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COVID-19 Vaccines – Rising to the challenge of emerging viruses

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Abstract

Vaccines candidates in response to COVID-19 pandemic are the major milestones in the history of scientific research. This review article aims to provide consolidated latest information regarding the available COVID -19 vaccines globally till date.

After the publication of the genetic sequences of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) on January 11 2020, a stable, safe, highly reactive vaccine was targeted globally. In more than two years of pandemic we have more than thirty vaccines approved/authorized by various organizations each having its own advantages and disadvantages. All vaccines till date have less immunogenic capacity and less production of effective neutralizing antibody (NAb) responses. Adding to the challenge were vaccine hesitancy, pediatric age group, pregnancy, lactation, rare serious adverse events in real world evidence and emergence of variants. Data is collected from the reliable sources from the literature, by searching "COVID-19 vaccines". The related data was collected through the web search from published articles in journals and newspapers, documents of organizations like World health organization (WHO), Centre of disease control (CDC) and Global alliance for vaccine and immunization (GAVI) and literature from the manufacturers of various vaccines. Though the challenge is reached but still, the non-pharmaceutical interventions, such as social distancing, face masks, and contact tracing, will remain the mainstay of health policy strategies to reduce viral spread and limit the demands of health care settings globally. Lately continuous emergence of new variants, is creating a serious concern and warning the health authorities to be well equipped and updated.

Keywords: Challenges, COVID-19, Efficacy, Immunity, Vaccines, Variants

Introduction

Timeline overview of vaccines dates back to hundreds of years and currently more than 20 life threatening diseases are vaccine preventable [1]. The struggle for the development of safe and effective vaccine for the existing disease, had provided us with the latest technologies like reverse vaccinology, recombinant / DNA vaccines and viral vectors, but still the scientific community is struggling to handle the emerging and re-emerging viruses effectively with vaccines. The human race has witnessed two epidemics of Coronaviridae family (MERS and SARS) in the present century, [2] with significant mortality but presently no effective vaccine is available for them till date. Unfortunately another virus of the same family (SARS-CoV2) posed great threat to the humanity in December 2019, subsequently its genetic sequence was published soon, in view of urgent response with the development of vaccine, to combat the pandemic.

Vaccine antigen and Immunity

Coronaviridae family have enveloped, positive-sense, single-stranded RNA viruses with four structural proteins, (surface (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein. [3] Among these the S-protein which is expressed on the surface of the virus is the main target for vaccines. S protein is the one which binds to the host cells and plays a crucial role in eliciting the immune response during disease progression. It has two subunits, S1 and S2, S1 subunit contains a fragment called the receptor-binding domain (RBD) and mediate binding while S2 subunit mediates membrane fusion. The RBD of S protein induces neutralizing antibodies (NAbs) and T-cell immune responses which provides long term protection, by the T-cell-mediated immune responses through CD4+ and CD8+ cells. CD4+ T-cells activate B-cells which lead to the production of virus-specific antibody and CD8+ T-cells being cytotoxic, kill cells that have been invaded by the virus [4]. These neutralizing antibodies (NAbs) were demonstrated in animal studies and also in COVID-19 recovered patients, establishing the role of S-protein in immunity development. Therefore, RBD of S-protein is particularly the target for SARS-CoV-2 vaccines [5].

Collations and vaccine production

Considering the pandemic scenario of COVID–19 worldwide a safe and effective vaccine was foresighted as the appropriate and effective method to combat the pandemic. Globally, scientific communities got actively engaged and the pandemic witnessed unprecedented partnerships among multiple International alliances for vaccine development. Pioneer alliance was, COVID-19 Vaccines Global Access (COVAX) for coordinating global vaccine development [6]. COVAX is the vaccine pillar of Access to COVID-19 Tools (ACT) Accelerator, it was co-led by World health organization (WHO), Global Alliance for Vaccines and Immunization (GAVI), Coalition for Epidemic Preparedness Innovations (CEPI) and United Nations International Children's Emergency Fund. (UNICEF) [7]. Diligent efforts worldwide are evident by the number of vaccine candidates under preclinical and clinical evaluation. Few among them have been authorized by the various authorities.

Vaccine platforms

In addition to the approved/ authorized vaccines, approximately 200 more vaccine candidates are under trial for COVID-19 worldwide [7]. These vaccines are all designed to boost the immune system targeting spike glycoprotein which promotes virus entry [8]. Multiple technologies were evaluated for rapid and effective product, various categories of vaccines are in clinical trials. Whole virus vaccines (Live attenuated or inactivated virus vaccines), Subunit vaccines (protein or polysaccharide), viral vector vaccines, Nucleic acid vaccines (RNA or DNA) and Virus like particles vaccines (VLPs). Table I, is the overview of various vaccine modalities available with reference to COVID-19. [9, 10, 11]

Vaccines in various phases

According to CEPI development stages for vaccines [12] are classified as "exploratory" (early research) – this is a basic stage where planning and designing of a candidate vaccine is done, with no in vivo evaluation. In vivo evaluation includes four stages, first is preclinical stage, during which, the vaccine is prepared and evaluated for immunogenicity and protective efficacy in animal models followed by three clinical trials (phase I, II & III). In Phase I trial, vaccines are evaluated for safety, dose and any potential side effects in a small number of people and in Phase II trial, vaccine candidates are further explored for safety and efficacy on larger groups. Phase III trial – In this stage vaccine is evaluated for efficacy, safety, immunogenicity and rare side effects in larger group (thousands) of people.

Authorized/approved vaccines – More than 30 vaccines have been approved /authorized till July 2022 [13] for adults by certain national/ international regulatory authorities for emergency use, details are in Table II [14-45]. In addition, other approved vaccines are Sinopharm (inactivated vaccines), EpiVacCorona (peptide vaccine), CoviVac Russia COVID-19 Vaccine (whole-virion vaccine), WIBP-CorV (Inactivated vaccine), QazVac (Inactivated vaccine), COVIran Barekat (Inactivated vaccine), Unnamed vaccine candidate from China (Inactivated vaccine), Abdala (CIGB 66) (Protein subunit vaccine), Soberana 02, (Conjugate vaccine), MVC-COV1901 (Protein subunit vaccine), ZyCoV-D (DNA plasmid vaccine), Corbevax (Adjuvanted protein subunit vaccine), Covifenz -CoVLP (Plant-

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based adjuvant vaccine), VLA2001 (Inactivated vaccine), Noora (Recombinant protein vaccine) [13].

Booster doses

Benefits of COVID-19 vaccine boosters has been supported by two large studies [46]. Boosters are vaccines doses, given to the population that has completed their primary vaccination series, with the object to maintain vaccine effectiveness which had fallen with time. Decline in the vaccine effectiveness over time has been reported in various studies [47, 48, 49, and 50]. More than 126 countries globally, including India has introduced booster vaccination program targeting health care workers, elderly and immune-compromised population. All the authorized vaccines for COVID-19 require boosters. The concept of heterologous prime post vaccination has also been reported to be beneficial in COVID-19 vaccines [51]. Heterologous prime boost vaccination, [51] involves two different vaccine types with same or similar antigen of the target, the first and / or second dose prime the immune response and the booster is given with different vaccine type to boost the immune response. Mix and match approach has reported to increase the protective efficacy, [52, 53, 54] moreover adapting this, the use of available vaccine will be rationalized globally.

Pediatric vaccination

Queries had always been raised regarding pediatric vaccination, as kids have multiple protective mechanisms and severe illness is rarely reported in literature. [55] Moreover long term effects are yet to be explored. But trials reported that the benefits outweigh its side effects. [56] World Health Organization regulated Interim statement on COVID-19 vaccination for children and adolescents in November 2021, [57] approving the mRNA vaccine BNT162b2 for the use in children aged 5-11 years. Centers for Disease Control and Prevention (CDC) [56] also gave emergency use authorization to Pfizer Biotech vaccine for use in children 5 years and older. It had prepared a separate vaccine formulation with orange cap and small needle for pediatric group. Other vaccines like Sinovac-CoronaVac, BBIBP-CorV, ZyCoV-D, Covaxin, Covovax and Ad 26COV.2S are also being considered for trials in pediatric populations. [56, 57, 58] India started with pediatric vaccination in the age-group of 15-18 years for COVID-19 from 3rd January 2022. [59] Initially two vaccines were authorized by drug controller general of India (DCGI) for children above 12yrs of age. Covaxin (Bharat biotech) and Zycov-D (Zydus cadila) for emergency use in children. ZyCoV-D is the first, Plasmid based DNA vaccine authorized for emergency use in India. It is administered through needle-free applicator (Pharmajet), 3 doses are recommended, 28 days apart. Further Biological E's Corbevax and Bharat Biotech's Covaxin, was also approved by DCGI for children under the age of 12 years. No vaccine is yet approved for children younger than 5 years of age, though clinical trials are in progress.

COVID-19 Vaccine status in India

In response to COVID-19 pandemic, vaccine production in India had also been on Fast track. More than twenty COVID-19 vaccine candidates are in different phases of development in India, of these 10 are in phase III trial. [60] Table III [61, 62] enlists various vaccine candidates in India in various trial phases. Nation vaccination drive in India started on 16 January 2021 with AstraZeneca's Covishield. This drive was considered "World's largest vaccination drive". [63] Approximately 1, 65,000 people got vaccinated on the first day of the campaign with no major side effects. Government of India developed a mobile application app, CoWin (Covid Vaccine Intelligence Network) to manage the inoculation drive. [60] The app is made user friendly which helps in booking vaccination slots and also getting vaccination certificates easily. Till 16th July 2022 approx. 199 crores vaccination doses had been given in the country, with approx. 67% population fully vaccinated. [64] The target to alter the course of the pandemic largely depends on the successful vaccination derive.

Present VOC (Variant of concern)

The present circulating strain and the variant of concern, since November 2021 is Omicron and its various lineages. The variant had reported to have unusual "constellations of mutations" and consequently decreased response to the vaccine with original Wuhan strain [65]. Bivalent formulations was prepared to widen the spectrum of these vaccines. The results of phase trials reported by Chalkias et.al. [66] in bivalent (Wuhan strain and BA.1) vaccines indicate that these vaccines may be a new tool in the response to emerging variants.

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Bivalent formulations of the Moderna COVID-19 Vaccine and the Pfizer-BioNTech COVID-19 Vaccine got emergency use authorizations (EUAs) by U.S. Food and Drug Administration on 31st August 2022 [67].These got authorized, as single booster dose, for > 18 years for Bivalent Moderna while Pfizer-BioNTech Bivalent got approval for individuals of > 12 years of age, after at least 2 months following primary vaccination. These vaccines have two messenger RNA (mRNA) components, one from the original strain of SARS-CoV-2 and the other have a common mRNA of both BA.4 and BA.5 lineages of the omicron variant of SARS-CoV-2.

Repurposed vaccines

In this ongoing search for COVID-19 vaccine number of approved vaccines for the other viral infections were also investigated. The affectivity of these vaccines is expected to be based on the hypothesis that these vaccines may modify the response of the immune system and enhance cytokine production to provide protection against COVID-19. Various vaccines under trial were BCG, oral polio vaccine (OPV) and MMR (measles, mumps, and rubella). [4] For BCG vaccine alone, number of multi-centric randomized controlled trials are ongoing in different countries and presently the vaccine is in trial phase 2/3. Measles vaccine and OPV vaccine is in trial to evaluate its protection against COVID-19 in Egypt and USA respectively. [4]

Challenges and struggle

Normally the process of validating a vaccine or drug for use in humans take several years. But with the advent of reverse vaccinology [68] this period is condensed, and to combat this pandemic two vaccine candidates were authorized for use within a year. This provision is Emergency use authorization (EUA), which allows U.S. Food and Drug Administration (FDA), to authorize the use of unapproved medical products, to be used in an emergency to diagnose, treat or prevent serious or life-threatening diseases or conditions when there are no adequate, approved and available alternatives. [69] In COVID-19 pandemic, EUA started with diagnostics PCR, then the drug Remdesivir and lately vaccines. Pfizer-BioNTech was granted EUA on 11th December 2021 and Moderna on 17th December 2021. [69, 70] Subsequently twenty others was also approved/ authorized. [13]

Although number of nations globally have been struggling to manufacture an effective vaccine against COVID-19, concerns over the hesitation in accepting the vaccine cannot be ignored. A fraction of the population had always been hesitant for accepting vaccination, though its protective role in multiple infectious diseases is noticeable. Thus "Vaccine hesitancy which refers to either delay in acceptance or refusal of vaccines despite the existence of vaccination services." has added to the pandemic challenge [71] WHO EURO Vaccine Communications proposed "3 Cs" model (complacency, convenience and confidence) [72] to understand vaccine hesitancy, which includes factors like, doubtful safety of the vaccine, misconceptions regarding vaccination effects eg. Infertility and stunting, lack of faith in the healthcare system, fear of sharps and lower education background etc. The Tuskegee Syphilis study in African population is a historical marker, which had contributed in vaccine hesitancy. [73] The adverse reactions reported during vaccine trials had also played a major role. During COVID-19 vaccine trials death and unexplained illnesses was reported with AZD1222 and Johnson & Johnson's and Covaxin [73] though later found to be unrelated. Therefore the measures to create awareness through media regarding the advantages of vaccination is necessary to reduce the panic and doubt within the population. Awareness programs should be scientifically sound, culture sensitive, as well as ethnically acceptable in the given population.

Despite all the hurdles, handful of COVID-19 vaccines were approved for vaccination in human population globally. Three main vaccines were from Pfizer, Moderna and Oxford. Though vaccination drive in many countries started early in 2021, aiming to end pandemic, still there were many unanswered questions regarding the protective period, adverse effects, efficacy and transmission of virus post vaccination. To answer these questions the use of vaccines had to be closely monitored at both at national and international level. For this various systems were formed in many countries like- Vaccine Adverse Event Reporting System (VAERS) in U.S. [74] and Adverse Events Following Immunization (AEFI) in India. [75] These systems are supposed to register any serious side effects or unexpected

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reactions post vaccination and subsequently their relatedness whether significant or co-incidental, to be analyzed. The results of vaccination are positive worldwide except some minor acute events. Side effects reported were redness or tenderness at the site of injection, fatigue, headache, muscle aches, chills, joint pain, and possibly some fever. These mild symptoms are body's immune response, to the vaccine. According to some observational studies [75, 76] the risk of acquiring COVID-19 after 12-14 days post vaccination is decreased, and if acquired will be less severe.

Despite successful results, the continuous emergence of variants is raising concerns about the limited effects of vaccines. These variants and viral mutations are being routinely monitored globally through sequence based surveillance and epidemiological investigations. Based on their transmissibility, disease severity and treatment response they are classified into three classes of SARS-CoV-2 variants by CDC Variant of Interest, Variant of Concern and Variant of High Consequence. [77] Variant of Interest are Eta (B1.525), Iota (B1.526), Kappa (B1.617.1) and Mu (B.1621). [77] These are **associated with changes in receptor binding, reduced neutralization by antibodies formed, increase transmissibility, disease severity, reduced treatment response and doubtful diagnostic results.** Variant of Concern (VOC) are Alpha (B1.1.7), Beta (1.351), Delta (B1.617.2) and Gamma (P.1). [75] Lately in November 2021, WHO designated B.1.1.529 also as a VOC and named it Omicron. [78] These variants have the **evidence of significant reduction in neutralization by antibodies generated, increase disease transmissibility, more severe disease with increased hospitalizations or deaths, reduced effectiveness of treatments or vaccines available and failure in diagnostics.** Variant of High Consequence have **clear evidence of reduced effectiveness of** preventive or medical countermeasures (MCMs) relative to previously circulating variants. [77] Currently, no SARS-CoV-2 variant is in this class.

Different vaccines are being scheduled, in different parts of the globe, depending on the availability and storage capacity of the countries. More than two vaccines are also been given in some countries, but only one type is given to a particular person, except in Europe where mix and match approach has been reported. [79] They started their vaccination drive with AstraZeneca, but with subsequent reports of the cases of thrombosis and thrombocytopenia syndrome its use was halted. These partially vaccinated population had the option of completing their vaccinations either with Pfizer or Moderna vaccine. Fortunately mixed-dosing demonstrated increased immunogenicity including both humoral and cellular responses to SARS-CoV-2. Subsequently mouse model studies was done with combination of three vaccines (adenovirus vectored vaccine, inactivated vaccine and recombinant subunit vaccine) and two vaccines (adenovirus vaccine and mRNA vaccine). [80] Responses elicited by heterologous prime-boost immunization significantly improved the Neutralizing Ab response but the trials in humans are needed to confirm the increased immunogenicity without significant adverse effects.

Tables and Figures

Table I - Overview of various vaccine modalities with reference to COVID-19 [9, 10]

Vaccines Category	Mechanism	Immune response	Advantages	Disadvantages	Vaccine candidates

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Live attenuated whole virus vaccine	Weakened version of the whole target pathogen is used.	Cellular immunity with both B and T cells.	Simple to manufacture. Produce immunity against all proteins, therefore may protect against all variants.	May revert to pathogenicity causing vaccine derived disease. Temperature sensitive.	Inhalational vaccines – COVI-VAC, MV-014-212, T-COVIDTM.
Inactivated whole virus vaccine	Genetic material of the micro-organism is destroyed, but the viral antigens are intact.	Only antibody mediated response is stimulated.	Micro-organism, cannot replicate and are unable to cause disease. Safe stable and do not require stringent storage facilities	Immune response generated is weaker and shorter. Require repeated boosters.	CoronaVac, Sinopharm, CoviVac, Covaxin, WIBP, QazVac, COVIran.
Viral vector vaccines	Genetically engineered vaccines with attenuated viruses used as vectors to deliver genetic code for antigens/ proteins.	Cellular immunity with both B and T cells.	Highly specific delivery of genes to the target cells with efficient gene transduction. Induction of robust immune responses, and increased cellular immunity. Easy to manufactured.	May cause genotoxicity. Potential for tumorigenesis is of concern.	Covishield, Sputnik-V, Sputnik light, Convidicea, JNJ etc.
Subunit vaccines	Only the very specific parts (the subunits) of a virus or bacterium that the immune system needs to recognize is used.	Only the antibody-mediated response is produced.	• Well-established technology. • No risk of the vaccine triggering disease (no live components). • Relatively stable.	• Complex to manufacture. • Adjuvants and booster shots may be required as immune response generated is weak.	ZF2001, Abdala, Soberana, MVC-COVI901.

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Nucleic acid vaccines Ribonucleic acid (RNA) & Deoxyribonucleic acid (DNA)	Genetically engineered RNA or DNA is used from the disease causing pathogen.	Induces both humoral immunity and cell-mediated immunity	No risk of acquiring vaccine derived disease as no live components are used. Low production cost.	New technology of developing vaccines therefore long term safety yet to be ensured. Requirement of ultra-cold storage.	Pfizer (RNA), Moderna (RNA), ARCoV (RNA), and ZyCoV-D (DNA).
Virus like particles vaccines (VLPs) [11]	Molecules that mimic the conformation of native viruses but are not infectious as they lack the viral genome.	Elicit both the antibody- and cell-mediated immune responses.	Potential to target Dendritic Cells is a main advantage of VLP vaccines, for activating the innate and adaptive immune responses, provide stronger and longer-lasting protection. Lack viral genetic material, therefore non-infectious.	• Complex production process. Risk of incorrect folding & assembly rendering the vaccine ineffective.	VIR-7831, ABNCoV2, EuCorVac-19, IVX-411, VBI-2902a

Table- II - Details of Approved/ Authorized vaccines for adult use.

Vaccine	Type	Storage	Dose schedule	Efficacy	Effect on variants	Cost [17]
Pfizer-BioNTech (Comirnaty) [14, 15, 16] - first FDA-approved COVID-19 vaccine.	Lipid nanoparticle–formulated, nucleoside-modified RNA (mod RNA) vaccine BNT162b2, encoding full-length spike protein of SARSCoV-2.	Require minus 70 degrees Celsius, once thawed to be used within five days.	Two doses intra-muscularly at 14-day interval.	95% efficacy after two doses	Alpha (B1.1.7) - 89.5% and 93.7%. Beta (B1.351) – 75%, and 88.0% in Delta variant. [18, 19] Neutralization effects against strains like B.1.429 (epsilon), B.1.526 (lota) [20] and B.1.617 (kappa) variant [21] are also elicited, expecting to be effective.	$19.5 (Rs 1,440) per dose.

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Moderna Spikevax (mRNA-1273) [22, 23] - successful results of various stages of the vaccine was published in The New England Journal of Medicine (29th September, July 28 and July 14).	Lipid nanoparticle (LNP)-encapsulated, Messenger ribonucleic acid (mRNA) based vaccine, encoding for stabilized form of the Spike (S) protein (S-2P antigen).	Require minus 20 degree Celsius for long term storage, remains stable at 2 to 8 degrees Celsius, for up to 30 days.	Two intra-muscular doses 28 days apart.	80% effective 14 days after the first dose and 90% effective 14 days after the second dose. [24]	Alpha (B1.1.7) - 100% and 96.4% - Beta (B1.351) [25] Neutralizing effect against all COVID-19 emerging variants, including beta, delta, eta and kappa variants has been elicited. [26]	$25 (Rs 1840)/ dose
Covishield (AZD1222) [13] – Vaccine trials paused twice in July and September but restarted soon after FDA reviewed all safety data from trials globally.	Recombinant replication-defective chimpanzee adenovirus vector (CdAd3, CdAd63) vaccine, expressing the SARS-CoV-2 surface glycoprotein.	Stored and transported at 2 to 8 degree Celsius.	Two doses are recommended 4-12 weeks apart intra-muscularly.	Efficacy is 76% and reduces hospitalizations by 94%, 15 days after vaccination. [27]	Alpha (B1.1.7) - 74.5% and Delta (B.1.617.2) - 67.0%. [28] Efficacy against the Omicron SARS-CoV-2 variant (B.1.1.529) is under trial.	$3 (Rs 220.68) per dose.
Sputnik V [29, 30] It is the world's first registered COVID-19 vaccine, named after the first Soviet space satellite. It is unique, as two vector (rAd26 and rAd5) based technology is used.	Heterologous recombinant adenovirus using adenovirus 26 (Ad26) and adenovirus 5 (Ad5) both for the first and second vaccination dose respectively.	Stored at temperature of minus 18 °C or below.	Two doses Intramuscularly, with a 21-day gap.	Efficacy reported is 91.6%. [31] Induces both humoral and cellular immune response.	Produces protective neutralizing titers against variants like Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617) and two local variants in Moscow. [32]	$10 (Rs 735).
CoronaVac [33, 34] by Sinovac Life Sciences (Sinovac LS). Phase III trials was in Brazil, Chile, Indonesia, Philippines, and	Formalin inactivated SARS-CoV 2 virus.	Transported and refrigerated between 2 and 8 degrees and can remain stable up	Two-doses schedule, at 28-day intervals, intra-muscularly in deltoid muscle.	Efficacy reported to be 66% against symptomatic COVID-19, 88% against	It is equally effective against the B.1.1.7 variant but less effective against B.1.351 [36] and does not appear to be effective against the Gamma P.1	

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Turkey.		to three years, at this temperature.		hospitalization, 90% against ICU admissions, and 86% against deaths, [35] after second dose.	variant. [37]	
JNJ-78436735 (Ad26.COV2.S) [38] vaccine is developed by Janssen Pharmaceutical Companies in collaboration with Johnson and Johnson (J&J).	Ad-Vac technology with Adenovirus serotype 26 (Ad26), a non-replicating viral vector	Stored at 2 to 8 degrees Celsius, till vials are opened.	A single intramuscular injection is recommended.	Efficacy of 85.4% against critical illness and 93.1 % against hospitalization. [39]	Low neutralizing titer have been elicited against the B.1.351 (Beta), B.1.617.2 (Delta), B.1.617.2 + AY.1 (Delta Plus), and C.37 (Lambda) variants.[40]	$10 per dose
ZF2001 COVID-19 Vaccine manufactured in the CHOZN CHO K1 cell line. [41]	Protein subunit recombinant vaccine using a dimeric form of the receptor-binding domain (RBD) as an antigen.	Stored at 2 to 8 degrees Celsius	3 doses Intramuscular over a period of 2 months.	Efficacy of 82% against the disease severity. [41]	Neutralization activity of ZF2001 found it to be effective against all Alpha (B.1.1.7 lineage), Beta (B.1.351 lineage), Gamma (P.1 lineage), Delta (B.1.617.2 lineage), Epsilon (B.1.429 lineage), Eta (B.1.525 lineage) and Kappa (B.1.617.1 lineages).[42]	
Covaxin (BBV152) [43] is developed in collaboration with the Indian Council of Medical Research (ICMR),	Whole-virion inactivated SARS-CoV-2 Vaccine (BBV152)	Stored at a temperature range of 2 to 8 degrees Celsius	Vaccine has two dose vaccination regime, 8 days apart, with IgG2 antibody	ICMR announced 77.8% overall efficacy and 93.4% efficacy a	Effective against the B.1.1.7 (Alpha) and B.1.617 (Delta) variant. [45] Trials for the efficacy of others variants are	₹275 per dose

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National Institute of Virology (NIV) and Bharat Biotech.			response.	gainst severe COVID-19. [44]	ongoing.	

Table III - Vaccine candidates in India in various trial phases. [61,62]

Vaccine candidate	Collaborators	Trial phase
COVAXIN- whole-virion inactivated SARS-CoV-2 Vaccine (BBV152)	Bharat Biotech in collaboration with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV).	Phase III clinical trial. DCGI approval for pediatric study trials. WHO issued an emergency use listing (EUL) in November 2021. [62]
Covishield (AZD1222) recombinant vaccine using adenovirus vector	Serum Institute of India (SII) and Indian Council of Medical Research (ICMR).	Approved in India.
ZyCoV-D – DNA vaccine	Cadila Healthcare Ltd. (Zydus Cadila) and Department of Biotechnology, India	DCGI approval for Phase III Human Clinical Trials
Sputnik V- recombinant vector based vaccine (Human adenovirus vector)	Dr Reddys Laboratories Limited and Sputnik LLC. Developed by Gamaleya Research Institute, Russia.	Phase II/ III clinical trials
Moderna COVID-19 Vaccine (mRNA-1273) - mRNA-based vaccine.	Moderna, BARDA, NIAID	Approved in India
Janssen (JNJ-78436735; Ad26.COV2.S) - Non-replicating viral vector vaccine	Janssen Vaccines (Johnson & Johnson)	Approved in India
Biological E's novel (BECOV2A/2B/2C/2D) Recombinant protein vector based vaccine.	Biological E. Limited	Phase I/ II clinical trial
BBV154 - intranasal vaccine	Bharat Biotech	Phase I Human Clinical Trial
NVX-CoV2373- protein subunit vaccine	Serum institute of India, Pune and Novavax.	Phase III under consideration.
COVOVAX recombinant spike protein nanoparticle vaccine	Indian Council of Medical Research and Serum Institute of India.	Phase II/ III clinical trial
HGCO-19- mRNA based vaccine	Gennova Biopharmaceuticals	Phase I/II Human Clinical Trial

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	Limited.	
Inactivated rabies vector platform	Bharat Biotech. International Ltd. Hyderabad and Thomas Jefferson University, USA.	Pre-clinical (advanced)

Conclusion

It is too early to know whether the COVID-19 vaccines will provide effective and long-term protection. Though the authorized vaccines are claiming promising results and have brought hope in the long fight against the coronavirus, but the WHO experts are of the opinion that vaccine on its own will not be sufficient to end this pandemic, we cannot afford to guard down the other precautionary measures like continue wearing masks, physically distancing and avoiding crowds. Further research and trials are needed to be sure of the safety of these vaccines, their doses, immune response and effect on emerging variants. Moreover it is still not clear the degree to which the vaccines can protect us, not only against the disease but also against infection and transmission of SARS-CoV-2 and its emerging variants.

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