

Covid-19 Vaccines: Insights into Efficacy, Safety, and Reported Adverse Drug Reactions

Rahul D. Kamble¹, Saniya F. Mulla², Pallavi Y. Patil³

¹Assistant Professor, Department of Pharmaceutical Chemistry, Ashokrao Mane Institute of Pharmaceutical Sciences and Research, Save

² Student, Department of B. Pharmacy, Ashokrao Mane Institute of Pharmaceutical Sciences and Research, Save

³ Student, Department of B. Pharmacy, Ashokrao Mane Institute of Pharmaceutical Sciences and Research, Save

Abstract –

This review explores the immunological and autoimmune side effects linked to COVID-19 vaccines, focusing on how often they occur, the cases that have been reported, and their connection to different types of vaccines.

A key idea in dealing with concerns about vaccines is vaccine-induced immune thrombotic thrombocytopenia. Grasping this concept is important for healthcare workers to recognize and handle any possible side effects after vaccination. Even though these side effects are rare, they can lead to worry and fear among people. To keep the public confident in vaccination efforts, healthcare providers and public health organizations need to keep a close watch on these side effects, quickly report any unusual cases, take steps to reduce risks, and share clear and correct information with the public. Ongoing research and monitoring are vital for learning more about these side effects and creating ways to prevent them from happening.

Keywords: COVID-19 vaccination, Myocarditis, Circulatory adverse effects, Immunization, Inflammation, Healthcare professionals.

Key Word : COVID 19, Vaccines, Myocarditis, Circulatory adverse effect

□INTRODUCTION

Brief overview of COVID-19 pandemic and global health impact

COVID-19 has caused a huge worldwide toll. More than 282 million cumulative confirmed cases and

5.4 million deaths were reported by the end of 2021; however, these figures are most likely a significant overestimate of the actual number of illnesses and deaths. 1

In both wealthy and resource-constrained nations, the pandemic's subsequent waves have placed tremendous strain on health systems. Health professionals themselves have been at the forefront of SARS-CoV-2 exposure in addition to rising patient loads; according to WHO estimates, 116,000 health workers died from COVID-19 between January 2020 and May 2021. 2

According to the International Monetary Fund, the pandemic will cause a total economic loss of US\$13.8 trillion by 2024. 3 There was a significant demand for quick access to reliable scientific advice due to the emerging pandemic. In response to the challenge, WHO established a new fast-track review mechanism in key COVID-19 response areas to guarantee the quality and consistency of interim guidelines and other outputs. It assessed over 1000 documents during the first 18 months of the epidemic and gave WHO technical teams permission or criticism within 24 to 48 hours.

In response to the COVID-19 pandemic, WHO has increased its efforts in every area of its operations. The pandemic has

had a direct or indirect impact on every aspect of health. All WHO levels—global, regional, and national—have performed at a higher intensity than at any other point in the organization's existence. Even though this situation has presented many difficulties, it has also made it easier to see the advantages and requirements of funding WHO.

In the context of the COVID-19 pandemic, internal and external evaluations of WHO's performance in pandemic preparedness and response have been conducted, and their findings have unanimously urged for additional financing for the WHO Health Emergencies Program.

•Role of vaccines in controlling pandemic

Some for COVID-19-risk individuals In the first two months following vaccination, the 2023–2024 COVID-19 vaccinations decreased older persons' risk of COVID-19 hospitalization by almost 50%. By four to six months following immunization, vaccine protection begins to diminish. One type of zoonotic virus is coronaviruses, which may naturally occur in bats. It is a member of the three families—

Coronaviridae, Arteriviridae, and Roniviridae—that make up the order Nidovirales. Particularly in elderly patients, certain coronaviruses caused serious pneumonia, lower respiratory infections, and organ failure, whereas others produced mild common cold infections including fever and cough.

The World Health Organization (WHO) proclaimed a COVID-19 pandemic on March 11, 2022, when the first case was discovered in Wuhan, China Coronaviridae, Arteriviridae, and Roniviridae—that make up the order Nidovirales. Particularly in elderly patients, certain coronaviruses caused serious pneumonia, lower respiratory infections, and organ failure, whereas others produced mild common cold infections including fever and cough.

The World Health Organization (WHO) proclaimed a COVID-19 pandemic on March 11, 2022, when the first case was discovered in Wuhan, China.

Objective of the review:

•summarize efficacy, safety, and adverse drug reaction(ADR) Give patients a thorough evaluation of the medication's overall benefit-risk profile to guarantee their safe and efficient use. This entails compiling information on the medication's therapeutic advantages (efficacy), determining any adverse effects (safety), and describing the type, frequency, and risk factors of any adverse reactions (ADRs) to direct clinical practice, public health campaigns, and policy choices. aims to offer a thorough, empirically supported evaluation of the drug's overall benefit-risk profile.

This entails assessing how well it treats an illness, determining any negative side effects and how frequently they occur, comprehending the risk factors connected to adverse drug reactions (ADRs), and eventually supporting the safe and

sensible use of medications in clinical practice and public health.

Types of COVID-19 Vaccines:

mRNA vaccines-(Pfizer-biotech)

The FDA approved Pfizer's COVID-19 vaccine for emergency use in December 2020, just about seven months after the vaccine's phase I/II trial in May 2020. This was the fastest vaccine to be developed. The pharmaceutical giant Merck set the previous record in 1967 when it took four years to create the first mumps vaccine that worked. Pfizer started Phase I/II testing in May 2020 as the number of cases was close to 5 million and the number of deaths was slightly under 150,000.

There were three groups of 15 participants each, totaling 45 participants in the study. Two 10 µg doses spaced 21 days apart were given to Group 1. Two doses of 30 µg were administered to Group 2, separated by 21 days. One dose of 100 µg was given to Group 3.

In order to test the immunogenicity of the vaccination to individuals who recovered from infection, human convalescent sera (HCS) were collected from 38 patients 14 days after the PCR-confirmed diagnosis.

□ Mechanism of action

The vaccines from Moderna and Pfizer have comparable modes of action. A modified mRNA sequence wrapped in lipid nanoparticles is delivered to cells as part of the Pfizer-BioNTech mRNA vaccine for COVID-19

Efficacy was assessed by binding antibody reactions against S2-P. By instructing the cells to create the SARS-CoV-2 spike protein, this mRNA initiates an immunological response that involves the activation of both B-cells and T-cells, which eventually results in the development of antibodies against the spike protein without the need for the virus.

The vaccination aims to stimulate T-cell and B-cell responses against the spike protein. To protect and facilitate its entry into host cells, the mRNA that codes for the spike protein is encased in a lipid nanoparticle.

Cellular instruction: Once within the cell, the mRNA gives the cell's machinery instructions on how to construct the spike protein, or more precisely, the transmembrane-anchored S2-P antigen.

• Moderna-

One of the earliest pharmaceutical companies to promise to create a COVID-19 vaccine was Moderna. On March 17, 2020, the National Institute of Allergy and Infectious Diseases initiated the first clinical studies for the self-replicating Moderna mRNA1273 vaccine

Our immune system views this spike protein, which is produced on the cell surface, as alien. As a result, the immune system produces antibodies to combat viral infections in the future.

A grant of up to \$483 million to expedite the vaccine's development was announced by BARDA one month later. A collaborative agreement to develop about 1 billion mRNA1273 vaccine doses annually was announced on May 1 by Moderna and Lonza.

Phase 3 trials of the mRNA-1273 vaccination started on July 26, 2020, after BARDA extended its sponsorship following favorable outcomes from Phase 1 and Phase 2 studies. The US and Moderna signed a preliminary supply contract. The cells are commanded to translate the lipid-encoded mRNA into a unique protein known as "spike protein," which is the SARS-CoV-2 surface marker protein, as soon as it is injected intramuscularly into the deltoid muscle.

The vaccine is immunogenic, and higher doses result in higher antibody titers; nevertheless, a subgroup of patients receiving higher doses (250 µg) experienced substantial side effects, with the incidence increasing after the second immunization.

On January 6, 2021, the Moderna mRNA vaccine was granted a conditional marketing authorisation that is valid throughout the European Union

□ Mode of action-

The vaccine works by inducing a primary immune reaction, which triggers a secondary immunological response based on memory cells after the individual has been exposed. Because of this, live attenuated, dead organisms—that is, a protein or portion of the virus—are used in traditional vaccines. However, a new class of mRNA vaccines uses inoculation of mRNA.

Because of this, live attenuated, dead organisms—that is, protein or portion of the virus—are used in traditional vaccines. However, a new class of mRNA vaccines uses inoculation of mRNA.

The Moderna vaccines are thought to have comparable modes of action and both employ mRNA technology.

1) Covidshield Vaccine

One crucial step in preventing COVID-19 is vaccination. On January 16, 2021, India began a phased vaccination campaign against COVID-19.

Clinical trials have a limited number of participants, therefore it is crucial that the protection provided by any vaccine be investigated in practical environments.

Assessing the effect of COVID vaccines in preventing infection—defined as the identification of viral RNA or antigen in a respiratory samples obtained from an individual after a predetermined amount of time has passed has been a widely utilized technique for determining the population-level efficacy of these vaccines

utilizing a case-control strategy, obtaining all prescribed dosages. Our institution began administering the Covishield vaccine on January 16, 2021, yet some of our healthcare workers were able to get the other vaccine by traveling to different locations

Our organization's ethical committee approved the study, and each participant provided oral informed consent.

The information was recorded using the EpiCollect5 application and analyzed using STATA V14.0. Between March and May 2021, our HCWs conducted almost 2200 tests, according to the database. 795 of them were positive. We contacted 963 test-negative HCWs (37.3%) and 547 test-positive HCWs (65.8%) in order to enroll 360 cases and 360 matched controls.

Assuming 50% vaccination coverage, 70% efficacy, and a matched case-control design pair, the sample size was calculated to be 346 case-control.

2) Covaxin vaccine:

Covaxin, a COVID-19 vaccine created by Bharat Biotech Ltd. and the Indian Council of Medical Research, has been authorized in India. The study's main goal was to determine how well Covaxin prevented HCWs from contracting breakthrough SARS-CoV-2. HCWs from a tertiary care hospital in Eastern India participated in a test-negative matched case-control research. The issue has become much more problematic due to the introduction of mutant strains of the virus. The pandemic has killed millions of people and infected hundreds of millions more worldwide. The institution's vaccine database and recall were used to gather

vaccination data. If there was a discrepancy, the CoWIN portal (cowin.gov.in) verified it. There is no increase in COVID-19 cases in India, and a third wave has not yet materialized. The strain B.1.617 that was found in India is currently a global issue, according to studies from the (WHO). The issue has become much more problematic due to the introduction of mutant strains of the virus. The main strategies for COVID-19 prevention and control The Indian Council of Medical Research (ICMR), National Institute of Virology, and Bharat Biotech collaborated to develop the domestic vaccine Covaxin. Alhydroxiqum-II was employed as an adjuvant in Covaxin's tried-and-true Whole-Virion Inactivated Vero cell-derived platform technology. It was authorized for emergency use in clinical trial mode on January 16, 2021. According to the interim report, its effectiveness was 81%. The AIIMS healthcare workers participated in this hospital-based test-negative case-control study from February to July of 2021. Eastern India's AIIMS Bhubaneswar is a tertiary care facility that offers both COVID and non-COVID services.

3) Sputnik vaccine

The two-vector adenovirus-based COVID-19 vaccine Sputnik V exhibited excellent efficacy (91.6% in Phase 3), but it was controversial because of its unreliability and lack of transparency regarding its raw data. It sought to address fair access to vaccines, especially for low- and middle-income nations.

As one of the so-called vector vaccines, the Sputnik V COVID-19 vaccine employs two distinct vectors to lower the possibility of the vaccination's efficacy declining.

The Real-world data show that the vaccine's effectiveness is more than 97%. Other benefits of the Sputnik V vaccination are its low cost and lack of requirement for extremely low storage temperatures. In Russia, the first approved vaccination was developed. The previous Ebola virus vaccine, which was similarly developed at the Gamaleya National Research Centre for Epidemiology and Microbiology (Moscow, Russia), used Ad5 and the vesicular stomatitis virus as the carrier viruses.

The results of the research show a robust protective effect that is consistent across all participant age groups.

□ **Protein subunit vaccine (novavax):** The first illnesses were discovered in Wuhan, China, in December 2019, two years after the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Similar to its COVID-19 vaccine, the Novavax protein subunit vaccine stimulates an immune response by using a modified SARS-CoV-2 spike protein instead of the entire virus. The spike proteins are produced by moth cells infected with an engineered baculovirus; these proteins are then collected and combined into recombinant nanoparticles, or virus-like particles, which are subsequently used to make the vaccine.

The immune system can recognize and train to combat this stable and identifiable form of the viral spike protein.

To guard against the Omicron type, new formulations for the 2023–2024 vaccination have been created. These proteins are extracted and put together to create recombinant nanoparticles, or particles that resemble viruses, which are subsequently used to make the vaccine. The immune system can recognize and learn to combat the stable and identifiable form of the viral spike protein produced by this mechanism.

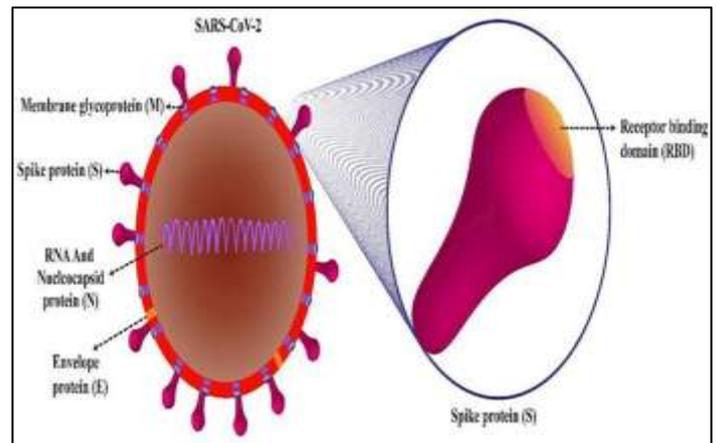


Fig No.3.6 Protein subunit vaccine (novavax)

Efficacy of COVID-19 Vaccines:

□ Clinical trial efficacy data (phase 3 result)

The World Health Organization's (WHO) official description, COVID-19 is a virus that is brought on by a novel coronavirus. In the Chinese province of Wuhan, it was first reported on December 31, 2019.

95%, in reducing symptomatic COVID-19 infection, and were followed by practical efficacy studies that demonstrated notable decreases in infection and severe sickness.

1.High Efficacy:

Pfizer-BioNTech and Moderna's initial Phase 3 trials for mRNA vaccines revealed high efficacy rates, with efficacy against COVID-19 symptoms reported at 90–95%.

2.Prevention of Symptomatic Disease:

The primary objective of the studies, which was to prevent symptomatic SARS-CoV-2 infection, was accomplished by the immunizations.

The viral coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was the cause of the coronavirus disease 2019 outbreak.

Since COVID-19 may only be regarded as a treatable disease from a clinical perspective once specific and effective antivirals are available, numerous trials have been carried out in an effort to develop viable medications to combat the illness.

3.Severe disease and hospitalization death:

The viral disease known as COVID-19 initially appeared in Wuhan, China, near the end of 2019. It quickly spread throughout the world and caused harm. The COVID-19 epidemiology has evolved over time, resulting in broken families, significant social and financial costs, and an uncertain outcome.

Every nation was affected, governments were imposing limits on citizens' freedoms, and national health services were pushed to the brink of collapse. The rate of spread was compared to none, and nations that were thought to have controlled spreading in one week were dealing with chaos in the weeks that followed, an uncontrollably high number of new cases, and widespread high death rates.

□ **Real world effectiveness against:**

•Symptomatic infection:

Real-world studies showed that licensed COVID-19 vaccines produced very high protection against symptomatic SARS-CoV-2 infection soon after a two-dose primary mRNA series (efficacy ≈90–95% in early trials and mass vaccination

settings). However, the emergence of immune-evasive variants— particularly Omicron and its descendants—caused a substantial reduction in vaccine effectiveness against symptomatic infection after the primary series.

Booster doses, including variant-updated (bivalent/XBBtargeted) boosters, restore partial protection against symptomatic disease (early surveillance estimates commonly report additional protection in the ~40–60% range), but protection against infection is lower and wanes faster than protection against severe outcomes. Hybrid immunity (prior infection plus vaccination) generally confers stronger protection than vaccination alone.

•Variant of concern (delta, omicron,XBB):

The World Health Organization(WHO) classified Omicron and Delta as Variants of Concern (VOCs). because they showed increased transmissibility, severity, or a reduced effectiveness of public health measures and treatments compared to earlier strains.

Omicron is the latest major VOC, while Delta was a previous variant characterized by high infectivity. The XBB lineage is a recombinant of Omicron subvariants, which itself is a further evolution of the virus

□Key Characteristics of Delta

1)High Transmissibility: The Delta variant was notably more contagious than previous strains. Increased Severity. It was linked to an increased risk of serious illness and hospitalization.

2)Global Impact: The Delta variant spread rapidly worldwide, impacting the course of the pandemic.

□Key Characteristics of Omicron

1)High Transmissibility: The Omicron variant was also characterized by significant transmissibility

2)Immune Evasion: It showed a greater capacity to circumvent the immunity acquired from a previous infection or immunization.

3)Subvariants: The Omicron lineage has given rise to numerous subvariants, including the XBB lineage.

□The Role of XBB-

1)Recombinant Variant:

The XBB lineage is a type of recombinant variant, meaning it's a combination of genetic material from different Omicron subvariants.

2)Continued Evolution:

The emergence of XBB demonstrates the ongoing evolution of the SARS-CoV-2 virus, with new variants continuing to arise and spread

□Duration of protection and need for booster dose: 250 million cases and over 5 million fatalities to far, the coronavirus disease 2019 (COVID-19) pandemic has spread throughout the world, posing a major healthcare emergency. Other aspects of life, including social, technological, and economic aspects, have also been affected.

Mass vaccination and achieving herd Despite the advent of new varieties, immunization against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appears to be the most effective approach to avert the pandemic.

The majority of vaccines only provide a short-lived immunity against a variety of common infections, and booster shots are frequently necessary to develop a robust immunity.

It is still up for contention whether COVID-19 vaccines produce long-term protection and whether booster shots for

various COVID-19 vaccines are required. Determining the length of time that humoral immune responses are effective enough against COVID-19 infection is crucial in light of this.

□Safety profile

•General safety of vaccine across population

COVID-19 vaccines are generally safe, though they can cause temporary side effects like fever or muscle pain in some individuals, with a lower occurrence of issues like swollen lymph nodes or anaphylactic shock.

Vaccines undergo rigorous testing before approval, and studies have found that having other immunizations, such as for the flu and pneumonia, may be associated with a reduced risk of experiencing side effects.

Randomized clinical trials (RCTs) and pivotal clinical studies offered vital safety information for vaccination licensing, but there was little information about these particular populations.

The ongoing fight against the pandemic has been greatly aided by the quick production and widespread distribution of COVID-19 vaccinations.

□Special populations:

1)Children and adolescents:

The morbidity and fatality rates from the SARS-CoV-2 pandemic were lower in children and adolescents than in adults. The clinical course, risk factors for severe COVID-19, mortality, treatment choices, and preventative measures in the juvenile and environment were the main topics of this review, with an emphasis on pediatric patients with haematological disorders. Children are more vulnerable to infectious infections than adults due to their developing immune systems.

Minors appear to be less susceptible to SARS-CoV-2 infection, with just a few fatal cases and a low incidence of severe COVID-19.

80–90% of children and teenagers who are infected (80%) 19, 20 exhibit symptoms, which are often mild or moderate.

No. 18 As a result, the hospitalization rate decreased, from 2.5 to 4.1%. 15% of hospitalized patients were admitted to the intensive care unit.

2)Pregnant and lactating women:

Since SARS-CoV-2 has spread around the world, there is an increasing need for efficient treatments. Preventive measures that could halt the disease's spread are now of utmost importance.

Women who are pregnant or recently pregnant (at least six weeks after the end of pregnancy) are more susceptible to serious COVID-19 disease, including hospitalization. admittance to an ICU.

Invasive mechanical ventilation is received.

Pregnant and nursing women have not been included in any of the randomized clinical trials that have been carried out to evaluate the safety and efficacy of the COVID-19 vaccines in these unique categories.

a)Immunocompromised patient

Approximately 3% of adult Americans have impaired immune systems, making them less equipped to fight off illnesses like COVID-19's causative agent, SARSCoV-2.

Individuals who take immunosuppressive drugs or treatments, as well as those with immunocompromising illnesses, are more vulnerable to serious COVID-19 consequences, such as hospitalization . admittance to an intensive care unit.

Be immunocompromised as a result of an underlying medical disease or immunomodulatory medications that alter the immune response. mRNA-based immunization typically

lowers COVID-19-associated hospitalization and mortality in immunocompromised persons, particularly after three or more doses. However, there is a wide range of COVID-19 vaccine-induced immune responses and a high risk of COVID-19 in the immunocompromised population.

b) Long term monitoring and pharmacovigilance data

To monitor the long-term safety of COVID-19 medical products, global pharmacovigilance systems adapted existing surveillance methods and launched new initiatives.

This produced extensive data showing that serious long-term adverse effects from COVID-19 vaccines are rare, while the risk of both long-term and short-term complications is significantly higher from COVID-19 infection itself.

Monitoring method- To gather extensive real-world evidence, global regulatory bodies and public health agencies enhanced pharmacovigilance by supplementing traditional passive reporting with advanced, active surveillance methods.

Traditional Pharmacovigilance Systems:

Active surveillance programs were established or expanded by health organizations such as the Food and Drug Administration and the U.S. Centers for Disease Control and Prevention. □ V-safe:

In the weeks and months after immunization, a smartphone-based system in the United States actively gathered health data through text messages and online surveys.

International partnerships: To evaluate the risks of particular adverse effects, large-scale, multi-country comparison studies were conducted through initiatives such as the Global Vaccine Data Network (GVDN®).

ADVERSE DRUG REACTION (ADRS):

Despite the fact that vaccinations were developed to stop the SARS-CoV-2 virus from spreading, they have had detrimental impacts on several Organ Systems,

such as circulation issues, migraines, fever and injection site reactions. Myocarditis, pericarditis, arrhythmias, thrombotic events, hypertension, acute coronary syndrome, cardiac arrest, and anaemia are examples of circulatory adverse effects.

Only a small percentage of COVID-19 vaccine users experience these rare adverse effects

1. Serious ADRs:

•Myocarditis:

First dosage of the vaccine, he experienced similar symptoms, though they were less severe. Studies conducted in the lab showed higher troponin levels and negative viral serology.

Males under 30 are more likely to experience these problems, especially following the second dosage of an mRNA vaccination. With only a few cases per million doses given, the incidence of these illnesses is still incredibly low.

•Thrombosis with Thrombocytopenia Syndrome (TTS):

Many explanations have been proposed, even though the exact reason of thrombocytopenia after COVID-19 vaccination is still unknown. It is called immune thrombocytopenic purpura is one instance of thrombocytopenia following COVID-19 vaccination, in which the body targets its platelets following vaccination, resulting in bleeding and bruises.

Vaccine-induced prothrombotic immune thrombocytopenia (VIPIT) is another potential mechanism, wherein aberrant blood post-marketing surveillance and pharmacovigilance are crucial. When low platelet counts coexist with clots, serious consequences including deep vein thrombosis or cerebral venous sinus thrombosis may result.

POST-MARKETING MONITORING AND PHARMACOVIGILANCE:

The COVID-19 pandemic vaccine development process can be expedited from 10 to 18 months, with pre-clinical testing and phase I taking approximately 6 to 9 months, and phases II and III taking an additional 6 to 9 months before the emergency authorisation is granted.

Phase III trials began after the intermediate assessment of phase I/II data, with many clinical trial stages carried out concurrently.

There are currently about 320 vaccine candidates, 17 of which are in use and 97 of which are undergoing clinical testing; seven of these have been granted emergency use authorization, the indication for use, and the safety studies to be continued after marketing clearance, all of the existing COVID-19 vaccines were awarded a EUA.

Importance of Continuous Surveillance Vaccine safety:

Monitoring is a difficult, continuous procedure. Vaccine safety needs to be aggressive, prompt, rigorous, and impartial.

Real-world observation:

Clinical trials are restricted and regulated. Vaccine safety in the general population, which comprises a broader spectrum of individuals with varying living conditions, is continuously monitored.

Finding uncommon side effects:

It's possible that uncommon side effects won't show up until millions of people have received vaccinations. Regardless of how uncommon these signals are, continuous monitoring systems are built Inclusion of vulnerable groups: Surveillance can reveal safety concerns that are unique to or more common in particular groups, such as immunocompromised individuals, pregnant women, or those with chronic illnesses, which were probably under-represented in clinical trials.(3)

Risk-Benefit Analysis:

The four primary surveillance techniques are sentinel, cohort event monitoring (CEM), passive (automated), and active. Enhancing current vaccine safety surveillance systems worldwide is essential for AEFI.

Countries with more reliable systems might think about using active surveillance to monitor adverse events of specific interest (AESI), even though passive systems are most commonly utilized to do so. Every stakeholder should be involved in order to enhance vaccine safety monitoring.

Following notice, inquiry, analysis, causality assessment, and communication, the system should incorporate data collecting and report.

Vaccines' Prevention of hospitalization And Death Far Outweighs Rare:

Hospitalization and death prevention from vaccines much outweighs Rarely assessed the risks and benefits per million stratified males.

The COVID-19 outcomes data collection stratified matched these age groups.

The model benefit targets included hospitalizations, intensive care unit (ICU) admissions, fatalities, and COVID-19 cases that may have been avoided with immunization.

The model risk endpoints included hospitalizations, ICU admissions, deaths, and cases of vaccine-related myocarditis/pericarditis

•Comparative risk and benefits of ADRs:

Our calculations consider the uncertainty of the regulatory question of whether, for the target group, the advantages of vaccination exceed the risks.

We determined the hospital's COVID-19 case count for the dangers and advantages that are most crucial to public health. We evaluated the advantages and disadvantages of the Moderna vaccination for each million males between the ages of 18 and 64 who receive two full doses.

These groups are expected to have a superior benefit-risk ratio than males between the ages of 18 and 64, according to the available data.

□FUTURE PERSPECTIVES:

The research changed the growing temperature of SARS-CoV-2 in Vero cells from 37°C to 22°C

Cold-adapted live-attenuated vaccine that people might spray into their nose One A robust B and T cell- mediated immune response was generated by a single vaccination dose.

The mice that were given the shot exhibited little signs of SARS-CoV-2 infection, including mild viral expression in many vital organs like the kidneys and brain, less weight loss, and fewer deaths. Useful strategy to promote a robust immunological reaction.

□CONCLUSION:

Protection (Efficacy) Vaccines work extremely well: The vaccines initially offered around 90-95% protection against getting sick with COVID-19. Protection against the worst outcomes lasts longer: Even as protection against mild illness fades over 4–6 months, the vaccines remain very strong at preventing severe illness, hospitalization, and death. Need for Boosters: Because the virus keeps changing (variants like Omicron) and protection decreases, booster shots are necessary to refresh your body's defense and restore protection, especially against symptomatic infection.

Generally Safe: The vaccines are safe and undergo strict testing. Most side effects are minor and temporary, like fever or muscle pain. Very Rare Serious Risks Blood Clots (TTS): Mostly associated with adenoviral vector vaccines. Monitoring is Continuous: Global systems are constantly watching for any long-term effects, and the data shows they are rare.

The Bottom Line (Benefit-Risk)-The benefits are much greater than the risks. Analysis consistently shows that vaccinating people prevents vastly more hospitalizations, ICU stays, and deaths from COVID-19 than the number of rare side effects caused by the vaccine.

ACKNOWLEDGEMENT

We gratefully acknowledge the valuable information and scientific data obtained from published literature, clinical trial reports, and official guidelines of international and national health organizations. Special reference has been made to documents and updates provided by the World Health Organization, U.S. Food and Drug Administration, European Medicines Agency, Ministry of Health and Family Welfare, and the Indian Council of Medical Research, whose publicly available reports and recommendations contributed significantly to this review.

REFERENCES

- 1) The true death toll of COVID-19: estimating global excess mortality. Geneva: World Health Organization; 2021 (<https://www.who.int/data/stories/the-true-death-toll-of-covid-19-estimating-global-excess-mortality>, accessed 17 March 2022)
- 2) The impact of COVID-19 on health and care workers: a closer look at deaths. Geneva: World Health Organization; 2021 (<https://apps.who.int/iris/handle/10665/345300>, accessed 17 March 2022).
- 3) Agarwal R, Gopinath G, Farrar J, Hatchett R, Sands P. A global strategy to manage the long-term risks of COVID-19. Washington (DC): International Monetary Fund; 2022 (IMF Working Paper 22/68; <https://www.imf.org/en/Publications/WP/Issues/2022/04/04/A-Global-Strategy-to-Manage-the-Long-Term-Risks-of-COVID-19-516079>).
- 4) Moderna . Emergency use authorization (EUA): Moderna COVID-19 Vaccine. Moderna. Published 2021. [Accessed 2021 Mar <https://www.modernatx.com/covid19vaccine-eua/> [Google Scholar].
- 5) National Institutes of Health (NIH). Clinical trial of investigational vaccine for COVID-19 begins [Internet]. 2020 [Updated 2020 March 16]. Available from: <https://www.nih.gov/news-events/news-releases/nih-clinical-trial-investnins>
- 6) Jackson LA, Anderson EJ, Rouphael NG, Roberts PC, Makhene M, Coler RN, et al. An mRNA vaccine against SARS-CoV-2: Preliminary report. *N Engl J Med.* 2020; 383(20):1920-31. [DOI:10.1056/NEJMoa2022483] [PMID] [PMCID]
- 7) European Medicines Agency (EMA). Recommends COVID-19 vaccine Moderna for authorization in the EU [Internet]. 2021 [Updated 2021 January 6]. Available from: <https://www.ema.europa.eu/en/news/ema-recommends-covid-19-vaccine-eu>
- 8) Blakney AK, Ip Sh, Geall AJ. An update on self-amplifying mRNA vaccine development. *Vaccines.* 2021; 9(2):97. [DOI:10.3390/vaccines9020097] [PMID] [PMCID]
- 9) C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, G. Fan, J. Xu, X. Gu, Z. Cheng Clinical features of patients infected with 2019 novel corona virus in Wuhan, China *Lancet* (2020), pp. 497-506
- 10) C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, G. Fan, J. Xu, X. Gu, Z. Cheng Clinical features of patients infected with 2019 novel corona virus in Wuhan, China *Lancet* (2020), pp. 497-506
- 11) A.E. Gorbalenya, S.C. Baker, R. Baric, R.J. Groot, C. Drosten, A.A. Gulyaeva, B.L. Haagmans, C. Lauberv, A.M. Leontovich, B.W. Neuman, D. Penzar, Severe acute respiratory syndrome-related coronavirus: the species and its viruses—a statement of the Coronavirus Study Group. *Nat Microbiol* doi: 10.1038/s41564-020-0695-z
- 12) World Health Organization. 2021. Interim recommendations for use of the ChAdOx1 S [recombinant] vaccine against COVID-19 (AstraZeneca COVID-19 vaccine AZD1222, SII Covishield, SK Bioscience). Available <https://apps.who.int/iris/rest/bitstreams/1343289/retrieve>. Last accessed 16 July 2021.
- 13) <https://doi.org/10.3390/vaccines11030682>
- 14) Ministry of Health and Family Welfare, Government of India. CoWIN Dashboard [Internet]. [cited 2021 July 16]. Available from: <https://dashboard.cowin.gov.in/>

15) R.W. Frencck Jr., N.P. Klein, N. Kitchin, et al. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents *N Engl J Med*, 385 (3) (2021), pp. 239-2

16) Logunov D, Dolzhikova I, Zubkova O, Tukhvatullin A, Shcheblyakov D, Dzharullaeva A. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: Two open, non-randomised phase 1/2 studies from Russia. *Lancet*. 2020;396(10275):887-97. [Google Scholar]

17) Dolzhikova I, Zubkova O, Tukhvatulin A. Safety and immunogenicity of GamEvac-Combi, a heterologous VSV- and Ad5-vectored Ebola vaccine: an open phase I/II trial in healthy adults in Russia. *H Vaccin Immunother*. 2017;13:613-33. [Google Scholar]

18) Krammer F. SARS-CoV-2 vaccines in development. *Nature*. 2020;586(7830):516–27. doi: 10.1038/s41586-020-2798-3. Oct; [DOI] [PubMed] [Google Scholar]

19) Collet J.P. Limitations of clinical trials. *Rev Prat*. 2000;50(8):833–837. [PubMed] [Google Scholar]

20) <https://cran.r-project.org/web/packages/metafor/metafor.pdf>

21) World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 2020. <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefin-covid19-11-march-2020> (accessed October 13, 2023)

22) Kandeel M, Yamamoto M, Tani H, et al. Discovery of new fusion inhibitor peptides against SARS- CoV-2 by targeting the spike s2 subunit. *Biomol Ther*. 2021;29(3):282 9

23) Kandeel M, Yamamoto M, Tani H, et al. Discovery of new fusion inhibitor peptides against SARS- CoV-2 by targeting the spike s2 subunit. *Biomol Ther*. 2021;29(3):282 9