REVIEW ARTICLE

ISSN: 2455-8095
doi: https://doi.org/10.21477/ijapsr.7.2.2

Impact of Anti-COVID-19 Vaccines on Emerging Variants of COVID-19

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ABSTRACT

COVID-19 is an acute infectious condition brought about by SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2). SARS-CoV-2 is largely a respiratory virus, although it can also impair other significant organs and systems. Several novel variants of concern (VOCs) have appeared after the outbreak of the SARS-CoV-2 pandemic, including the Alpha (B.1.1.7); Beta (B.1.351); and Gamma (P.1); Delta (B.1.617.2), and Omicron (B.1.617.2) (B.1.1.529). According to preliminary studies, some of these VOCs can evade immune responses produced against earlier variants, reducing the efficiency of existing vaccinations. Several presently offered vaccinations give partial to total protection against these strains, if further mutant variations evolve, current vaccinations may have to be revised, either by generating vaccines that match the existing strain or by creating multivalent vaccines that cover a wider range of mutations. A vaccine may prove efficacious against a variant but show no effect on the other. The effects of currently existing anti-COVID-19 vaccinations on distinct SARS-Cov-2 VOCs have been discussed in this article.

Keywords: COVID-19, SARS-CoV-2, Vaccination, Vaccine, Variants of Concern (VOCs).

1. INTRODUCTION

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) is the highly transmissible virus that provoked an infectious disease in 2019 in Wuhan, China, resulting in an outbreak of acute respiratory condition known as coronavirus disease 2019 (COVID-19). The continuing epidemic has resulted in about 162 million reported cases and more than 3.3 million people died by mid-May 2021. Vaccinations are the most common strategy for preventing viral illnesses, and the effectiveness of this strategy has already been demonstrated by the rapid invention of COVID-19 vaccines. Numerous vaccines have been tested (Figure 1), and most of them can produce immunity in diverse animal models via antibody production or T-cell responses. Since the commencement of the COVID-19 pandemic, researchers have been working to develop effective vaccination techniques worldwide.

Adaptive changes in the genetic material can change how harmful the virus is. Even a single nucleotide substitution can significantly impact a virus's capacity to elude the immune response, making vaccine development more difficult. SARS-CoV-2, like other RNA viruses, is susceptible to genetic mutation as it adapts to new human hosts. Mutations occur in the virus over time, leading to the establishment of various variants with distinct features from the original strains. Although significant advancement in clinical trials gave rise to a clearer appreciation of SARS-CoV-2 as well as the COVID-19 management, restricting the virus and its variants' transmission has become a growing concern as SARS-CoV-2 remains to cause mayhem around the globe, with several countries experiencing a 2nd or 3rd wave of pandemic pertaining primarily to the emergence of new virus variants.

1.1. Variants of SARS-Cov-2

Variants are divided into variants of concern (VOCs), variants of interest (VOIs) and variants of high consequence. Basic definitions of VOCs and VOIs have been presented by the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), which will be revised as needed. Greater spread, severity (increased incidence of hospital stays or mortality rate), dramatic drop in antibodies' neutralization obtained during previous infection or through vaccine, lowered response to therapeutic interventions or vaccine, and

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Received: 19-02-2022 **Accepted:** 29-03-2022 **Available Online:** 01-04-2022

error detection protocols are all examples of the VOCs. Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and Omicron (B.1.1.629) have been identified as VOCs in recent times. The VOI mutations cause amino acid alterations with potential or verified phenotypic effects.[1] Epsilon (B.1.427/B.1.429), Iota (B.1.526), Eta (B.1.525), Kappa (B.1.617.1), Mu, have been identified as VOIs. Mutation D614G is commonly seen in all VOIs; findings revealed that this mutation makes the variant spread faster than other variants lacking it.

1.2. Pharmacological Treatment for COVID-19

Antiviral agents, anti-SARS-CoV-2 monoclonal antibodies, and immunomodulators drugs are currently available or being studied to treat COVID-19 (Figure 2). Remdesivir, molnupiravir, and lufotrelvir were found to be effective in treating individuals affected with the omicron strain.[2] According to the results, monoclonal antibodies authorized by the Food and Drug Administration (FDA) may be ineffective against the omicron variant. The alpha and delta versions were possibly neutralized by several combinations of monoclonal antibodies (Bamlanivimab + Etesevimab, Casirivimab + Imdevimab, and Cilgavimab + Tixagevimab). When etesevimab was combined with bamlanivimab, neutralizing action against gamma was significantly decreased, whereas neutralizing effect against omicron and beta variants was eliminated. The imdevimab-casirivimab combination preserved anti-beta variant and anti-gamma variant action but decreased anti-omicron activity. The combination of tixagevimab and cilgavimab blocked beta, gamma, and omicron receptors.[3] Efficiency of interferon β-1a as well as interleukin-1 receptor antagonists on all the SARS-CoV-2 VOCs are still unknown.

Other drugs such as Duvelisib (NCT04372602), Infliximab (NCT04425538), Tramadol (NCT04454307) are under clinical trials for the treatment of COVID-19.

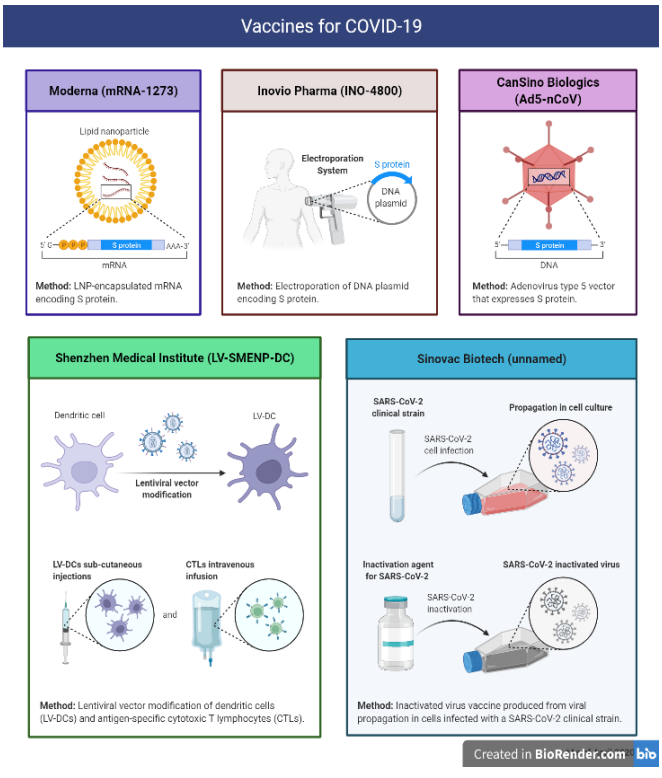

Figure 1: Anti-COVID-19 Vaccines designed using different methods
LV, Lentiviral; nCOV, Novel coronavirus; CTLs, Cytotoxic T lymphocytes; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2.

2. VACCINATION AGAINST COVID-19

Vaccination campaigns for the BBV152 (Covaxin) and ChAdOx1 (Covishield) vaccines started in India in January 2021. Even though over 3 million single doses of vaccine were being administered every day in India, the percentage of people completely immunized against COVID-19 was still lower than the world average and lower than other countries with relatively larger COVID-19 burden, like Brazil. To add to these concerns, novel VOCs and VOIs could evade protection established by primary infection or vaccinations. However, more research is required on this conception.[4]

Several SARS-COV-2 vaccines have been approved for use in clinical settings to limit the transmission of the viral pandemic and minimize death rates. The spike protein of SARS-COV-2 is perhaps the primary target, and numerous vaccines, such as viral vector vaccines and mRNA vaccines, have been created using diverse technologies (Table 1).

Apart from the vaccines listed above, other vaccines, such as protein-based vaccines and inactivated vaccines, have already been created in India (Covaxin), Russia (Sputnik V), and China (CoronaVac) and have been certified or given urgent use permission in so many countries all over the world to avert COVID-19.

2.1. Clinical Trials for COVID-19 Vaccines

COVID-19 vaccinations are now being investigated in over 135 countries. Some vaccines are still in preclinical studies, while just a handful have progressed to the various stages of clinical trials (Table 2).

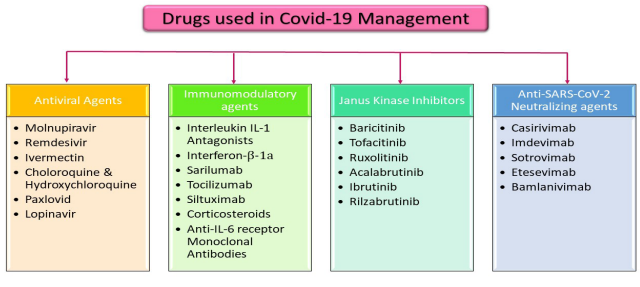

Figure 2: Pharmacological agents for COVID-19

Table 1: Efficacies of currently available vaccines[5]

Vaccine	Type	Dose regimen	Efficacy
BNT162b2 vaccine	mRNA vaccine	two-doses given 21 days apart	95%
Ad26.COV2.S vaccine	Non-Replicating Viral Vector	single dose	73.1%
NVX-CoV2373 vaccine	Protein subunit	single dose	92.6%
ChAdOx1 nCoV-19 vaccine	Non-Replicating Viral Vector	two doses	70.4%
mRNA-1273 vaccine	mRNA Vaccine	two doses given 28 days apart	94.1%

Table 2: Anti-COVID-19 vaccines under clinical trials

NCT ID	Title	Status	Primary purpose
NCT05228613	Safety and Immunogenicity Study of COVID-19 Protein Subunit Recombinant Vaccine Adjuvanted With Alum+CpG 1018	Recruiting	Treatment
NCT04780035	Study of the Tolerability, Safety, Immunogenicity and Preventive Efficacy of the EpiVacCorona Vaccine for the Prevention of COVID-19	Completed	Prevention
NCT05218070	Safety and Immunogenicity Study of EgyVax Vaccine Candidate for Prophylaxis of COVID-19 Infection (Sphinx)	Recruiting	Prevention
NCT04691947	Safety and Immunogenicity of Two Different Strengths of the Inactivated COVID-19 Vaccine ERUCOV-VAC (ERUCOV-VAC)	Recruiting	Prevention
NCT04833101	Study on Heterologous Prime-boost of Recombinant COVID-19 Vaccine (Ad5 Vector) and RBD-based Protein Subunit Vaccine	Completed	Prevention
NCT04952727	Study on Sequential Immunization of Inactivated COVID-19 Vaccine and Recombinant COVID-19 Vaccine (Ad5 Vector) in Elderly Adults	Recruiting	Prevention
NCT04560881	Clinical Trial to Evaluate the Efficacy, Immunogenicity and Safety of the Inactivated SARS-CoV-2 Vaccine (COVID-19)	Completed	Prevention
NCT04568811	The Phase I Clinical Trial of Booster Vaccination of Adenovirus Type-5 Vectored COVID-19 Vaccine	Completed	Prevention
NCT05165966	Safety and Immunogenicity Study of Booster Vaccination in Different Doses of COVID-19 Vaccine (Vero Cell), Inactivated for Prevention of COVID-19	Active, not recruiting	Prevention
NCT05293548	A Clinical Trial on Sequential Immunization of Recombinant COVID-19 Vaccine (CHO Cell, NVSI-06-09) and Inactivated COVID-19 Vaccine (Vero Cell)	Not yet recruiting	Prevention

2.2. Post-vaccination Complications of COVID-19

Despite the safety and effectiveness of COVID-19 vaccinations in clinical trials, many case studies and case series have revealed occasional but severe adverse effects involving multiple organs, including the brain, heart, and vascular system.[6] Two cases of Guillain-Barre Syndrome (GBS)[7] and cerebral venous sinus thrombosis[8] have been recently reported following immunization with the Pfizer - COVID-19 vaccine. Other complications include thrombosis,[9] thrombotic thrombocytopenia,[10] Acute Transverse Myelitis (ATM),[11,12] myocarditis,[13-18] lymphadenopathy,[19] and Central Serous Retinopathy (CSR)[20] have also been noticed. With the continuing global mass immunization program, doctors must be able to diagnose neurological problems or other adverse effects linked with COVID-19 vaccine quickly.

3. EFFECTS OF ANTI-COVID-19 VACCINES ON DIFFERENT VARIANTS

The recent identification of new SARS-CoV-2 strains underscores one of the pandemic's key difficulties. Variants with improved disease transmission and antibody resistance can harm pandemic mitigation and management attempts. The Indian government claims that both Covaxin® and Covishield® are potent against all SARS-CoV-2 VOCs; regrettably, Oxford University experts claim that both Pfizer/BioNTech and AstraZeneca vaccines are efficacious against the kappa and delta variants, albeit the potency against the delta plus variant is unknown.[21]

The vaccination BNT162b2 offered 89.5% protection against alpha variants and 75.0 percent against beta variants.[22] A two-dose AZD1222 (AstraZeneca) immunization fails to protect against Beta (B.1.351) variant-mediated COVID-19, according to investigations.[23] For delta variants, the vaccines mRNA-1273 (Moderna), BNT162b2 (Pfizer/BioNTech), and ChAdOx1 (Oxford/AstraZeneca) have shown to decrease new infections, although effectiveness and maximum viral load reductions are reduced.[24-26] Those immunized with the BNT162b2 (Pfizer/BioNTech) and ChAdOx1 (Oxford/AstraZeneca) vaccines had a 5.11-fold decrease in neutralizing potential against delta plus variant.[27] During broad Gamma variant transmission, completing the ChAdOx1 vaccination schedule led to considerably enhanced protection from moderate and severe COVID-19 in aged people compared to a single dose.[28]

People affected with the alpha or delta strain were given two shots of either BNT162b2 or AZD1222, and PCR Ct values revealed that the delta variant seemed to have a lesser reduction in transmission as compared to the alpha variant, and the benefits of immunization diminished with time.[29] Cross-neutralization of the beta and delta variants remained constant following vaccination with ChAdOx-1 S, Ad26.COV2.S, mRNA-1273, or BNT162b2, while neutralization of omicron was much reduced or undetectable.[30]

The omicron spike was more effectively neutralized by antibodies generated by recombinant ChAdOx1 (Astra Zeneca-Oxford)/BNT162b2 immunization or vaccination using three shots of BNT162b2, although the omicron spike eluded neutralization more readily compared to the delta spike.[31]

A booster dose is required following vaccination with the mRNA-based vaccines for achieving effective protection against the omicron form, as two doses of mRNA-based vaccinations generate weak neutralization of omicron.[32] Initial vaccination with 2 doses of ChAdOx1 nCoV-19 or BNT162b2 vaccine produced modest protection from symptomatic illness brought about by the omicron form, but this protection diminished with time.[33]

Even though some of these studies suggest that vaccination-dependent induction of an immune response towards newer VOCs is significantly reduced, the findings are nevertheless encouraging and demonstrate the effectiveness of available vaccinations in combating current and future VOCs.

4. FUTURE PROSPECTS

The use of nanotechnology in vaccine development might be a viable strategy in fighting against the COVID-19 pandemic. SARS and MERS nanoparticles made of mRNA and lipids are now being tested. Conventional vaccines, which use a weakened virus or refined, unique viral proteins to provoke the body to effectively elicit immunity, may be manufactured almost as quickly as a virus's genomic code. It is possible to think of it as a new era for vaccinations and vaccinology. It is expected that mRNA modification will achieve substantial progress in the development of newer vaccines , and that will be extremely beneficial for future variants that may evolve.

To facilitate the faster genetic evaluation of evolving variants with both in vitro and in vivo studies, the Coalition for Epidemic Preparedness Innovation (CEPI) established a collaborative project called "Agility" in association with Public Health England (PHE), the National Institute of Biological Standards and Controls (NIBSC), and the GISAID Initiative. The Agility program seeks to offer accessible, high-quality data on the biological consequences of developing variants to highlight necessity for vaccine alterations or adaptations to retain the efficacy.

5. CONCLUSION

Considering the global COVID-19 pandemic situation, which we briefly discussed here, long-term research to track the progression of COVID-19 vaccine-induced protective immunity will be required. The research for vaccination and drugs to combat COVID-19 must progress. It's unclear how long such variants will persist, or to what degree current vaccines would be capable of protecting against such variants. However, warning bells have already been ringing about plausible and unexpected corona virus mutations and the likelihood of current vaccines' effectiveness is reduced.

5.1. List of Abbreviations

SARS-Cov-2: Severe Acute Respiratory Syndrome Coronavirus 2

COVID-19: Corona Virus Disease 2019

SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus

MERS-CoV: Middle East respiratory syndrome coronavirus

WHO: World Health Organization

CDC: Centers for Disease Control and Prevention

VOCs: Variants of Concern

VOIs: Variants of Interest

FDA: Food and Drug Administration

GBS: Guillain-Barre Syndrome

ATM: Acute Transverse Myelitis

CSR: Central Serous Retinopathy

mRNA: Messenger RNA

CEPI: Coalition for Epidemic Preparedness Innovation

PHE: Public Health England

NIBSC: National Institute of Biological Standards and Controls

GISAID: Global Initiative on Sharing all Influenza Data

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How to cite this article: Devi A, Sharma I, Kumar A, Sharma S, Nanika, Bala S. Impact of Anti-COVID-19 Vaccines on Emerging Variants of COVID-19. Int. J. Appl. Pharm. Sci. Res. 2022;7(2): 24-29. doi: https://doi.org/10.21477/ijapsr.7.2.2

Source of Support: Nil.

Conflict of Support: None declared.