Review Article

A Comparative Review of mRNA, Viral Vector, Inactivated, and Protein Subunit COVID-19 Vaccines

Ghode Payal[1] , Jambhulkar Vaishnavi[2] , Rathod Sunil[3]
Students of Sahakar Maharshi Kisanrao Varal Patil College Of Pharmacy, Nighoj, Maharashtra, India.

ABSTRACT:
The COVID-19 pandemic prompted an unprecedented global response in vaccine development. Multiple platforms, including mRNA, viral vector, inactivated, and protein subunit vaccines, were rapidly developed to curb the spread of SARS-CoV-2. This review provides a comparative analysis of these vaccine types, focusing on their mechanisms of action, efficacy, safety profiles, storage requirements, and global distribution. mRNA vaccines such as Pfizer-BioNTech and Moderna demonstrated high efficacy, while viral vector vaccines like AstraZeneca and Johnson & Johnson offered logistical advantages. Inactivated vaccines such as Covaxin and Sinopharm are based on traditional methods and showed good safety profiles. Protein subunit vaccines like Novavax are emerging as a promising alternative with minimal side effects. Understanding these differences is essential for informed public health decisions, vaccine acceptance, and future pandemic preparedness.

KEY-WORDS:
COVID-19 vaccines, mRNA vaccines, viral vector vaccines, inactivated vaccines, protein subunit vaccines, SARS-CoV-2, vaccine efficacy, vaccine safety, immunogenicity, vaccine platforms

INTRODUCTION:
The outbreak of coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, led to a global health emergency, necessitating rapid development of effective vaccines. Several vaccine technologies, some novel and others traditional, were explored to deliver safe and effective protection against the virus. This review focuses on four main types of COVID-19 vaccines—mRNA, viral vector, inactivated, and protein subunit—highlighting their mechanisms, clinical performance, advantages, and limitations. A comparative understanding of these platforms can support public confidence, guide healthcare decisions, and enhance preparedness for future pandemics. COVID-19 vaccines are safe and effective, and benefits outweigh the noks as vaccine help in protecting adults and children aged 12 years and sider against getting severe illness, hospitalization, and death with COVID-10 infection. However, some COVID-19 vaccinated people (who is vaccinated with either a primary series or a primary series plus a booster dose can still have a vaccine breakthrough infection because none of the available vaccine is 100% effective.Currently vaccines which have been given emergency use authorization are:

- ❖ mRNA vaccines (Pfizer-BioNTech and Modernal)
- ❖ Protein subunit vaccine (Novavax, Corbevac)
- ❖ Viral vector vaccine (Johnson & Johnson's Janssen
- ❖ Inactivated coronaviruses (Covaxin, CoviShield

MECHANISM OF ACTION OF COVID-19 VACCINE TYPES:

1) MRNA VACCINES:
mRNA vaccines work by delivering messenger RNA encoding the SARS-CoV-2 spike protein into host cells. The mRNA is translated into the spike protein, which is recognized as a foreign antigen, triggering both humoral and cellular immune responses. Examples: Pfizer-BioNTech (BNT162b2), Moderna (mRNA-1273) Advantages: High efficacy, fast production Challenges: Requires cold-chain storage, initial concerns about long-term effect.

2) VIRAL VECTOR VACCINES:
These vaccines use a harmless adenovirus as a vector to deliver DNA encoding the spike protein into human cells. The host cells produce the spike protein and stimulate an immune response. Examples: Oxford-AstraZeneca (ChAdOx1 nCoV-19), Johnson & Johnson (Ad26.COV2.S), Sputnik V Advantages: Stable at 2–8°C, single-dose options available Challenges : Pre-existing immunity to vector may reduce efficacy

3) INACTIVATED VACCINES:
These contain whole virus particles that have been killed or inactivated. They cannot replicate but can still stimulate an immune response.Examples: Covaxin (Bharat Biotech), Sinopharm, Sinovac Advantages: Traditional method, safe and well-established .Challenges: Require adjuvants, multiple doses, lower efficacy than mRNA

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4) PROTEIN SUBUNIT VACCINES:
These vaccines contain purified fragments of the virus, typically the spike protein or its receptor-binding domain (RBD), along with adjuvants to enhance the immune response. Examples: Novavax (NVX-CoV2373), Covovax Advantages: Good safety profile, minimal side effects Challenges: Newer platform, may need boosters

COMMON SIDE EFFECTS (USUALLY MILD AND TEMPORARY) :

- Pain, redness or swelling at the injection site
- Fever , Fatigue , Headache
- Muscle or joint pain

These typically resolve within a few days.

LESS COMMON / RARE SIDE EFFECTS

1. **MYOCARDITIS/PERICARDITIS**
   (Inflammation of the Heart or surrounding tissue) Mostly seen in younger males (usually under 30) after mRNA vaccines (Pfizer, Moderna)Usually mild and resolved with treatment

2. **THROMBOSIS**

- Rare blood clotting disorder
- Seen with viral vector vaccines like Astra Zeneca and Johnson & Johnson
- Occurred mostly in younger women
- Very rare : a few cases per million doses

3. **ANAPHYLAXIS**

- Severe allergic reaction
- Occurs shortly after vaccination , very rare
- Vaccination sites are equipped to treat it immediately

4. **GUILLAIN – BARRE SYNDROME (GBS)**

- Rare neurological condition
- Reported after J & J vaccine, but also occurs after infections , including COVID itself

5. **MENSTRUAL CYCLE CHANGES**

- Some women reported irregularities
- No long – term fertility effects found

TYPES OF COVID-19 VACCINES AVAILABLE

Vaccines	Dose schedule	Dose, route, site	Common adverse effect	Contraindication	Precaution
BCG (Freeze-dried)	At birth	0.1 ml intradermal left deltoid	Axillary lymph adenitis	Immunodeficiency	Instruct patient to not to squeeze or scratch, rub or massage the site or use ointments, oils, or herbs on the site or put a sticking plaster over the site.

DTwP (whole cell vaccine) DTaP	6.10.14 week booster 16 to 18 month 2 booster 4 to 6 years: 3rd booster10 to 12years (T dap/Td)	0.5 ml IM anterolateral aspect of thigh	Fever, local pain induration, incessant crying, rarely encephalo pathy	Progressive neurological disease, severe reaction to first dose Severe allergic reaction (eg, ana-phylaxis after a previous dose or to a vaccine component Encephalopath y (eg, coma decreased level of consciousness, prolonged seizures), not attributable to another identifiable cause, within 7 days of administration of previous dose of DTP or DTaP	
IPV	610, 14 weeks: booster 16 to 10 months: 2nd booster 4 to 6 year s	Infants and small children, anterolateral aspect of the thigh Older children and adults: deltoid muscle for Mor the posterior aspect of the upper arm for SC Injection	Local itching, skin rash, soreness, hard lump, tenderness or pain, fever, crying persistentl y, Irritability, less of appetite. ti redness.	Severe allergic reaction (eg, ana-phylaxis) after a previous dose or to a vaccine compo nent	Pregnancy Moderate or severe acute illness with or without fever
OPV	At birth	2 drops orally	Vaccine-associated paralytic poliomyeli tis rarely	Immunodeficie ncy, HIV disease	

MMR (lyophilized)	9 months. 15 months booster 4 to 6 years	0.5 ml SC deltoid thigh	Mild fever, mild rash after 7 days	Severe allergic reaction (e.g., ana-phylaxis) after a previous dose or to a vaccine component Pregnancy Known severe immunodeficiency Family history of altered immunocompetence. Systemic hypersensitivity to neomycin	Recent (≤11 months) receipt of antibody-containing blood product (specific interval depending on the product) History of thrombocytopenia or thrombocytopenic purpura Need for tuberculin skin testing or interferongamma release assay (IGRA) testing. Moderate or severe acute illness with or without fever
Hepatitis B 10 mcg of purified HBsAg	At birth, 6,14 weeks	0.5 ml IM anterolateral aspect of thigh	Local pain, erythema	Severe allergic reaction (e.g., ana-phylaxis) after a previous dose or to a vaccine component Hypersensitivity to yeast	Moderate or severe acute illness with or without fever
Hepatitis A ln activated)	12 months, 18 months 2 dose 6 to 18 months apart	0.5 ml IM Thigh	Local pain, erythema: fever, and headache are cases of severe side effects like the elevation of liver enzymes, ITP (idiopathic thrombocytopenic purpura), and Guillain-Barré syndrome (GBS)	Severe allergic reaction leg, ana -phylaxis) after a previous dose or to a vaccine component, safety in pregnancy remains undetermined	Moderate or severe acute illness with or without fever

Varicella (lyophilized)	15 months: 4 to 6 years	0.5ml SC Deltoid	Milder varicella type rash	Severe allergic reaction (e.g., ana-phylaxis) after a previous dose or to a vaccine component Known severe immunodeficiency (e.g., from hematologic and solid tumors, receipt of chemotherapy. congenital immunodeficiency, long term immunosuppressive therapy or w patients with HIV infection who are severely immunocompromised) Pregnancy Family history of altered Immuno-competence	Recent (<11 months) receipt of antibody-con-taining blood product (specific interval depends on product) Moderate or severe acute illness with or without fever Receipt of specific anti viral drugs (acyclovir, famciclovir, or valacy clavir) 24 hours before vaccination (avoid use of these antiviral drugs for 14 days after vacci nation) Use of aspirin or aspirin-containing products
Typhoid Vi antigen vaccine 30 mcg of inactivated Vi capsular poly sacch aride	9 to 12 months: booster 2 years	0.5 ml IM Deltoid	Mild local reaction and pain, fever and headache, and general dis comfort	Allergic reaction after a previous dose of typhoid vaccine, or history of severe, life-threatening allergies: immunosuppressed; pregnant or breastfeeding; on antibiotics or anti-malarial drugs	Acute febrile illness or acute Gl illness
Meningoccal lyophilized) 50 mcg each sero type of inactivated capsular polysaccharide (Men ACWY)	11 to 12 years: booster at 16 years, no booster if 1 dose given after 16 years	0.5 ml IM or SC deltoid/thigh	Mild fever, local reaction	Severe allergic reaction (eg: ana-phylaxis) after a pervious dose or to a vaccine component	Moderate or severe acute illness with or without fever Preterm birth (MenACWY-CRM)

Serogroup meningococcal (MenB)	16 to 18 years (10 year or older in high-risk group) two or three doses	IM: 2 doses at least 1 month apart	Local pain, redness or swelling, tiredness, fatigue, headache, muscle/joint pain, fever, chills, nausea or diarrhea	Severe allergic reaction(e.g., anaphylaxis after a previous dose or to a vaccine component	Moderate or severe acute illness with or without fever Pregnancy Latex sensitivity (MenB-4c)
Japanese encephalitis (lyophilized)	9 months, 15 months: Travelers two-dose series spaced 28 days apart and at least 1week before travel. A 3d booster if a person has received the two-dose primary vaccination series one year or more previously and there is a continued risk for JE virus infection	2 months 1 years: 0.25 ml 1 to 3 years: 0.5 ml >3 years: 1.0 ml SC deltoid	Local pain, tenderness, headaches, myalgia, and low-grade levers, rarely encephalitis	Allergic reaction after a previous dose (allergy to Protamine component) or any severe, life threateing allergies, pregnancy	Moderate or severe acute illness with or without fever
Rotavirus	6,10,14 weeks for infants upto 24 weeks of age	Oral	Irritability or mild. temporary diarrhea or vomiting ear ache fever headache irritability muscle pain or cramping in the abdomen	Severe allergic reaction (eg. anaphylaxis) after a previous dose or to a vaccine component history of Intussusception	Altered Immunocompetence other than SCID Chronic gastrointestinal disease Spina bifida or bladder exstrophy Moderate or severe acute illness with or without fever

			or stomach, sore throat, stuffy of runny nose, unusual tiredness o r weakness		
***Recom binant Zoster Vaccine (RZV) Zoster vaccine liv e (ZVL)	Two doses of RZV (0,2 to 6 months) one dose of ZVL for 60 years and older (allergic to RZV)	0.5 ml in the deltoid region of the upper arm, reconstitute using adjuvant suspension component; use it within 6 hours of reconstitution	Diarrhea, difficulty in moving, fever, headache, muscle aches, cramps, pains, or stiffness nausea pain, redness, and swelling at the Injection site shivering stomach pain, unusual tiredness or weakness, vomiting	Severe allergic reaction (eg, anaphylaxis) after a previous dose or to a vaccine compo nent	Moderate or severe acute illness with or without fever, may Increase the risk for nervous system prob lems, including Guillain-Barré syndrome.
PCV 13 (pneumoc occal conjugate vaccine)	Infants to 5 years: 4 doses at 2, 4, 6 and 12-15 months. 6-18 years age with certain medical conditions single dose if not already rec eived	0.5 ml, IM antero lateral aspect of the thigh deltoid muscle in Toddlers/childr en/adults: Do not administer in the gluteal area or near major nerve trunks or blood vessels Do not mix with other vaccines/produc ts in the same syring e	Fever common, rarely chest pain, chills coughing, difficult breathing and swallowin g, tachycardi a, seizures skin itching, rash, or redness, a naphylaxis	Severe allergic reaction (e.g anaphylaxis) after a previous dose of PCV13 or any diphtheria-tux-old-containing vaccine or to a component of a vaccine (PCV13 or any diphtheria-toxoid-containing vaccines, inclu ding yeast	Moderate or severe acute illness with or without fever
PPSV23 Pneumoco ccal polysaccha ride vaccin e	6 weeks	0.5 ml IM or SC anterolateral aspect of thigh/deltoid	Local reaction	Severe allergic reaction (e.g, anaphylaxis) after a previous dose or to a	Moderate or severe acute illness with or without fever

				vaccine compo nent	
Haemophil us influenzae B 10 mcg of capsular polysaccha ride	6, 10, 14 weeks: 12 months, booster 16 to 18 mont hs	0.5 ml IM antero lateral aspect of thigh	Local pain, erythema, mild fever	Severe allergic reaction (eg, ana phylaxis) after a previous dose or to a vaccine component Ag e 5 weeks	Moderate or severe acute illness with or without fever
Live attendu- ated influenza vaccine (LAIV) quadrivale nt Seasonal I nfluenza	Every year to 2 through 49 years of ag e	0.2-ml prefilled single-use intranasal spray er	Fever, malaise, myalgia, and other systemic s ymptoms	Severe allergic reaction (eg, ana phylaxis) after a previous dose or to a vaccine component. Pregnant, immunocompr omised persons. Concomitant use of aspirin or salicylate containing medication in children and adolescents. LAIV4 should not be administered to persons who have taken oseltamivir or zanamivir within the previous 48 hours, peramivir within the previous 5 days, or baloxavir within the previous 17 days Children aged 2 through 4 years with diagnosis of asthma or wheezing: episode has occurred during the preceding 12 months Persons with active cerebrospinal fluid/orophary	GBS <6 weeks after a previous dose of influenza vaccine Asthma in persons aged 5 years old or older Medical conditions which might predispose to higher risk of complications attributable to influenza. Moderate or severe acute illness with or without fever

				ngeal communica tions/leaks Close contacts and caregivers of severely Immunosuppre ssed persons who require a protected environment. Persons with cochlear implants (dur to the potential for CSF lesk, which might exist for some period of time after implantation, Providers might consider consultation with a spe cialist concerning risk of persistent CSF leak if an age-appropriate inactivated or recombinant vaccine cannot be used. Altered immunocompe tence Anatomic or functional asplenia (eg, sickle cell disease)	
RIV (Recombin ant influenza vaccine) egg free Quadrivale nt inactivated influenza vaccine [IIV4] egg protein	every year to 18 years and older Every year to 6 months of age and older ever y year	0.5-ml prefilled syringe (PFS) 15 µg/0.5 ml IM	Fever, malaise, myal-gia, and other systemic symptoms Pain, redness at the injection site, head-ache, muscle aches, and malaise.	Severe allergic reaction (eg:, ana-phylaxis) to any component of the vaccine, egg free	GBS <6weeks after a previous dose of influenza vaccine Moderate or severs acute illness with or without fever

CONCLUSION

COVID-19 vaccine development marked a significant milestone in medical science, showcasing rapid innovation across various platforms. While mRNA vaccines offered high efficacy, viral vector vaccines brought logistical convenience. Inactivated vaccines provided a familiar and safe approach, and protein subunit vaccines offered a well-tolerated alternative with strong immunogenicity. Each platform has contributed uniquely to controlling the pandemic, and understanding their differences is essential for guiding policy, public trust, and future vaccine innovation.

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