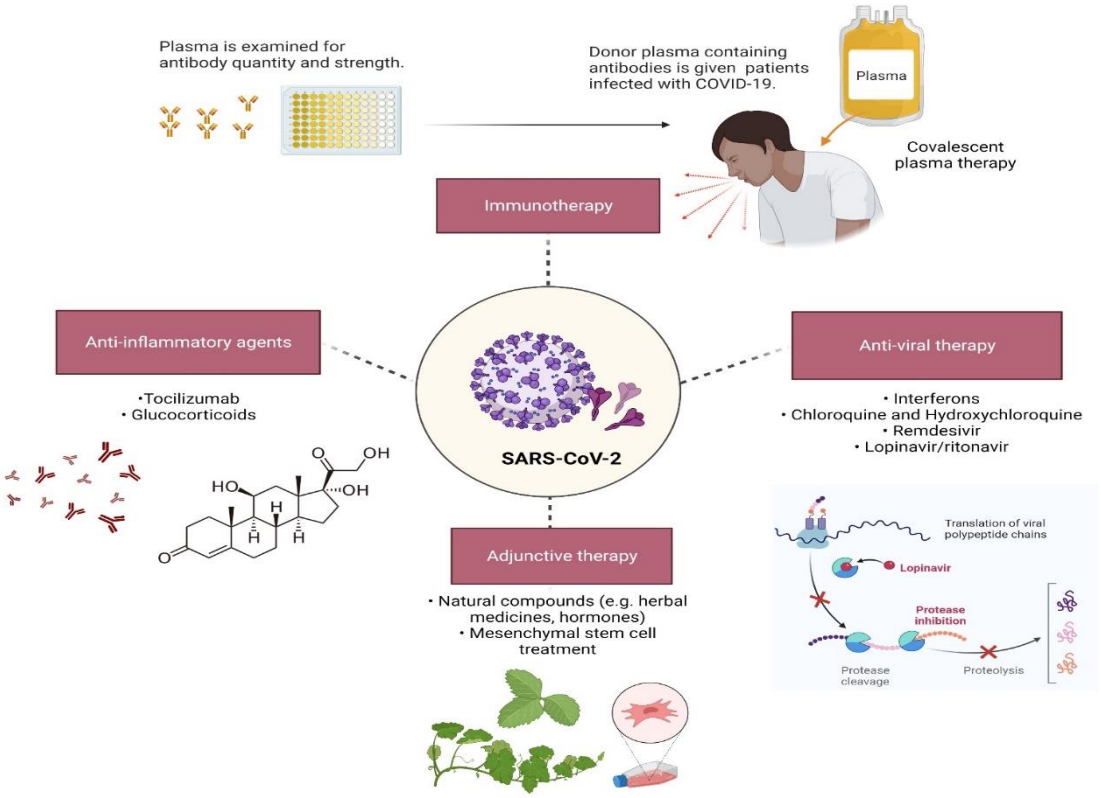

Figure 4. Therapies of SARS-CoV-2

ii. Prevention for SARS-CoV-2:

- *Personal Protection:*

The most effective strategy for the general public to lower the risk of infection is to take appropriate protection and measures, such as good personal hygiene, wearing a medical mask, obtaining enough rest, and avoiding crowded locations [57]. Maintaining a 2-meter interpersonal distance can be regarded a good way to reduce the probability of transmission [74]. A recent study found that wearing a community-wide face mask can help minimise COVID-19 transmission by minimising the emission of infectious saliva and respiratory droplets by people who have subclinical or mild COVID-19 [75]. When performing aerosol-generating procedures, healthcare practitioners should take normal measures and use personal protective equipment (PPE) such as gloves, gowns, eye protection, face masks, and N95 respirators. Early detection, isolation, and treatment are critical for governments to stop the virus's spread and the recurrence of positive cases. The use of an online geographical tracking system and big data analysis to map COVID-19 instances allows for rapid and accurate tracing and mapping of super-spreaders in the community for epidemic monitoring and response [76,77].

- *Vaccination:*

With a greater understanding of the SARS-CoV-2 genome, most vaccine development techniques target the S protein-coding sequences or antigens generated from the S protein. Live-attenuated vaccines, inactivated virus vaccines, subunit vaccines, viral vector-based vaccines, DNA vaccines, and RNA vaccines are now being developed for SARS-CoV-2 [78]. Vaccines are typically used to prevent infection (i.e., sterilisation immunity). The actual value of a vaccines is the avoidance of the disease. This can be accomplished either instantly in the immunised person or indirectly by reducing population-wide transmission. High rates of sterilising immunity to SARS-CoV-2 may be difficult to achieve, given

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that natural immunity to other common CoVs (e.g., 229E) is incomplete, and neutralising antibodies to SARS-CoV-1, Middle East respiratory syndrome CoV, and SARS-CoV-2 are not always induced by infection and can wane quickly [79]. Effective vaccinations administered to a significant number of people are expected to significantly lower infection in a population that is otherwise susceptible. Even if transmission could be effectively halted by immunization of children and young adults, mortality rate would not be significantly decreased except if the immunization is also directly beneficial among the elderly [80].

8. Long term Strategies to Prevent Future Pandemic:

i. Periodic surveillance on wildlife:

Between the onset of SARS and the present outbreak, serological evidence indicated that people living near the wildlife-human interaction in rural regions were exposed to SARS-related coronaviruses, possibly the same virus as nCoV-2019 [81,82]. Coronaviruses of wildlife origin are now considered a "clear and present risk," according to these findings. They also bring up a critical concern in the present outbreak: the large range of virus strains seen in wildlife, all of which have the potential to infect humans. Moreover, many of other CoV' s are thought to exist in bats throughout Southeast Asia, most of which might cause a pandemic. Scientists in high-risk countries should endeavour to find all of these viruses so that they can be catalogued, a reference library developed for rapid pathogen identification and risk assessment, and vaccines and medicines tested against them. [83,84]

ii. Surveillance among inhabitants who have direct contact with wildlife:

Patients with acute respiratory infection (ARI) or influenza-like illness (ILI) signs with unknown aetiology, as well as people with frequent contact with wild or domesticated animals as part of their livelihood or occupation, can be included in the monitoring as a cost-effective method for identifying novel virus spill overs. In partnership with research institutions, this 'pre-outbreak surveillance' method can be integrated with many areas of public health, healthcare, agriculture, and forestry to implement sample collecting and testing of wildlife, domestic animals, and people. These efforts will aid in the identification and characterization of viral genetic sequences, the identification of high-risk populations with antibodies and cell-mediated immunity responses to CoV' s of wildlife origin [85], and the identification of risk factors in human behaviour and living environment through interviews. Then, evidence-based risk-reduction strategies can be implemented. After that, evidence-based risk-reduction initiatives can be designed and deployed in the areas where viral spill over has been detected.

iii. Enhancing biosecurity on markets and labs:

Decreased levels of environment sanitation and excessive levels of human-animal interaction were identified as important risk variables for zoonotic disease transmission in behavioural risk research, notably in community wet and animal markets [86]. While current wildlife trading limitations may aid disease control for the time being, market biosecurity in terms of cleanliness and basic sanitation and rules, as well as the origin of animal traded at the market, must be enhanced to avoid future disease outbreaks. Farmed animals are expected to be at a lower risk of viral outbreak than wild-caught animals. Risk monitoring and veterinary treatment on farms and during shipping to marketplaces would need to be enhanced on a regular basis. The link seen between outbreak and the wildlife trade has been established, sparked widespread opposition to wildlife consumption, prompting scientists to call for an immediate amendment to the Wildlife Protection Law to standardise as well as handle wildlife trade as a public health and security issue. To address this issue as a long-term aim, collaboration between the State Forest management and Grassland

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Administration, Department of Agriculture and Ministry of natural resources, State Management for Market Regulation, and public health agencies is required [87,88].

iv. Utilization of Artificial Intelligence:

Artificial intelligence (AI) may play a role in health-care system governance and response to health-care catastrophes like the present COVID-19 outbreak. AI could aid in the analysis of large amounts of data in a rapid manner, as is required during times of crisis, allowing health authorities to respond quickly. The use of AI to analyse medical records, treatments, and laboratory results could speed up the decision-making process and enhance patient management. It has been suggested, for example, that AI could assist radiologists in reading CT scans. While a conventional read takes roughly 15 minutes, AI can finish it in a matter of seconds.

Block chain and artificial intelligence could be employed for remote patient monitoring and clinical data transfer to health authorities. A SARS-CoV-2 positive patient could be assigned to a quarantine facility for monitoring and treatment in order to prevent the virus from spreading. Similarly, data from a specific geographic area may be used to follow positive individuals and/or quarantine that area to prevent the virus from spreading. [89,90]

9. Conclusion:

The origin, transmission capability, and innate immunity potential of the Omicron variety remain unknown in the aftermath of its appearance. It's also unclear whether further varieties based on Omicron may emerge in the future. However, there is no question that the Omicron version of SARS-CoV-2 would not be the last. The COVID-19 pandemic has become more difficult to control due to the constant appearance of new SARS-CoV-2 mutations. Thankfully, we have a wealth of expertise and strategies for dealing with novel coronaviruses, and we understand what we must do to prevent viral variations from spreading. Human society would win this battle against COVID-19 with worldwide coordination and speedy data sharing.

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