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Review Article

COVID-19: VARIANTS, VACCINES, AND ADVERSE REACTIONS

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ABSTRACT

Coronavirus Disease 2019 (COVID-19) not only jeopardized the health condition of humankind but also bruised the economy. Researchers found several dominant and predominant strains of the coronavirus and variants, in which B.1.1.7, B.1.351, and P.1 being the most prevalent. In all the variants of severe acute respiratory syndrome coronavirus 2, modifications occur in the spike protein deciphering variants that differ based on characteristics and properties such as the extent of virulence, severity of the disease, or probability of reinfection. The development of a vaccine against the pandemic causing COVID-19 is considered a major milestone in the history of vaccines due to the speed at which the vaccine was made. The vaccine against COVID-19 vaccines are classified under nucleic acid vaccines, protein-based vaccines, viral vector vaccines, and whole virus vaccines. At present, there are 22 vaccines approved under the category of emergency use authorization. COVID-19 prevention has been the main principle behind early vaccine availability, although none of the approved vaccine candidates have completed large scale clinical trials to evaluate the efficacy. This review presents a brief idea on types of COVID-19 vaccines, approved vaccines, and vaccine candidates under development.

Keywords: Vaccines, COVID-19, Immunology, Infectious diseases, Approved vaccines.

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INTRODUCTION

Coronavirus Disease 2019 (COVID-19) pandemic has created a whirlwind of fear not only among the vulnerable people in the society such as adults aging above 60, people with other underlying complications, and the economically backward class but also healthy and economically sound individuals [1,2]. Based on the severity, three categories of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants are seen, namely, variant of concern (VOC), variant of interest (VOI), and variant of high consequence. The variants that come under the category of VOC are B.1.1.7, B.1.351, B.1.427, B.1.429, and P.1.Variants coming under VOI are B.1.525, B.1.526, B.1.526.1, B.1.617, B.1.617.1, B.1.617.2, B.1.617.3, and P.2. In the present scenario, no SARS-CoV-2 variant has emerged to a state of high consequence [3]. So far, 22 vaccines have been authorized across several countries [2,3]. Few drugs such as hydroxychloroquine and remdesivir have been approved for Emergency Use Authorization (EUA) as desperate measures to fight COVID-19 [4,5]. Increased rates of immunization may prevent another wave of infection and might control seasonal outbursts [3,6-8].

COVID-19 IMMUNOLOGY

COVID-19 is an infectious disease that mainly affects the respiratory system and is caused by SARS-CoV-2 virus [14]. Countries across the world have made their ways to stop the spread of pandemic by setting up isolation wards, canceling large gatherings, shutting down travel, and by closing of schools temporarily [5,7]. Coronaviruses are spherical, single-stranded positive Riboxynucleic acid (RNA) viruses composed of matrix proteins. The name coronavirus is derived from the Latin word corona, meaning "crown" referring to the spike-like surface protein projections on the surface of the virus [1,9-13]. Numerous glycosylated-S proteins are present on the surface of CoV2 virus that helps in mediating viral entry by binding to the host cell receptor such as angiotensin-converting enzyme 2 (ACE2). Whenever the S protein binds to the receptor, a transmembrane protein serine 2 activates the S protein promoting the entry of virus into the cell. On the entry, the viral RNA is released into the cell, translation of the polypeptide from the RNA genome occurs, further replication and transcription through the cleavage of protein, and finally the complex assembly of replicase-transcriptase, after which the viral particles are released [14-18]. The S protein in CoV2 is highly regulated in receptor identification, attachment, and entry of virus into the host cells which represent an important target in the COVID-19 vaccine search [16,18]. As an emergency measure in response to the COVID-19 pandemic, the first trial in humans targeting the S protein was started on March 16, 2020 under the category of mRNA based vaccine [17,19-21]. In the process of developing a vaccine against COVID-19, the S protein and it's subunit (S1) which has the receptor binding domain is being frequently worked on as vaccine antigens as it has the ability to release neutralizing antibodies that can deny the entry into the host cell and thereby preventing infection [16,18,19].

KEY POINTS TO CONSIDER IN VACCINE DEVELOPMENT

To develop a potent and safe vaccine against COVID-19, few factors need to be considered about SARS-CoV-2 and its immune response against the vaccine and the infection [23,30].

Type of mutation

Several variants of SARS-CoV-2 have been reported globally in this pandemic. There are around 30,000 letters of RNA included in one SARS-CoV-2, which enables the virus to attack and replicate. However, these mutations are found to be slow and mild, and mutants nearly replicate similar sequences as in the parent strain providing us with a relief in the development of vaccines [22,23].

Immune response

Blood analysis of COVID-19 recovered patients have shown to possess antibodies against SARS-CoV-2 virus. Studies report that neutralizing antibodies may decrease or disappear after 3 months from recovery. Researchers need to focus on the strength and the nature of response of the vaccines toward the virus and its effect on the immune system [15,17].

Reinfection probability

Question seems to arise on how long any immunity can last if reinfection occurs. Concerns on the possible mechanism of reinfection in a person who has already been infected once before seem to hang

in the air. The possible mechanism of reinfection by the virus would be by targeting the memory B-cells specifically and killing them [24]. Over time, we have to create new vaccines and revaccinate people, but if the virus interferes with the immune memory; then, we might be in trouble and the reinfection rate may increase. An epidemiological study on 1,300 individuals conducted by Indian Council of Medical Research reported that 4.5% of people have been found to be reinfected, raising concerns on the potential of the vaccines [24,25]. Another study in the UK has identified that the antibodies developed against the coronavirus declines swiftly post-recovery from COVID-19 indicating the risk of reinfection is more [26].

Duration of resistance

The delay or the time gap between the doses of vaccines especially due to the current situation is a worry factor associated with immunity against the virus. Antibodies, T-cells, and B-cells have been found in people who have recovered from COVID, but the reports on how long it can last after the infection remains unclear. Reports of reinfection have raised doubts on the duration of immune response to the virus [27,28].

Antibody-dependent enhancement (ADE)

Studies have shown that when the patients are infected with one variant of the virus, they produce neutralizing antibodies against it, but when they are later infected by another variant of the same strain of virus, the former antibodies will not be able to neutralize the virus. These types of non-neutralizing agents are responsible for ADE [22,29].

VACCINATION STRATEGIES

Different vaccination strategies have been proposed to develop a vaccine against COVID-19. Fig. 1 shows that the vaccination strategies involved in developing a vaccine against COVID-19.

Nucleic acid vaccines

They are the newer technology vaccines. It is made up of the genetic code similar to COVID-19 virus that regulates the production of the spike protein of the virus. There are two types of vaccines: Deoxyribonucleic acid (DNA) vaccines and RNA vaccines. DNA vaccines should reach the nucleus of the host cells, whereas RNA vaccines should reach only the cytoplasm of the host cell [30-32].

DNA vaccines

The genetic material of SARS-CoV-2 virus is taken, it undergoes transcription to form mRNA and then at the nucleus of host cells translation takes place; then, it codes for the spike protein. Thus, the immune system recognizes the spike protein thus producing antibodies against the spike protein. The antigen-presenting cell (APC) is the prominent target cell to receive the genetic material. Myocytes also play an important role. After translation, the protein is then made up into peptides then it binds to major histocompatibility complex (MHC) class I or II. MHC I is taken to the surface of a macrophage by myocytes and MHC II is taken to the surface of a macrophage by dendritic cells, thus presentation of cells to CD4+ and CD8+ T-cells [31]. It is stable and can be prepared and produced easily in bulk quantities [33-35].

RNA vaccines

In RNA vaccines, the vaccine contains mRNA that encodes the antigen. When it reaches the cells, the mRNA gets translated into proteins called the antigens thus recognized by the immune system. The mRNA can be synthesized using a DNA template in a cell free system. The naked mRNA cannot enter the cytoplasm and can be degraded easily. Thus, they are encapsulated in lipid nanoparticles. RNA strands get degraded after the antigens are made [36]. RNA vaccines are cheaper, easier, and safer to produce [37,38].

Protein-based vaccines

This is the conventional form of vaccines. They are easy and cheap to produce. Its efficiency is limited and can produce an unbalanced immune response [39].

Protein subunit

It uses fragments of COVID-19 viral particles such as the spike proteins. They are not capable of causing disease to the host cells, but the immune system may not recognize them or produce weaker immunity. Adjuvants are added, which helps to produce stronger innate immune response and activates the APCs and improves the presentation of antigen to the CD4 T helper cells[39-41].

Viral like particles

They have similarity to that of a virus but are non-infective without genetic material of the virus. They contain viral surface proteins that consist of viral epitopes which produce stronger T-cell and B-cell immune responses [42-46].

Viral vector vaccines

They are newer technology vaccines. The vector virus used for vaccine production is harmless and contains the genetic part of SARS-CoV-2 virus which helps transport the antigen to targeted regions [47]. They can directly infect APCs. They may induce prior immunity to the vector [47,48].

Non-replicating viral vector

They can induce immune response but cannot replicate in the host cells. The various vectors which are used to make vaccines include adenovirus, measles virus, and parainfluenza virus. Adenovirus is used frequently to manufacture vaccines which produce both antibody

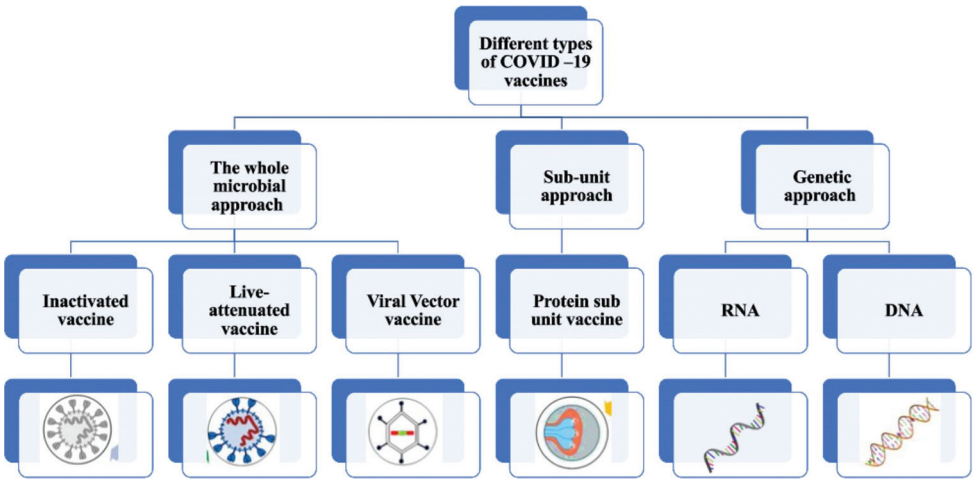

Fig. 1: Classification of COVID-19 vaccines

mediated as well as T-cell mediated immune response. To synthesize non-replicating viral vectors of adenovirus, E1A and E1B genes replaced with transgene expression cassette [48].

Replicating viral vector

The virus is alive and has the ability to divide and can produce high immune responses since they sustain in the body for longer duration and can infect cells. The vaccine also contains the viral proteins that enhance the immune system which produces more antibodies and immunity for a longer period of time [48-50].

Whole virus vaccines

It is synthesized using a weakened or inactivated COVID-19 virus. They can be easily synthesized, but the disadvantage is that irrelevant antigen may produce the immune response [51,52].

Live attenuated vaccines

Attenuated vaccines are formed by reduction in the virulence of the virus but making it alive [53]. It is more effective than inactivated vaccines [54-56]. It has the capability to activate the immune system by stimulating toll-like receptors such as TLR 9, TLR 7/8, and TLR 3 thus activating CD8 T-cells, CD4, and B-cells [57].

Inactivated virus vaccines

Inactivated viral vaccines also called whole-killed vaccines are in the form of pathogens without any ability to infect or replicate but have the capability to activate the immune system. The vaccine exposes the same type of epitope of the desired virus, which, thus, produces the immune response [49,58,59]. The pathogen is inactivated either by chemicals such as formaldehyde or heat or radiation. Ghost techniques can also be done by gentle poring method, in which the cell contents are emptied which assures the safety of the vaccine [60].

APPROVED VACCINES

Understanding the need to develop and provide safe and potent vaccines against COVID-19, FDA has been utilizing various companies to facilitate vaccine availability at the earliest. At present, there are 22 vaccines approved by FDA under the category of EUA, as shown in Table 1. There are also few COVID-19 vaccine initiatives that are happening under different health regulatory agencies in different countries such as OWS, ACTIV, COVPN, and COVAX [2,3,61-65].

Lineages of SARS-CoV-2

A mutation in the spike protein results in the development of multiple variations, three of which have distinct properties such as ease of transmission and longer infection duration [66]. B.1.1.7, B.1.351, and P.1 were the variants' names. VOC-202012/01 or 201/301Y, a prominent circular variant of SARS-CoV-2, was redesigned from variant of investigation to VOC. V1, also known as B117, began spreading from England in September 2020 [67]. Due to a major change in the receptor-binding domain's conformation caused by a mutation in the N5014 S protein, this strain swiftly affects the immunocompromised. There are 13 additional mutations that cooccur, the most significant of which is the deletion at positions 69 and 70. This strain is feared due to its rapid transmission rate; mutational variations in the spike proteins, primarily the N501Y mutation paired with the 60–70 deletion, are responsible for the increased seizing ability. Scientists found a total of 23 mutations in the Wuhan strain (just eight of them in the spike region), so this cannot reduce vaccine-induced immunity, because it requires the virus to be modified in large numbers [68]. The disease caused by B.1.17 is now efficiently treated, due to the ease with which the deletion in position 69–70 can be detected using the quantitative polymerase chain reaction test [69]. B.1.351, also known as 501Y.V2, was discovered in the early October 2020 in South Africa [70,71] and contains nine spike mutations, as well as the D614G mutation, which includes three mutations in the receptor-binding domain, a group of mutations in the N-terminal domain, and a single mutation in the furin cleavage site [70]. Unlike the B.1.1.7 lineage, there is no evidence of deletion at position 69/70. Recent research has discovered that one of the spike mutations, E484K, is resistant to neutralization by vaccine sera and convalescent plasma, posing a danger to the efficacy of monoclonal antibody therapy, and current vaccines for disease prevention. In mid-November 2020, the third dangerous Variant, P.1, was discovered for the 1st time in Brazil [72]. The spike protein in this strain undergoes ten mutations, eight of which are attributable to positive selection. When compared to the other two strains, the P1 strain is lethal, because it is 1.7–2.4 times more transmissible, resulting in a 1.2–1.9 times higher death rate. Aside from the three strains listed above, two more strains, B.1.427 and B.1.429, were discovered in February 2021 in California (thus the moniker CAL-20C) [68]. The spike (S) glycoprotein, which contains the receptor-binding domain (RBD) and the N-terminal domain (NTD), which are the two main targets of neutralizing antibodies, is responsible for SARS-CoV-2 entrance. L452R mutation in RBD and S13, W1S26 mutation in NTD are among the strains that fall under the "VOC" category. These variations are highly contagious, according

Table 1: List of approved vaccines

S. No.	Developer	Vaccine	Mechanism	Country
1.	Anhui Zhifei Longcom	RBD-Dimer	Protein Subunit	China, Uzbekistan
2.	Bharat Biotech	Covaxin	Inactivated	India
3.	CanSino	Ad5-nCoV	Non-replicating Viral Vector	China
4.	Chumakov Center	CoviVac	Inactivated	Russia
5.	FBRI	EpiVacCorona	Protein Subunit	Russia
6.	Gamaleya	Sputnik V	Non Replicating Viral Vector	Russia
7.	Janssen (Johnson & Johnson)	Ad26.COV2.S	Non Replicating Viral Vector	Netherlands, US
8.	Kazakhstan RIBSP	QazVac	Inactivated	Kazakhstan
9.	Minhai Biotechnology Co	SARS-CoV-2 Vaccine (Vero Cells)	Inactivated	China
10.	Moderna	mRNA-1273	RNA	US
11.	Oxford/AstraZeneca	AZD1222	Non Replicating Viral Vector	UK
12.	Pfizer/BioNTech	BNT162b2	RNA	Multinational
13.	Serum Institute of India	Covishield	Non Replicating Viral Vector	India
14.	Shifa Pharmed Industrial Co	COVID-19 Inactivated Vaccine	Inactivated	Iran
15.	Sinopharm (Beijing)	BBIBP-CorV	Inactivated	China
16.	Sinopharm (Wuhan)	Inactivated (VeroCells)	Inactivated	China
17.	Sinovac	CoronaVac	Inactivated	China
18.	Takeda	TAK-919	RNA	Japan
19.	Gamaleya	Sputnik Light	Non Replicating Viral Vector	Russia
20.	Center for Genetic Engineering and Biotechnology	CIGB-66	Protein Subunit	Cuba
21.	Medigen	MVC-COV1901	Protein Subunit	Taiwan
22.	Zydus Cadila	ZyCoV-D	DNA	India

to studies, and current generation vaccinations are ineffective. The variations B.1.525 (from Nigeria) and B.1.526 (from New York) cause the spike protein to alter in several ways. In B.1.525, the E484K mutation decreases the host's immune response, and a substantial Q677H mutation is also present, but its advantage on the virus is yet to be described. Similarly, virologists discovered that the E484K mutation in B.1.526 reduces the host's immunity, while the S477N mutation improves the virus's capacity to connect to the host cell. B.1.526.1, which was first discovered in New York in October 2020, has eight spike mutations [73]. Researchers were concerned about this variation due to the possibility of vaccination resistance. The B.1.617 lineage, also known as G/452R.V3, was first discovered in India in October 2020. There are 13 mutations in the spike protein, three of which are particularly concerning: P681R, L452R, and E484Q. In comparison to other versions, the E484Q mutation allows the virus to easily elude the immune system. Due to its strong affinity, the L452R mutation reduces the ability of the host's immune system to recognize the virus, whereas P681R is responsible for the increase in infectivity rate. When looking at the mutations in the sub lineages, B.1.617.2 had an extra T478K mutation not found in the other two [74,75]. P618R, L452R, and E484Q mutations are found in B.1.617.3, but not in B.1.617.2. The P2 variety, which originated in Brazil, is made up of five spike protein mutations, one of which is E484K, and it is found all across the country [72,76].

ADVERSE EVENT REPORTS AND EFFICACY OF COVID-19 APPROVED VACCINES

It is very important to establish the safety and efficacy of COVID-19 vaccines.

Sputnik

Two forms of the heterologous COVID-19 vaccine (frozen and lyophilized) were tested in a two phase non-randomized studies in Russia. The adverse events include pain at the site of injection, afterward by headache, hyperthermia, and joint pains. The threshold of virus neutralizing antibodies in participants vaccinated with Sputnik V is 1.3×–1.5× higher than the amount of antibodies in COVID-19 recovered patients. The phase 1 and phase 2 clinical trials of sputnik were completed on August 1, 2020. Every one of the participants are doing well, and no unexpected or unwelcome side effects have been observed. The vaccine elicited a powerful immune response. After receiving the vaccine, not a single participant in the existing clinical trials became infected with COVID-19. It was developed by Gamaleya National Research Institute of Epidemiology and Microbiology in Russia [77-79].

Pfizer-BioNtech

On December 11, 2020, the Pfizer-BioNtech mRNA vaccine was given approval as EUA for COVID-19 to be administered as two doses separated by 21 days based on the phase 1/2/3 clinical trials. Pfizer-BioNtech mRNA vaccine asserted 95% effectiveness in preventing COVID-19. Symptoms such as fever, joint pains, and chills were observed after the second dose. Post-vaccination allergic reactions and anaphylaxis were reported. The early data from December 14 to 23, 2020 have reported 21 cases of anaphylaxis and less severe non-anaphylaxis reactions after administration of 1,893,360 doses of the vaccine. Seventeen patients were treated in the emergency department and four were hospitalized. Most of the reported anaphylactic cases of the vaccine were seen in women [80,81].

Covaxin

It is developed by Bharat biotech, in collaboration with ICMR, and the vaccine was authorized for emergency use on January 3, 2021 by India's drug regulatory authority, the Central Drugs Standard Control Organization. The vaccines phase1 and phase 2 clinical trials data show no major adverse events other than fatigue, body ache, vomiting, and chills were reported. Two doses (3/6 μg) were administered to 380 participants as a part of phase 1 clinical trials in a double blind randomized-controlled manner. Seventeen people had shown injection related reactions mainly at the site of the vaccine shot and 23 participants exhibited body pains and fever. After the second dose also, similar adverse events were reported [82,83].

Moderna

On December 18, 2020, FDA approved Moderna under EUA against COVID-19 in individuals aged above 18 years. It belongs to the category of mRNA vaccine and is given in the dose of 100 μg with 28 days of gap from the first dose. The vaccine has shown an efficacy rate of 94.1% against COVID-19. In the phase 1, clinical trial of the moderna vaccine adults aging from 18 to 55 was administered with the three concentrations (25 μg, 100 μg, and 250 μg) with 15 participants in each group of the 45 in total and the adverse events reported were from mild-to-moderate which included myalgia, fatigue, chills, and pain at the injection site. The adverse reaction rate was found to be 33% in 25 μg, 67% in 100 μg, and 53% in 250 μg. Unsought events reported during clinical trials are lymphadenopathy, hypersensitivity reactions, delayed reactions at the injection site, and bell palsy [84,85].

CoronaVac (Sinovac life sciences)

CoronaVac is an inactivated type of vaccine produced by Sinovac Biotech and is a two-dose vaccine which is recommended for individuals aged above 18. It has shown to have an efficacy rate of 50.4% in preventing symptomatic infection. The endpoint in terms of safety and efficacy for both the phases was the incidence of any adverse reactions within 28 days of vaccination in participants who have at least received one dose of test vaccine. The participants were classified as 3μg, 6μg, and placebo groups and the incidence of adverse events was found to be 13%, 17% and 13%, respectively, in phase 1. The majority of adverse events reported from participants were from mild-to-moderate and almost all patients recovered within 48–72 h of occurrence except one participant in 6 μg, a group who had an acute hypersensitivity reaction which was manifested as urticaria. In phase 2, the rate of adverse reaction was 19%, 19%, and 18% in 3 μg, 6 μg, and placebo groups, respectively. The most common side effects were pain at the site of injection which was observed in 62 participants out of 300 [86,87].

Janssen Ad26.COV2.S COVID-19 vaccine

Also called Johnson and Johnson, COVID-19 vaccine was developed by Janssen vaccine, Netherland and belongs to the viral vaccine type. Clinical trials were initiated in June, 2020 and the ongoing phase 3 trials involved 43,000 people. The efficacy of the vaccination was found to be 66% in preventing symptomatic COVID-19 and has an 85% efficacy in preventing COVID-19 severity and 100% efficacy in preventing hospitalization or death caused due to the disease. The adverse cases reported include hypotension, bilateral nephrolithiasis, legionella pneumonia, multiple sclerosis, and a case of fever leading to hospitalization. Commonly seen side effects include pain at the site of injection, thrombosis with thrombocytopenia, allergic reactions that included anaphylaxis, capillary leak syndrome, and Guillain–Barre syndrome [88,89].

AZD1222

Also known as ChAdOx1 nCoV-19 vaccine. The vaccine developed by Oxford university. It consists of non-replicating adenovirus from chimpanzees that consist of structural surface glycoprotein of SARS-CoV-2 virus [90]. Phase 1 clinical trial was in the UK on April 23, 2020 among healthy adults aged 18–55 years. The trials were also conducted at Brazil, Kenya. Phase 2 was conducted among older adults >56 years [91]. In phase 3, population with comorbidities, we also included [90]. The vaccine efficacy is 90% when administered with low dose in first dose and standard dose in boost dose [92,93]. The vaccine has a good safety profile and after the second dose has a higher antibody titer. Adverse effects such as hemolytic anemia, transverse myelitis, fever, and multiple sclerosis were reported by the population [93].

Covishield

Covishield is a non-replicating vector vaccine. Also known as ChAdOx1 nCoV-19 coronavirus vaccine. The vaccine adverse events were monitored in northern India such as Varanasi, Durgakund. The second dose timing was changed from 28 days to 12 weeks. Fever, headache, dizziness, pain in injection site, and malaise body pain were most common adverse event [94]. In Nepal Oxford/AstraZeneca, COVID-19 AZD1222 (Covishield) vaccination was conducted and observed the adverse events. Mood irritability, fever, tenderness at injection site, myalgia, nausea, fever, chills, myalgia, and head heaviness are the adverse events reported [95].

BBIBP-CorV

It is an inactivated vaccine and is a mature technology. This method is also used for the prevention and control of influenza and poliovirus [96,97]. Phase 1 was from April 29, to June 28, 2020. The most common adverse event was pain on injection site, swelling, induration, fever, fatigue, mucocutaneous abnormalities, and mild-to-moderate abnormality which was seen in blood glucose levels, and serum total bilirubin. Neutralizing antibody of SARS-CoV-2 was seen among all vaccinated groups. Phase 2 was from May 18, to July 30, 2020. BBIBP-CorV have acceptable adverse events and have immunogenic effects among health individuals. The vaccine duration with 28 days has more neutralizing antibody titer when compared to 14 days and single dose immunization .

Inactivated SARS-CoV-2

Phase 1 and phase 2 clinical trials were between April 12, and May 2, 2020. Systemic reactions, local reactions, pain in the injection site, and fever were the common adverse events. Neutralizing antibody response against SARS-CoV-2 was not seen among any of the vaccinated individuals during follow-up after 1st vaccination. Participants generated antibody response after the 2nd dose and maintained high levels for 14 days after the 3rd dose. The vaccine has a better safety profile with better immune response [98-101].

RBD dimer

It is composed of antigen, thus producing antibody responses. It acts on cellular receptor human ACE2 to generate immunity [102-104]. It is produced in Chinese hamster ovary cells [105]. Three doses of vaccines enhances immune response. The phase 1 and 2 was between June 22, and September 15, 2020. Neutralizing antibodies of more than 90% were seen among vaccinated groups. The adverse events include pain and itching in the injection site, cough, headache, swelling, redness, and rhabdomyolysis [106].

Ad5-nCoV

The vaccine was developed by Cansino. It is a non-replicating viral vector. It consists of the spike protein of SARS-CoV-2 virus. Clinical trials were conducted between March 16, and March 27, 2020. It is administered through an intramuscular route, thus defending the virus rapidly [107]. Pain in the injection site, fever, fatigue, muscle pain, and headache was reported as adverse events. The vaccine produces both humoral and T cell immunity in most of the immunized individuals [108].

CoviVac

The whole virion vaccine used which inactivated vaccine developed by Chumakov center, Russia. It is safe to use at an age group of 18–60 years. It is more than 90% effective against SARS-CoV-2 virus. It produces better immunity when given 2 shots vaccination with a duration of 14 days between the doses. It is stored at 2–8°C temperature. The trial started on September 21, 2020 [109].

EpiVacCorona

It is a protein subunit developed by FBRI, Russia. The vaccine is 100% effective and the trials were at the age group between 18 and 60 years. It contains two shots of intramuscular vaccines 21–28 days apart and immunity provided within 45 days after 1st dose. Pregnant women and children were excluded from the trials [110,111].

QazVac

It is an inactivated vaccine manufactured in Kazakhstan. The age groups for the trial were from 18 to 50 years. It should be stored between 2–8°C. Efficacy of the vaccine reached 96%. It helps to accelerate herd immunity [112].

Inactivated (VeroCells)

It is an inactivated vaccine manufactured by Sinopharma, Wuhan. It has an efficacy of 79% against SARS-CoV-2 infection. Two doses should be administered at a dose interval of 21 days. It is recommended to administer at an age above 18 years. It is administered intramuscular route in the deltoid muscles. It should be stored at 2–8°C. People with comorbidities, age >60 years, pregnant and lactating women, HIV population, and immunocompromised population have insufficient data on the safety and efficacy of vaccines. The common adverse events are pain at the injection site, redness, swelling, induration, and itching [113,114].

TAK-919

It is a RNA vaccine developed by Takeda, Japan. It is also known as the Moderna vaccine. It is an intramuscular injection with two doses with a gap of 28 days. It can be administered to the age group above 18 years [114].

Sputnik Light

It is a non-replicating viral vector developed by Gameleya, Russia. It has an efficacy rate of 79.4%. The vaccination trials were between December 5, 2020 and April 15, 2021. It develops viral neutralizing antibodies. Cellular immune response seen for 100% of the vaccinated population. It showed efficacy of 78.6–83.7% among elderly population. No serious adverse events were reported [115].

CIGB-66

It is a protein subunit vaccine developed by Center for Genetic Engineering and Biotechnology, Cuba. It is also known as Abdala vaccine. It is 92.28% effective against SARS-CoV-2 virus. It consists of three doses with a duration of 14 days and 28 days between the first dose [116].

MVC-COV1901

It is a protein subunit vaccine developed by Medigen. The adverse events were mild. The immunoglobulin G and neutralizing antibodies were elevated among individuals after vaccination. Th1-skewed immune responses were seen among vaccinated groups. It consists of two doses with 28 days duration. The vaccine is well-tolerated with high immune response [117,118].

CONCLUSION

COVID-19 can spread rapidly and widely and vaccination can slow down the spread of the disease. Various methods such as relaxation of patent rule and giving the methodology to various production companies help to increase vaccine availability. Higher vaccination rates in the community can make outbreaks less likely and also reduce the need for preventive measures such as lock-downs and implementing curfews across the states. Escape variants impose a serious threat to vaccines and therapeutics and an immense global research of viruses will enable in controlling the cross species spread. Thus, it is the need of the hour to have a detailed understanding of the virus structure, pathogenic mechanisms, and scope of vaccine development to tackle the key challenges of management of this pandemic and to come up with a better therapy of COVID-19 for a better future. Research companies need to be supported financially to develop large scale manufacturing plants, allocation of facilities, and to protect them from financial loss. Studies should be continued to know the effect of spreading after taking COVID-19 vaccination, side effects associated with it, duration of immunity in the vaccinated people, possibility of reinfection, and the time to achieve herd immunity. The adverse effects related to the vaccines from a larger sample size that is needed to establish the safety profiling. After all, taking a vaccine is better than having this virus.

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