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

Ghode Payal¹, Jambhulkar Vaishnavi², Rathod Sunil³ Students of Sahakar Maharshi Kisanrao Varal Patil College Of Pharmacy, Nighoj, Maharashtra, India.

ABSTRACT:

COVID-19 pandemic prompted The 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 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 sider against getting severe 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 wellestablished. 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 | 6.10.14 | 0.5 ml IM | Fever, | Progressive | |
|----------|-------------------------|------------------|----------------------|----------------------|------------------------------|
| (whole | 0.10.14 week | anterolateral | local pain | neurological | |
| cell | booster 16 | aspect of thigh | induration, | disease, severe | |
| vaccine) | to 18 | aspect of thigh | incessant | reaction to first | |
| DTaP | month 2 | | crying, | dose | |
| 2 1 441 | booster 4 | | rarely | 4000 | |
| | to 6 years: | | encephalo | Severe allergic | |
| | 3 rd | | pathy | reaction (eg, | |
| | booster10 | | | ana-phylaxis | |
| | to | | | after a previous | |
| | 12years (T | | | dose or to a | |
| | dap/Td) | | | vaccine | |
| | | | | component | |
| | | | | Encephalopath | |
| | | | | y (eg, coma | |
| | | | | decreased level | |
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| | | | | another identifiable | |
| | | | | cause, within 7 | |
| | | | | days of | |
| | | | | administration | |
| | | | | of previous | |
| | | | | dose of DTP or | |
| | | | | DTaP | |
| IPV | 610, 14 | Infants and | Local | Severe allergic | Pregnancy Moderate or |
| | weeks: | small children, | itching, | reaction (eg, | severe acute illness with or |
| | booster 16 | anterolateral | skin rash, | ana-phylaxis) | without fever |
| | to 10 | aspect of the | soreness, | after a previous | |
| | months: | thigh Older | hard lump, | dose or to a | |
| | 2 nd booster | children and | tenderness | vaccine compo | |
| | 4 to 6 year | adults: deltoid | or pain, | nent | |
| | S | muscle for Mor | fever, | | |
| | | the posterior | crying | | |
| | | aspect of the | persistentl | | |
| | | upper arm | y, | | |
| | | for SC Injection | Irritability, | | |
| | | | less of appetite. ti | | |
| | | | redness. | | |
| OPV | At birth | 2 drops orally | Vaccine- | Immunodeficie | |
| OF V | Atolitil | 2 drops orany | associated | ncy, HIV | |
| | | | paralytic | disease | |
| | | | poliomyeli | discase | |
| | | | tis rarely | | |
| | | l | ustately | | |

| MMR (lyophilize d) | 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 immunodeficie ncy Family history of altered immunocompe tence. Systemic hypersensitivit y 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 H BsAg | 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 Hypersensitivit y to yeast | Moderate or severe acute illness with or without fever |
| Hepatitis A ln activated) | months, 18 months 2 dose 6 to 18 months ap art | 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 thrombocy topenic purpura), and Guillain- Barré synd rome (GB S) | Severe allergic reaction leg, ana -phylaxis) after a previous dose or to a vaccine component, safety in pregnancy remains undete rmined | Moderate or severe acute illness with or without fever |

| Varicella (lyophilize d) | 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 immunodeficie ncy (e.g., from hematologic and solid tumors, receipt of chemotherapy. congenital immunodeficie ncy, long term immunosuppre ssive therapy or w patients with HIV infection who are severely immunocompromised) Pregnancy Family history of altered Immuno- | 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: immunosuppre ssed; pregnant or breastfeeding; on antibiotics or anti- malarial drugs | Acute febrile illness or acute Gl illness |
| Meningoc occal lyophilize d) 50 mcg each sero type of inactivated capsular polysaccha ride (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 | 16 to 18 | IM: 2 doses at | Local | Severe allergic | Moderate or severe acute |
|-------------|-----------------------|------------------|--------------|------------------|--------------------------------|
| meningoco | years (10 | least 1 | pain, | reaction(e.g., | illness with or without fever |
| ccal | year or | month apart | redness or | anaphylaxis | Pregnancy |
| (MenB) | older in | month apart | swelling, | after a previous | Latex sensitivity (MenB-4c) |
| (1.15112) | high-risk | | tiredness, | dose or to a | |
| | group) two | | fatigue, | vaccine compo | |
| | or three do | | headache, | nent | |
| | ses | | muscle/joi | 110110 | |
| | 565 | | nt pain, | | |
| | | | fever, | | |
| | | | chills, | | |
| | | | nausea or | | |
| | | | diarrhea | | |
| Japanese | 9 months, | 2 months 1 | Local | Allergic | Moderate or severe acute |
| encephaliti | 15 | years: | pain, | reaction after a | illness with or without |
| s | months: | 0.25 ml 1 to 3 | tenderness | previous dose | fever |
| (lyophilize | Travelers | years: 0.5 ml >3 | , | (allergy to | |
| d) | two-dose | years: 1.0 ml | headaches, | Protamine | |
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| | days apart | | grade | threateing | |
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| | least | | rarely ence | pregnancy | |
| | 1week | | phalitis | | |
| | before | | | | |
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| | n series | | | | |
| | one year | | | | |
| | or more | | | | |
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| | and there | | | | |
| | is a | | | | |
| | continued risk for | | | | |
| | risk for JE virus | | | | |
| | infection | | | | |
| Rotavirus | 6,10,14 | Oral | Irritability | Severe allergic | Altered Immunocompetence |
| 100011105 | weeks for | J | or mild. | reaction | other than SCID Chronic |
| | infants | | temporary | (eg. | gastrointestinal disease Spina |
| | upto 24 | | diarrhea or | anaphylaxis) | bifida or bladder exstrophy |
| | weeks of a | | vomiting | after a previous | Moderate or severe acute |
| | ge | | ear ache | dose or to a | illness with or without |
| | 5 | | fever | vaccine | fever |
| | | | headache | component | |
| | | | irritability | history | |
| | | | muscle | of Intussuscept | |
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| (pneumoc 5 years: 4 antero lateral common, reaction (e.g illness with or without fever |
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| occal doses at 2, aspect of the rarely anaphylaxis) |
| conjugate 4, 6 and thigh deltoid chest pain, after a previous dose of PCV13 |
| |
| months. 6- Toddlers/childr coughing, or any 18 years en/adults: Do difficult diphtheria-tux- |
| 18 years en/adults: Do difficult diphtheria-tux- age with not administer breathing old-containing |
| certain in the gluteal and vaccine or to a |
| medical area or near swallowin component of a |
| conditions major nerve g, vaccine |
| single trunks or blood tachycardi (PCV13 or any |
| dose if not vessels Do not a, seizures diphtheria- |
| already rec mix with other skin toxoid- |
| eived vaccines/produc itching, containing |
| ts in rash, or vaccines, inclu |
| the same syring redness, a ding yeast |
| e naphylaxis |
| PPSV23 6 weeks 0.5 ml IM or SC Local Severe allergic Moderate or severe acute |
| Pneumoco anterolateral reaction reaction (e.g, illness with or without fever |
| ccal aspect of anaphylaxis) |
| polysaccha thigh/deltoid after a previous |
| ride vaccin dose or to a |
| e e |

| | 1 | | I | vaccino compo | |
|---|---|--|---|--|---|
| | | | | vaccine compo nent | |
| Haemophil us influenzae B 10 mcg of capsular polysaccha ride Live attendu- | 6, 10, 14 weeks: 12 months, booster 16 to 18 mont hs Every year to 2 | 0.5 ml IM antero lateral aspect of thigh 0.2-ml prefilled single-use | Local pain, erythema, mild fever Fever, malaise, | Severe allergic reaction (eg, ana phylaxis) after a previous dose or to a vaccine component Ag e 5 weeks Severe allergic reaction (eg, | Moderate or severe acute illness with or without fever GBS <6 weeks after a previous dose of influenza |
| ated influenza vaccine (LAIV) quadrivale nt Seasonal I nfluenza | through 49 years of ag e | intranasal spray er | myalgia, and other systemic s ymptoms | 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 | 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 |

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| | | | | communica | |
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| | | | | Close contacts | |
| | | | | and caregivers | |
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| | | | | Immunosuppre | |
| | | | | ssed persons | |
| | | | | who require a | |
| | | | | protected | |
| | | | | environment. | |
| | | | | Persons with | |
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| | | | | might consider | |
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| | | | | cialist | |
| | | | | concerning risk | |
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| | | | | CSF leak if an | |
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| | | | | appropriate | |
| | | | | inactivated or | |
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| | | | | vaccine cannot | |
| | | | | be used. | |
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| | | | | Altered | |
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| | | | | functional | |
| | | | | asplenia (eg, | |
| | | | | sickle cell | |
| | | | | disease) | |
| RIV | every year | 0.5-ml prefilled | Fever, | Severe allergic | GBS <6weeks after a |
| (Recombin | to 18 years | syringe (PFS) | malaise, | reaction (eg:, | previous dose of influenza |
| ant | and older | 3,111160 (1115) | myal-gia, | ana-phylaxis) | vaccine Moderate or severs |
| influenza | una order | | and other | to any | acute illness with or |
| vaccine) | | | systemic | component of | without fever |
| egg free | | | symptoms | the | winiout ievei |
| cgg nee | | 15 | symptoms | | |
| | Every vee | 13 μg/0.5 ml IM | Pain, | vaccine, egg free | |
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CONCLUSION

COVID-19 vaccine development marked a significant milestone in medical 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 vaccine innovation.

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