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COVID-19 Vaccines - A Narrative Review

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ABSTRACT

Since the pandemic started, various clinical trials have been going on to develop COVID vaccines. Vaccines which have passed the clinical trials include live attenuated vaccines, inactivated vaccines, protein subunit vaccines, virus like particles vaccines, viral vector vaccines, and nucleic acid vaccines. There are several vaccines in phase III and IV trials, and more than ten vaccines have been approved or authorized. Most of these vaccines are efficacious and safe. However, there are various pros and cons of these vaccines. This review explains how these vaccines have been developed, their mechanism of action, advantages, and disadvantages of these vaccines, along with costing and post vaccination challenges.

Keywords: Covid-19 vaccines, efficacy, safety, post-vaccination challenges

INTRODUCTION

The COVID 19 has taken the whole world by storm. Every region of the world is trying to develop a successful vaccine to treat COVID 19 at the earliest. Various trials have already been carried out, and different vaccines have become available in different countries. Before understanding how these vaccines work, let us briefly overview the structure of the SARS-CoV-2 virus. The SARS-CoV-2 virus consists of four structural proteins: Spike (S), an envelope (E), hemagglutinin Esterase (HE), membrane (M), and a nucleocapsid (N) Protein.

Development of COVID Vaccines

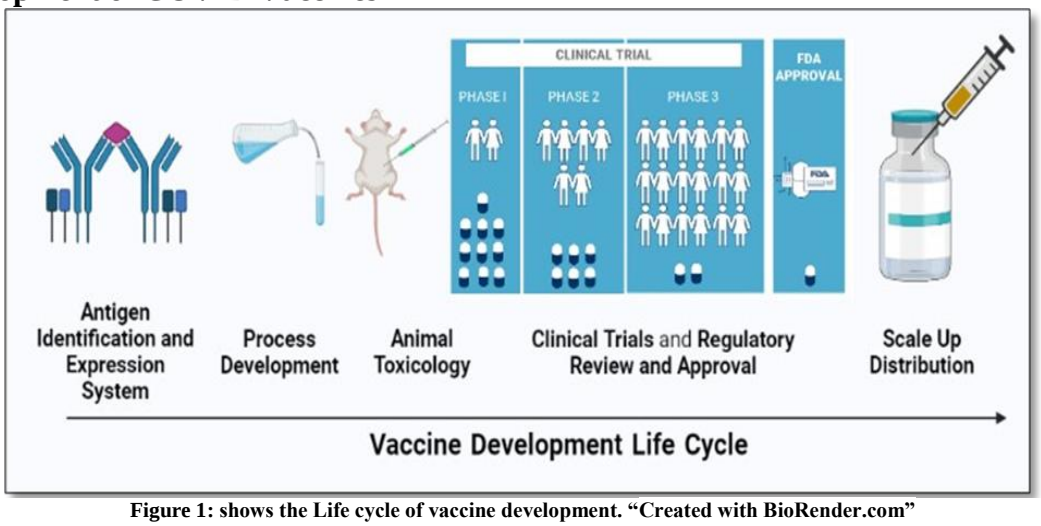


Figure 1: shows the Life cycle of vaccine development. "Created with BioRender.com"

Majorly three types of coronavirus vaccines are in development, Protein-based, Viral vectors, and mRNA based[2]. The primary aim of all vaccines is to expose the body to an antigen that won't cause disease but will elicit an immune response against

the virus[3]. The life cycle of vaccine development is shown in Figure 1

The Life cycle of SARS-CoV2

The surface spike (S) protein of SARS-CoV-2 binds to angiotensin-converting enzyme 2 (ACE2) and enters host cells. Subsequently, viral genomic RNA is released and translated into viral polymerase proteins. Subgenomic(-) RNAs are synthesized and used as a template to create subgenomic(+) messenger RNAs in this step (mRNAs). In the cytoplasm, the nucleocapsid (N) structural protein and viral RNA are replicated, transcribed, and synthesized. In contrast, in the endoplasmic reticulum (ER), other viral structural proteins such as the S protein, membrane (M) protein, and envelope (E) protein are transcribed and then translated.At the ER–Golgi intermediate compartment (ERGIC), the structural proteins are assembled into the nucleocapsid and viral envelope to form a mature virion. The budding virion is then released from the host cell[4].There are various approaches to develop COVID 19 vaccines[5], as depicted in Figure 2.

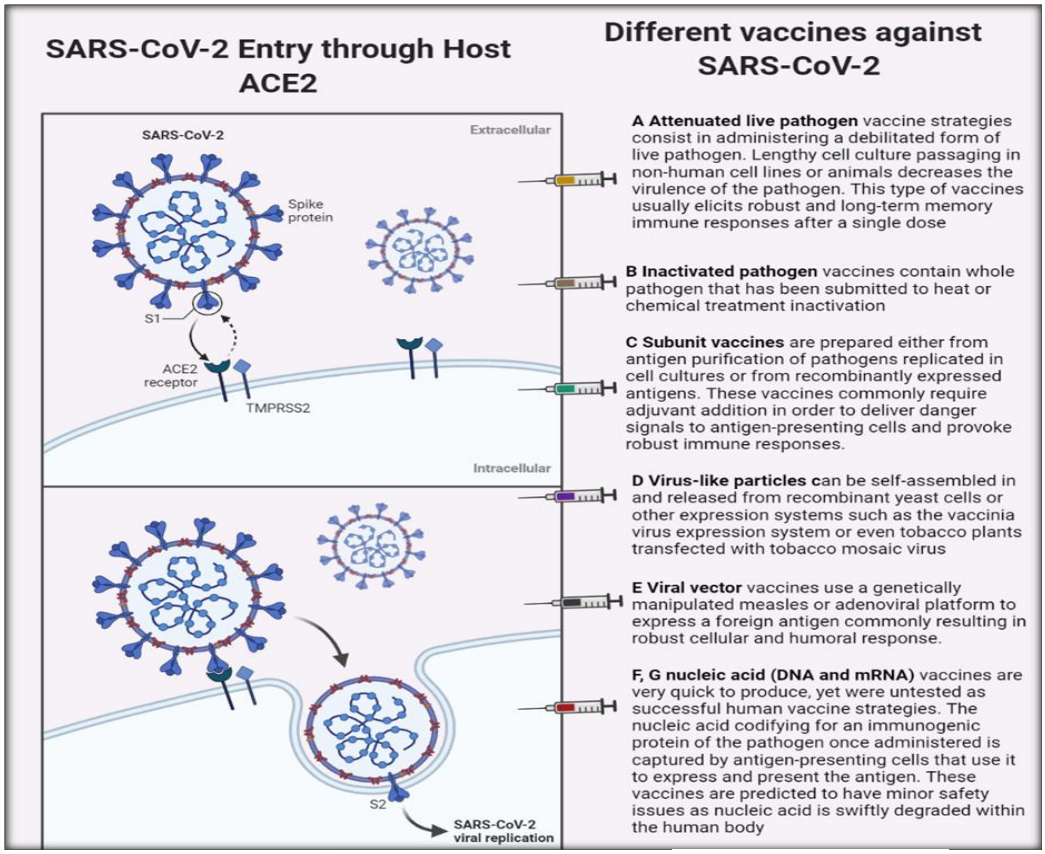


Figure 2: depicts how different vaccines against SARS-Cov-2. "Created with BioRender.com"

How COVID Vaccines Work?

COVID vaccines produce an immunogen which is an antigen that can elicit an immune response. It trains the immune system to identify the pathogen when it is confronted naturally by triggering: CD4+ helper T cells that in turn stimulate B-cells to generate neutralizing antibodies specific to the virus and CD8+ cytotoxic T cells to identify and kill cells affected by the virus[6-9].

Advantages and Disadvantages of Vaccines available in the healthcare field

The advantages and disadvantages of vaccines based upon the type of vaccine are mentioned in Table 1[10].

Table 1: depicts the advantages and disadvantages of vaccines based on vaccine type

Vaccine type	Description	Pros	Cons
Live attenuated vaccine	Vaccines contain viruses modified to hamper their replication and infection rate.	Rapid development, induce high immune response, mimic natural infection, create cross reactivity	Phenotypic or genotypic reversion, not suitable to all age groups, can revert and cause disease, might be harmful in immunocompromised.
Inactivated Vaccine	Inactivated vaccines are constituted by a virus treated physiochemically to inhibit its pathogenicity. Upon injection, the inactivated viruses are engulfed by antigen processing cells (APCs) and different epitopes are presented to the immune system	Easy to prepare, safe, high-titre neutralizing antibodies, very stable	possible cause of hypersensitivity, short memory
Protein subunit vaccine:	The subunit vaccines are composed of viral surface proteins formulated with adjuvants to elicit strong neutralizing antibody responses. Once injected, the proteins are engulfed by the APCs.	High safety, consistent production, can induce cellular and humoral immune response, do not cause disease	High cost, lower immunogenicity, require repeated dose and adjuvants, short memory
Virus Like Particles (VLP) vaccine:	They are constituted by one or more viral proteins assembled into a particle without viral genetic material. As such, these viral particles do not cause a disease while having a better uptake profile and more efficient circulation to the lymph nodes. Thus, they produce stronger immune responses	Increased uptake by lymph node, do not cause disease	Dependant on efficient expression platform, difficult to make VLP stable in long term
Viral Vector vaccine	Recombinant virus vaccines composed of viral vectors containing proteins from the target virus. It completely mimics natural viral infection, creating a strong immune response against it	Specific delivery tool required, Lower immune responses, repeated doses may cause toxicity	May induce prior immunity to vector
mRNA Vaccine	These vaccines deliver RNA coding targeting viral proteins into human cells. Then, they will produce viral proteins and, if a polymerase is encoded, also replicate themselves. This way RNA-based vaccines mimic ongoing viral infection including toll-like receptor activation and IFN production. Such vaccines containing different versions of mRNA for the spike protein have been developed.	Easy to design, higher degree of adaptability, induce strong immune response	Highly unstable, safety issue, low immune priming if efficacy of delivery is low
DNA Vaccine	DNA vaccines are appropriate for emerging infectious diseases because they allow for the rapid design of multiple candidates for novel antigens they are directly injected or otherwise inoculated into recipients	Easy to design and scale up, high safety, high-titer neutralizing antibodies	Specific delivery tool required, Lower immune responses, repeated doses may cause toxicity.

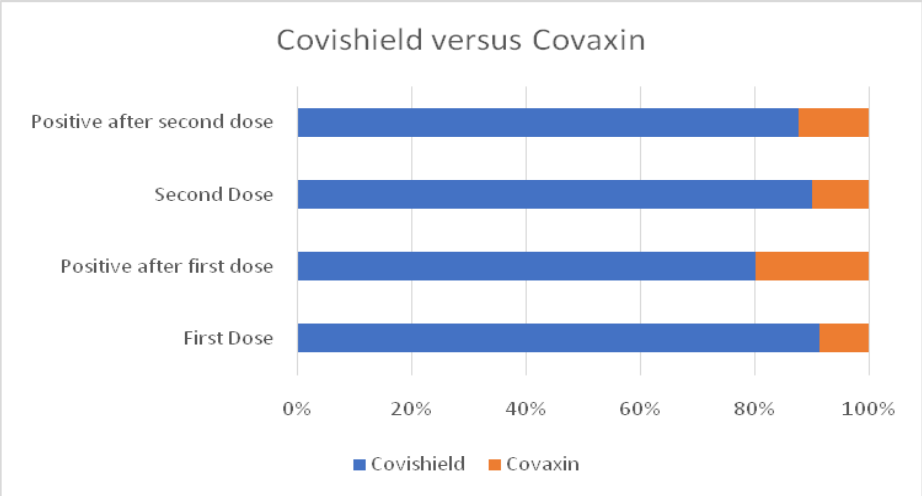
Table 2: depicts the name of vaccine, country of origin, dose, administration, advantages and disadvantages of each vaccine

S No.	Vaccine Name and Country of Origin	Vaccine Dose and Administration	Advantages	Disadvantages
1	Moderna, US	Dose: 100µg, Two doses-28 days apart	- Simple standardization - Simple manufacturing - Easy scaling up	- Storage and Transport difficulties
2	Pfizer BioNTech, US	Dose: 30µg, Two doses-21 days apart	- Simple standardization - Simple manufacturing - Easy scaling up	- Storage and Transport difficulties
3	AstraZeneca, UK	Dose: 0.22 ml or 0.5 ml, Two doses-4-12 weeks apart	- Better immune response	- Complex manufacturing
4	Sputnik V, Russia	Dose: 0.5 ml or 1.0 ml, Two doses-21 days apart	- Better immune response	- Complex manufacturing
5	Janssen, The Netherlands, US	Dose: 1 ml, One dose	- Better immune response	- Complex manufacturing
6	Sinovac, China	Dose: 3 µg with aluminium hydroxide adjuvant, Two doses-14-28 days apart	- Better safety profile as dead pathogen is used	- Requirement of additional adjuvants as chemically inactivated pathogen may lose immunogenicity
7	Sinopharm, China	Dose: 4 µg with aluminium hydroxide adjuvant, Two doses-21 days apart	- Better safety profile as dead pathogen is used	- Requirement of additional adjuvants as chemically inactivated pathogen may lose immunogenicity
8	Covaxin, India	Dose: 0.5 ml, Two dose-28 days apart	- Better safety profile as dead pathogen is used	- Requirement of additional adjuvants as chemically inactivated pathogen may lose immunogenicity

The vaccines that are available for use in the healthcare market, their administration, dose, advantages, and disadvantages of each vaccine are mentioned in the Table 2[11, 12].

Challenges after Vaccination

Though the focus of developing vaccines is to provide immunity against the virus, the challenges experienced after vaccination cannot be ignored. One of the major challenges some individuals have come across is getting COVID even after getting the vaccination. This could be due to two reasons, either the body is still in the phase of developing immunity against the virus, or the body has been attacked by mutant strain of the COVID virus[13]. Graph 1 shows the number of individuals that have been vaccinated for each dose and the number of individuals who got infected after each dose for Covishield and Covaxin[14].



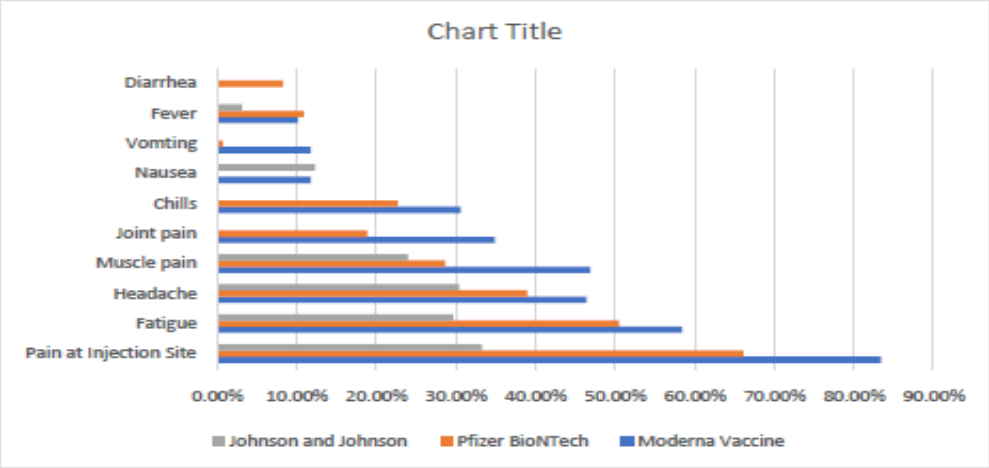
Graph 1: shows the comparison of Covishield versus Covaxin for the number of individuals vaccinated with first and dose and the number of cases positive after first and second doses as per the report of MOFHW till 20th April 2021.

Another challenge after vaccination is experiencing side effects, which could be local or systemic. After vaccination, the common side effects experienced by individuals most commonly include injection site reactions such as pain, redness, and swelling. Other side effects include fever, headache, chills, nausea, feeling of sickness, fatigue, and enlargement of lymph nodes. Oral side effects include blisters, halitosis, ulcers, angular cheilitis, bleeding gingiva, tongue tingling, taste disturbances, vesicles, xerostomia, presence of white or red plaque, and swollen lips[15].The comparison of side-effects of Sputnik V, Moderna, Pfizer-BioNTech, Covaxin, and Covishieldis shown in Table 3[16-18].

Table 3: showing comparison of side-effects of Sputnik V, Moderna, Pfizer-BioNTech, Covaxin, and Covishield

Sputnik V	Moderna	Pfizer-BioNTech	Covaxin	Covishield
• Headache • Fatigue • Pain at Injection Site • Flu like illness	• Fever • Chills • Redness at Injection Site • Swelling at Infection Site	• Headache • Myalgia • Arthralgia • Injection Site Pain • Fatigue • Chills • Fever	• Redness, Swelling, Pain at the Injection Site • Fever • Sweating and/or Chills • Malaise, Body ache • Nausea and Vomiting • Itching and Rashes • Headache	• Pain at the Injection site • Redness • Moderate or high fever • Drowsiness and Lethargy • Arm stiffness • Body ache and pain

The side effects in adults after the second dose of Moderna vaccine, Pfizer-BioNTech vaccine, and Johnson & Johnson vaccine are shown in Graph 2 as per the data collected from trials by U.S. Centres for Disease Control and Prevention[19]



Graph 2: shows comparison of side effects of Johnson and Johnson, Pfizer BioNTech, and Moderna Vaccine after second dose

Rare side effects of COVID Vaccine[20]

The severe side effects experienced is shown in Figure 3.

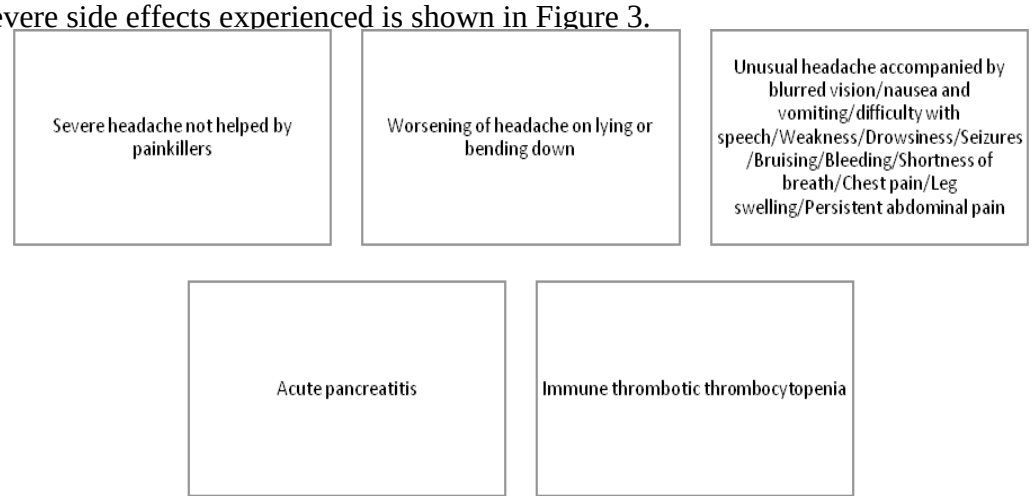


Figure 3: shows the rare/severe side-effects due to COVID Vaccine

The Debate regarding Antibody Dependent Enhancement

No ADE cases have been reported related to the COVID vaccine during the preclinical animal studies and human clinical trials. So far, there is no clear evidence that ADE may or may not be involved in the immunopathological processes associated with COVID-19 or re-infection with different variants after recovery or post-vaccination[21]. More studies are required to understand the correlation of protection against SARS-CoV-2 in natural human infection and as vaccines and antibodies in humans.

CONCLUSION

There is a constant comparison of the COVID vaccines which are coming out in the healthcare market. Several types of vaccines are available mainly, including mRNA, viral vectors, inactivated virus, and protein subunit on the majority. To better understand COVID vaccines, it is crucial to know how these vaccines work, their advantages and disadvantages, and what side effects can occur after vaccination? Despite the COVID vaccine data being promising, there is still a debate going on towards antibody dependent enhancement. We still need to have more studies to have better clarity regarding these challenges.

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