REVIEW

Vaccines for Covid-19: An insight on their effectiveness and adverse effects

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Abstract
An era of SARS-COVID-19 outbreak with a high contagious percentage around the globe has been the subject of multi-agency research aimed at generating vaccines for active immunization. Scientists across the world are joining hands for advanced tie-ups between medical start-ups and pharmaceutical industries for devices and vaccines development to hinder the progress of this outbreak. Moreover, the questions that need to be answered are how to improve the effectiveness and efficacy of vaccines with reduced side effects and the required doses of vaccines for enhanced surveillance. In this review article, we have discussed the effectiveness and efficacy of different Covid-19 vaccines.

KEYWORDS
efficacy, relative risk rate, SARS-COVID 19, Sinovac, vaccines

1 INTRODUCTION

Coronavirus belongs to the family coronaviridae, and it is a single-stranded virus, it infects humans and a wide range of animals.1 The COVID-19 pandemic is sweeping the globe at breakneck speed.2 A pandemic called SARS-COVID-19 broke out in many countries of the world in December 2019.1,3 It shocked the world into silence and motivated thoughts to figure out the methods to tackle the pandemic1; as there was no cure discovered for the virus, the authorities collectively decided to implement a lockdown to maximize social distancing.4 Many organizations including both public and private sectors were affected. The SARS-CoV-2 virus is spread from China to other countries.5 At the end of 2019, SARS-COVID-19 cases appeared in the city of Wuhan, China, and till April 15, 2020, less than 1.9 million SARS-COVID-19 cases were reported with nearly 120 000 confirmed mortalities around the globe.5 On January 30, 2020, WHO declared this a global health pandemic based on rapidly increasing rates of Covid-19 at Chinese and international locations.1

The common symptoms of Covid-19 are loss of taste and smell, cough, flu, fatigue, fever, and loss of appetite.6 It spreads from person to person via touch and respiratory droplets, but there should be no uncertainty about its airborne, fecal, or intrauterine transmission.7,8 Inhaling microscopic airborne droplets, direct contact with infected persons or contaminated surfaces, and bigger respiratory droplets are all possible routes of infection.7 Nasal swab, tracheal aspirate, or bronchoalveolar lavage samples are employed in a real-time polymerase chain reaction as a diagnostic technique.10 Several in-house and commercially available assays for detecting the Covid-19 are currently being developed. Some assays can only detect the unique virus, while others (e.g., SARS-CoV) can detect other genetically similar strains.11 No specific treatment has been achieved for COVID-19 even after 10 months of this pandemic, some potential therapies produced encouraging results.12 The most common precautionary measures during Covid-19 were social distancing, use of disinfectant substances like bleach, quarantine, wearing of N95 face masks, and so forth.12 Mostly the healthcare personnel is at high risk of exposure to Covid-19, both in the workplace like laboratories, in in-hospital emergencies, and community, when providing care to Covid-19 patients.13 Furthermore, they develop herd immunity through natural immunity and concluded infections are possible, consequences and the death rate would be destructive.13,14 This method was seen in Sweden where authorities presumed that the infection rate is up to 60% of the population, so herd immunity would be sufficient to protect the population.15 However, they failed and the deaths per million population attributed to COVID-19 in Sweden is at least five
times more than that of Germany. So, developing an effective vaccine against this SARS-COVID-19 is an important step and the only way of establishing herd immunity.

The most therapeutic drugs for SARS-Covid-19 cases and the effective vaccines for the people were urgent needs. As there is no specific drug to treat SARS-COVID-19 worldwide but the four vaccines that is, COVID-19 messenger RNA (mRNA) vaccine BNT162b2 (Pfizer), mRNA-1273 vaccine (Moderna), ChAdOx1 nCoV-19 vaccine/AZD1222 (AstraZeneca), and Sinovac that have low safety risk and higher efficacies of 95%, 94.1%, 70.4%, and 78%, respectively were used in many countries. The Oxford AstraZeneca, Johnson and Johnson, and Sputnik vaccines use engineered live viral vectors to demonstrate the coronavirus spike protein, while the vaccines developed by Pfizer and Moderna make use of recent technology, such as messenger RNA. In general, China's coronavirus vaccines may need to be replaced or administered differently to be successful resist the SARS-CoV2 virus, according to the head of China's Center for Disease Prevention and Control.

The vaccine efficacy is assessed by using the relative risk (RR) method, the relation of COVID-19 attack rates with and without a COVID-19 vaccine which is stated as 1–RR. The effectiveness of the vaccine was assessed by using the cohort study design which compared the incidence in the general cohort of persons with the incidence of COVID-19 infection in the vaccinated persons who were antibody negative. The effectiveness of different vaccines was estimated as 87.0% is the efficacy of the B117 variant of the Pfizer vaccine and 72.1% is the efficacy of the B1351 variant of the Pfizer vaccine.

As of January 8, 2021, the death rate due to COVID-19 vaccination was 8.2 per million the population which exceeded 53.4 per million among the populations of long-term care facilities. Most of the reported deaths from Covid-19 were in the people ≥85 years of age with serious underlying diseases like hypertension, dementia, heart failure, diabetes, chronic obstructive pulmonary disease, and anemia. Further certain vaccine-drug and vaccine-disease interactions in polypharmacy users might have contributed to worsened health outcomes in already weak populations.

For effective vaccine development, clinical and preclinical trials are important to minimize the associated adverse effects. However, the worldwide collaborations among the different organizations such as the Gavi alliance, Accelerating COVID-19 Therapeutic Interventions and Vaccines, World health organizations, Coalition for Epidemic Preparedness Innovations, Bill and Melinda Gates Foundation shows cooperation to the SARS-COVID-19 pandemic and ensure the acceptable funding for the vaccines development. In this review, we have summarized the efficacy as well as the adverse effects of different types of COVID-19 vaccines (Table 1).

### 1.1 AstraZeneca vaccine

The AstraZeneca is a monovalent vaccine comprised of a single recombinant, adenoviral vector (the icosahedral virions, nonencapsulated with a single linear molecule of DNA) encoding the S glycoprotein of Covid-19. Furthermore, the AstraZeneca vaccine also contains polysorbate 80, disodium edetate dihydrogen, magnesium chloride hexahydrate, sucrose, l-histidine hydrochloride monohydrate, l-histidine, sodium chloride, ethanol, and water for injection. The efficacy of the AstraZeneca vaccine was 63.09% (95% confidence interval). The time of vaccine opening to administration requires 2–8°C temperature due to the small shelf-life of vaccines which is 6 months.

The vaccine developed by AstraZeneca, a British-Swedish company, has been a source of considerable promise. The Oxford AstraZeneca vaccination is inexpensive and may be stored in a regular refrigerator because it is projected to be manufactured in large quantities, it could be significant in limiting the pandemic. For the time being, “the AstraZeneca vaccine is the only one that will be available in considerable quantities in many places, particularly on the African continent.” The vaccine shows some adverse reaction which is mild to moderate in some cases. Most adverse reactions were reported after the second dose such as injection site pain, headache, injection site tenderness, fatigue, malaise, myalgia, arthralgia, and nausea.

The Oxford AstraZeneca COVID-19 vaccine has a low level of perceived safety, particularly among vaccine skeptics. Some European governments banned the use of the AstraZeneca vaccine on March 15, 2021, as a precautionary measure following the deaths of a few hundred patients who developed blood clots because of deep vein thrombosis. Tenderness, discomfort, warmth, redness, itching, inflammation, and blisters at the injection site are common Indian AstraZeneca adverse effects. Recent studies of thrombocytopenia-related cerebral venous sinus thrombosis, repeated thrombosis, and hemorrhage occurring within a short time after receiving the vaccination are alarming, and health officials are paying close attention. Multiple thrombosis, bleeding, and thrombocytopenia, all of which seem to be symptoms of disseminated intravascular coagulation.

### 1.2 Sinopharm vaccine

This SARS-CoV-2 vaccine is established in the collaboration of the Beijing Institute of Biological Products, Prevention China, National Biotech Group Company Limited, and the Chinese Center for Disease Control. This Sinopharm vaccine has been approved as a 2-dose vaccine first given at 0 and 21 days for the prevention of Coronavirus disease. This vaccine is composed of aluminum hydroxide adjuvant in phosphate-buffered saline and inactivated antigens of Covid-19 and the shelf-life of the Vaccine is 24 months at 2–8°C.

The 14,301 participants were enrolled in the Vaccine Phase trial, from this 98% were aged between 18 and 60 years while 893 applicants are of 59 years of age, and 294 were registered in the COVID-19 vaccine BIBP group. Of this 85% of applicants were male, 87% of applicants were recognized as Asian and 13% were Chinese. The vaccine efficacy was demonstrated among
### TABLE 1  Efficacy as well as the adverse effects of different types of COVID-19 vaccines.

| S/N | Vaccine name            | Nature of vaccine | Effectiveness of vaccine | Efficacy of vaccine | Side effects                              | Age groups                      | References         |
|-----|-------------------------|-------------------|--------------------------|---------------------|-------------------------------------------|---------------------------------|--------------------|
| 1   | Pfizer vaccine          | RNA               | 89.5%                    | 95%                 | Fatigue, fever                            | Children, adolescents, and older | [19, 21]          |
| 2   | Moderna vaccine         | RNA               | 92.1%                    | 92.1%               | Headache, myalgia, fever                  | Children, adolescents, and older | [16, 21]          |
| 3   | AstraZeneca vaccine     | Viral vector      | 62%–90%                  | 63.09%              | Injection site pain, headache, fatigue, Malaise | 65 years and older              | [22–24]          |
| 4   | Sputnik V vaccine       | Viral vector      | 92%                      | 91.6%               | Headache, flu symptoms                     | 18 years and older              | [25, 26]          |
| 5   | Johnson & Johnson vaccine | Viral vector   | 66%                      | ......               | Headache, muscle pain, fatigue             | 18 years and older              | [27, 28]          |
| 6   | Sinovac vaccine         | Inactive vaccine  | ......                    | 80.7%               | Injection site pain, fever, pruritus, myalgia, cough, | 18 years and older              | [29, 30]          |
| 7   | Sinopharm               | Inactivated vaccine | 49.6%                  | 79%                 | Fatigue, fever, anorexia                   | 18 years and older              | [31, 32]          |
| 8   | CanSino                 | Viral vector      | 65.28%                   | Injection site pain, headache, muscle pain, fatigue | 18 years and older              | [33]              |
| 9   | Covishield              | Adenovirus vaccine| 70%                      | fever/chills, cough, dyspnea, fatigue, myalgia, headache, new loss of taste or smell, sore throat, runny nose, nausea/vomiting, diarrhea | 18 years and older              | [34]              |
| 10  | Covaxin                 | Inactivated vaccine| ......                  | 80.6%               | Fever, headache, fatigue, nausea, vomiting | 18 years and older              | [35]              |
| 11  | Novavax                 | Protein subunit   | 87.5%                    | Injection site pain, headache, joint pain, fatigue | 18 years and older              | [36]              |
participants is 80.7% while the adverse effects were seen during the clinical trials such as injection site pain, fever, pruritus, fatigue, headache, erythema, myalgia, cough, dyspnea, arthralgia, nausea, diarrhea, vomiting, and dysphagia. The Clinical Event Committee confirmed that 142 cases of SARS-CoV-2 were reported after the second vaccination.

1.3 | Sinovac/CoronaVac vaccine

The Inactivated Sinovac vaccines used against SARS-Cov-19 are developed by some vaccine manufacturers. This vaccine is used as a 2-dose vaccine for individuals aged 18 years and older. The Sinovac vaccine was approved by the NMPA on February 6th, 2021. It is used in different countries in the time of emergency. April 21, 2021, more than 260 million doses were distributed to the public in China and more than 160 million individuals have been vaccinated through Sinovac. The Sinovac vaccine is composed of 3 µg of inactivated SARS-CoV-2 virus, sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium chloride, aluminum hydroxide, or water for injection. Sinovac, a Beijing-based pharmaceutical company, created the Corona-Vac vaccine. It’s also based on an inactivated SARS-CoV-2 strain with an efficacy of 56.5%. According to the study conducted by the University of Chile, one dose was just 3% effective (increasing to 27.7% within 2 weeks after the second dose, while 56.5% after 2 weeks.) Corona-Vac, created by Beijing-based Sinovac, was found to be 50.4% effective in late-stage trials in preventing severe and mild COVID-19. This is far less than the 90% efficacy of several popular vaccines. The adverse reactions which was reported during the Sinovac trial is fatigue, fever, muscle pain, anorexia, muscle distention, acute allergic reaction, and diarrhea.

1.4 | Pfizer vaccine

The Pfizer-BioNTech BNT162b2 is a messenger RNA vaccine that shows 95% efficacy against SARS-COVID-19. The Pfizer-vaccine is composed of ALC-0315, potassium chloride, cholesterol, sodium chloride, disodium hydrogen phosphate dihydrate, potassium dihydrogen phosphate succrose, and water for injection. The effectiveness of the Pfizer vaccine was assessed by using a cohort study design in which they measure the effectiveness of the vaccine by comparing the incidence in the general cohort of persons with the incidence of COVID-19 infection in the vaccinated persons who were antibody negative. The Pfizer vaccine effectiveness in the B117 variant was 89.5% and the B1351 variant was 75.0% at 14 days after the second dose. In May, its Phase 2 trial was introduced on two varieties of the vaccine and both varieties lead to the production of antibodies against SARS-COVID-19 and T cells in response to COVID-19. The one version of the vaccine known as BNT162b2 produces some adverse effects like fatigue or fevers, so they move for the next Phase 2/3 trials. On July 27, the companies revealed the second Phase 2/3 trial in which 30,000 volunteers participated in the United States and other countries also participate Brazil, Germany, and Argentina.

1.5 | Moderna vaccine

This vaccine is composed of such components as messenger ribonucleic acid, PEG, cholesterol, DSPC, tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate trihydrate, and sucrose. The efficacy of the Moderna vaccine after one dose was 50.8% however, after the second dose it was 92.1% effective. This messenger-RNA-based Moderna vaccine was approved by the FDA and was used for the emergency during the SARS-COVID-19 pandemic in 2020. In efficacy trials of the Moderna vaccine, 15,185 participants were enrolled and they receive one dose of vaccine and 228 cases were reported showing the adverse side effects such as injection site rash and urticaria, which manifests for 48 h postvaccination. Those who received one dose of Moderna COVID-19 have adverse effects in participants 18 years of age or older, Pain at the injection site, Headache, Myalgia, fever, arthralgia, chills, vomiting, and axillary swelling sometimes erythema at the injection site.

1.6 | Gamaleya (Sputnik V)

Gamaleya vaccine is also known as Gam-COVID-Vac/Sputnik V vaccine. The Gamaleya vaccine is developed through heterologous recombinant adenovirus and using adenovirus 5 and adenovirus 26 as vectors for the appearance of Covid-19 spike protein. The Sputnik V Vaccine is two vector vaccines, that is, composed of sodium chloride, Tris aminomethane, Sodium EDTA, ethanol, magnesium chloride hexahydrate, polysorbate 80, sucrose, and water for injection. The Gam-COVID-Vac vaccine was approved by the WHO in the short-term study of Phase 3 trials which were conducted in Russia in the middle of Sept 7 and Nov 24, 2020. The Sputnik vaccine is not commonly used in Russia but is used in other countries such as Chile, Hungary, and Argentina.

Some side effects were reported such as headache, fatigue, Flu-like symptoms, and injection site reaction. From June 18 to August 3rd, 2020, they registered 76 volunteers for two studies and two groups each with nine participants receives adenovirus-26-S and adenovirus-5-S in 1st phase, respectively, while 20 received adenovirus-26-S or adenovirus-5-S in 2nd phase. So, both formulations of vaccines are well tolerated and safe with better efficacy.

2 | EFFICACY OF COVID-19 VACCINES AMONG CHILDREN, TEENS, AND PREGNANT FEMALES

Among the children, COVID-19 is a mostly asymptomatic and mild disease with <2% of children having symptoms and requiring hospitalization. Covid-19 vaccination among children and teens
remains highly discussed internationally with extensive policy divergence which was not part of an initial plan with the emergence of the original strain of the SARS-CoV-2 virus because these groups seemed very a little affected by COVID-19. But new mutations in the genome of SARS-CoV-2 led to its increased virulence. After the successful vaccination roll-out to older and at-risk populations, the virus started to spread among younger populations to a greater extent which turn into a new concern. Resulting in the safety and efficacy testing of vaccines in children and adolescents by biotechnological and pharmaceutical industries along with this many countries started vaccine roll-out under 18 years of age for protection against newer and more virulent viral strains.63

Though most of the COVID-19 vaccines are only approved for use in adults (18 years and older) but many countries have given the authorization for emergency use of mRNA vaccines (BNT162b2; Pfizer, and mRNA 1273; Moderna) in the adolescent groups (12–17 years of age).64,65 And later in November 2021, the mRNA vaccine BNT162b2; by Pfizer was approved by a stringent regulatory authority for the use in children 5–11 years of age.65 Pfizer was shown to be 91% effective against symptomatic COVID-19 among aged 5–11 years with minor side effects such as tenderness of the arm, headache, fatigue, joint pain, muscle pain, chills, and fever while the trial of Moderna among children of 6–11 years shown to be 88% effective with the following side-effects after the first dose like pain at the injection site, headaches, fever, tiredness, and muscle pain.66

Clinical trials for two inactivated vaccines, that is, Sinovac-CoronaVac and BBIBP-CoV were completed in children as young as 3 years of age and were approved by Chinese authorities for use in children of 3–17 years of age. Additionally, an adjuvanted inactivated vaccine Covaxin and a novel DNA vaccine (ZycoVd) developed by Bharat, were authorized to use in India among the age of 12–17 years; but have not yet received WHO Emergency use Listing (EUL) for children.65

The impact of Covid-19 vaccination on pregnant women remains uncertain due to inadequate data availability. In fact, because of the unique physiological changes in the cardiopulmonary and immune systems, pregnant women are still at a higher risk of getting pneumonia and viral respiratory infections. The efficacy of Moderna and Pfizer–BioNTech vaccines67 (96%–97% effectiveness)68 in pregnant women was demonstrated by many studies. Following these vaccinations, most pregnant females showed injection-site pain/soreness, headache, fatigue, chills, fever, myalgia, and nausea.67 highly vaccinated peoples has challenged the effectiveness of available vaccines.70

A test-negative case-control design was used to estimate the vaccine effectiveness against symptomatic disease due to omicron, delta variant of Covid-19, or the predominant alpha strain over the period of delta variant emergence in England.70,71

The effectiveness of the vaccine was calculated after prime immunization with two dosages of ChAdOx1 nCoV-19 (AstraZeneca), BNT162b2 (Pfizer–BioNTech), or mRNA-1273 (Moderna) vaccine. The investigations for all combinations of primary dosages of vaccines were found to be highly effective against the delta variant than the omicron. While the partial protection was provided against the omicron variant by the prime immunization with two dosages of BNT162b2 or ChAdOx1 nCoV-19 vaccine.71

4 CONCLUSION

Development of a vaccine is a laborious process with many stages, that is, the preclinical and clinical stages, etc hence, the novel approaches to COVID-19 have therefore enforced the research community to adopt unconventional methods to accelerate the process of vaccine development. Researchers used a Cohort Study design to measure the effectiveness of the vaccine by comparing the incidence in the general cohort of persons with the incidence of COVID-19 infection in the vaccinated persons who were antibody negative. The need of the hour is to develop an effective and safe vaccine against COVID-19 with enhanced efficacy and reduced side effects.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

This manuscript has no associated data to make it available.

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