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Review Article

Efficacy and Safety of COVID-19 Vaccines in Different Variants and Doses: A Systematic Review

Hamed Delam[1], Sara Moghaddam[2,3], Reza Zare[1*]

[1]Student Research Committee, Larestan University of Medical Sciences, Larestan, Iran
[2]Department of Nursing, School of Nursing, Larestan University of Medical Sciences, Larestan, Iran
[3]Department of Nursing, School of Nursing and Midwifery, Jahrom University of Medical Sciences, Jahrom, Iran

*Corresponding Author:
Reza Zare,
Email: rezazr1080@gmail.com

Abstract

Background and aims: Today, with the outbreak of the coronavirus disease 19 (COVID-19) pandemic, we have witnessed many efforts by different countries to produce a vaccine for this disease. Each vaccine has been marketed with different efficiencies, thus this research was designed to determine the efficacy of different types of these vaccines in 2022.

Methods: The present research was a systematic review. Researchers surveyed six international databases, including Medline/PubMed, ProQuest, Scopus, EMBASE, Google Scholar, and the ISI Web of Science, in January 2022. After reviewing the titles and abstracts of articles, 60 articles entered the final stage, and their full texts were reviewed based on the study purpose. All the vaccines included in the study were approved by the World Health Organization (WHO) or the Ministry of Health of the manufacturer country in the third phase of the clinical trial.

Results: All current vaccination platforms provide adequate protection against severe acute respiratory syndrome *coronavirus 2* (SARC-CoV-2) infection and significantly reduce the risk of serious infection. In addition, people who receive two vaccine doses have higher efficacy than those who only receive one dose of each vaccine. The results of the studies demonstrated that the effectiveness of vaccines is different in various groups and countries. According to the results of the reviewed studies, the Pfizer vaccine had an overall effect of 100% on the age group of 12-15 years. The overall effect of the Moderna vaccine varied from 78.6% to 97% in different groups. In general, the available vaccines for COVID-19 are less effective in the Omicron variant. On the other hand, it seems that the COVID-19 vaccines had better efficacy on the alpha variant.

Conclusion: Overall, the vaccines used in the COVID-19 pandemic have acceptable efficacy. Although serious side effects caused by the injection of the vaccine have been rarely reported in some studies, it seems that the safety of these vaccines is acceptable in general.

Keywords: COVID-19 vaccines, Vaccine efficacy, Safety, Systematic review

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Introduction

Respiratory viral infections and pandemics occurred more than 130 years ago. The Russian flu is known as the first severe pandemic in the world that occurred from 1889 to 1892, and a few years later, the Spanish flu spread all over the world.[1] After 100 years of Spanish flu, another severe viral infection, namely, coronavirus disease 19 (COVID-19) broke out in December 2019 and was the virus's starting point in Wuhan, China.[1,2] COVID-19 expanded globally, and the World Health Organization (WHO) reported it as an outbreak on January 30, 2020.[3,4] COVID-19 is caused by a positive-strand RNA virus that belongs to the Coronaviridae family and contains structural and non-structural proteins in its genome.[5-7] By encoding these proteins, researchers discovered that the Novel Coronavirus genome is 79% identical to the severe acute respiratory syndrome (SARS) coronavirus and 50% similar to the Middle East respiratory syndrome virus sequence.[1,8] In comparison to other coronaviruses, SARS-CoV-2 tends to spread more quickly.[9] This disease is growing worldwide and has a significant impact on global health, society, and the economy, resulting in lockdowns, anxiety, and stress.[10-12] Antiviral (against virus replication) and immunomodulatory/anti-inflammatory medicines are the main treatment options for COVID-19 in order to avoid tissue damage. Dexamethasone, tocilizumab, remdesivir, and the like are among the most common symptomatic therapies, but none of them is perfect.[10] Vaccine immunity is critical to decreasing illness burden, the implementation of the existing public health initiatives, and the consequent economic recovery.[11] Over 200 COVID-19 vaccines are in development. According to the WHO, there are more than 50 candidate vaccines in human clinical trials, 18 of which are undergoing efficacy testing.[13,14] *AstraZeneca*, *Moderna*, *Pfizer*, *Sinopharm*, *Sputnik V*, *Sinovac Biotech*, and *Johnson & Johnson* are among the companies that have acquired emergency use authorization.[15] To date, several platforms have

been developed for vaccine development, and currently, many platforms and methodologies have been employed to generate COVID-19 vaccines, some of which are as follows:

(I) Among numerous vaccination platforms, nucleic acid mRNA-based vaccines are the most recent generation of vaccines.[5,16] In modern ribosome mRNA vaccination, a single-stranded RNA polynucleotide sequence containing part of the codon corresponding to the amino acid and protein components of the virus can be produced in the cytoplasm. The resulting antigen causes an immunological response, which includes the development of antibodies. For example, companies such as Pfizer and Moderna, which produce vaccines based on new biotechnologies, insert a synthetic mRNA into the cell that encodes the Coronavirus S protein.[5,17] The vaccines were developed by Sputnik V, Johnson & Johnson, and AstraZeneca introducing a DNA sequence encoding the S-protein into the genome of a harmless modified adenovirus. A pathogen is made of a vaccine containing the entire virus, which is produced from the whole viruses or pieces of viruses that have been destroyed or inactivated. Heat, chemicals, or radiation damage the pathogen's genetic material, preventing it from replicating, but its presence can still trigger immunogenicity.[5,18] Sinopharm and Sinovac Companies produced their vaccines by inactivating SARS-CoV-2 with B-propiolactone while keeping all of the virus protein. Subunit vaccines have a pathogen fragment in the form of a protein, a polysaccharide, or a combination of the two, but no live pathogen particles.[5] Since the COVID-19 pandemic, multiple strains, including alpha, beta, gamma, and delta, have spread to various regions of the world, raising public health worries and fears due to rapid transmission rates and high safety evasion.[19] On November 26, 2021, the WHO identified Omicron as a new COVID-19 variant of concern; because of its contagious and vaccine-escape mutations, Omicron has caused worldwide panic.[20] According to a recent research study, the household-confirmed secondary infection rate for Omicron was about 21.6%, which is double the delta variant.[20] This research was designed to determine the efficacy of different types of these vaccines in 2022.

Methods

The present research is a systematic review of the efficacy of COVID-19 vaccines in different variants and doses designed and implemented in 2022. All the vaccines included in the study had been approved by the WHO or the Ministry of Health of the manufacturer country in the third phase of the clinical trial.

The reporting method of the present research was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist.

Search Strategy

In January 2022, researchers in the study surveyed 6 international databases, including PubMed/Medline, ProQuest, Scopus, EMBASE, Google Scholar, and the ISI Web of Science.

Different keywords were searched, including "COVID-19", "SARS-CoV-2 Infection", "2019 Novel Coronavirus Disease", "2019 nCoV Disease", "Coronavirus Disease 2019", "Severe Acute Respiratory Syndrome Coronavirus 2 Infection", and "COVID-19 Pandemic". The other keywords were "COVID-19 Vaccines", "COVID-19 Virus Vaccine", "SARS-CoV-2 Vaccines", "Coronavirus Disease 2019 Vaccines", "2019-nCoV Vaccine", "2019 Novel Coronavirus Vaccine", "Vaccine Efficacy", "Pfizer-BioNTech", "Moderna", "Novavax", "Sputnik V", "Sinopharm", "AstraZeneca", "Oxford–AstraZeneca", and "Vaccine dose".

Duplicate articles were removed from further analysis. The two investigators separately studied the papers. Papers referring to the efficacy of COVID-19 vaccines were included in the research. On the other hand, articles published in conferences, posters, and congresses were excluded from the study.

Qualitative Evaluation of Articles

The Newcastle-Ottawa Quality Assessment Form was used to assess the quality of the selected papers. The present tool has 3 different parts, including selection (4 items), comparability (1 item), and outcome (3 items), and based on the final scores, it is divided into good, fair, and poor categories. The first one included 3 or 4 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome/exposure domain. The second part contained 2 stars in the selection domain, 1 or 2 stars in the comparability domain, and 2 or 3 stars in the outcome/exposure domain. The final category consisted of 0 or 1 star in the selection domain or 0 stars in the comparability domain or 0 or 1 stars in the outcome/exposure domain.[21]

All articles were assessed based on information relevance and methodological accuracy.[22]

Screening Studies

The initial search was performed by two researchers (HD, SM), who were familiar with scientific databases and the subject of the study. If the results of the two were different, the third researcher (RZ) searched again. The articles were screened and the information was extracted separately by two investigators (HD, RZ). Finally, 1630 papers were obtained for analysis. Most articles were simultaneously indexed in Scopus, PubMed, and ISI databases, thus they were excluded from the study because they were duplicates (n = 825). By checking the title of the article and its abstract, a total of 357 articles were excluded from the study. After eliminating duplicate papers, 215 articles remained the review phase in terms of the title and abstract. At this stage, clinical trials, as well as cohort and cross-sectional studies were included in the study, and review articles, meta-analyses, case reports, and letters to the editor were excluded from the study.

Further, some articles were excluded from the study due to the lack of access to the full text. Eventually, 60 articles remained in the final phase, in which the full text of the articles was reviewed based on the study purpose. Figure 1 shows the study protocol.

Results

Efficacy data for five vaccines at different doses were reported in various studies presented in Table 1. The results of the studies revealed that the effectiveness of vaccines is different in various groups and countries. According to our findings, all the existing vaccine platforms provide adequate protection against the SARS-CoV-2 infection and lower the risk of severe illness considerably. In addition, people receiving two vaccine doses have higher efficacy than those who receive only one dose of each vaccine. For example, the efficacy of the *Moderna* vaccine was reported to be 78.6% in the study by Bajema et al on 1896 US adults over 65 years of age.[23] However, in the study by Vokó et al on 20 658 adults aged 25-34 in Hungary, the overall effectiveness of the *Moderna* vaccine was about 97%.[24] The *Sputnik* vaccine also had a wide range of results in different studies so that the effect of this vaccine in the study by Vokó et al conducted on 55 632 people aged 16-24 in Hungary was nearly 75.5%.[24] The highest effect of this vaccine among the reviewed studies was approximately 90.9%, which was reported in the population over 85 years old.[24] Overall, the efficacy of mRNA vaccines is highly close, while *Moderna* has a higher efficacy than *Pfizer*, and *Sputnik V* has a higher efficacy than *AstraZeneca* in the adenovirus recombinant vector. The *Pfizer* vaccine has shown 100% efficacy in the 12-15-year-old age group in the United States.[25] Based on the results of the reviewed studies, in the adenovirus recombinant vector, the *Sputnik V* vaccine had the highest efficacy (90.9%) in persons over 85 years old, and *AstraZeneca* has the highest efficacy (83.5%) in people over 65 years old. The results demonstrated that among the several platforms of the COVID-19 vaccine, mRNA vaccines had higher efficacy than inactivated and adenovirus recombinant vectors, whereas inactivated vaccines had the lowest efficacy. Table 2 presents the efficacy statistics for five vaccines in various variants. By examining various studies, it was found that the effectiveness of vaccines will probably change due to the emergence of different variants of COVID-19. The results of Table 2 represented that, in general, the available vaccines for COVID-19 are less effective in the Omicron variant. Moderna had the most effective vaccine (48%), while Sinopharm had the least effective vaccine (35%). On the other hand, it seems that COVID-19 vaccines had better efficacy on the alpha variant.

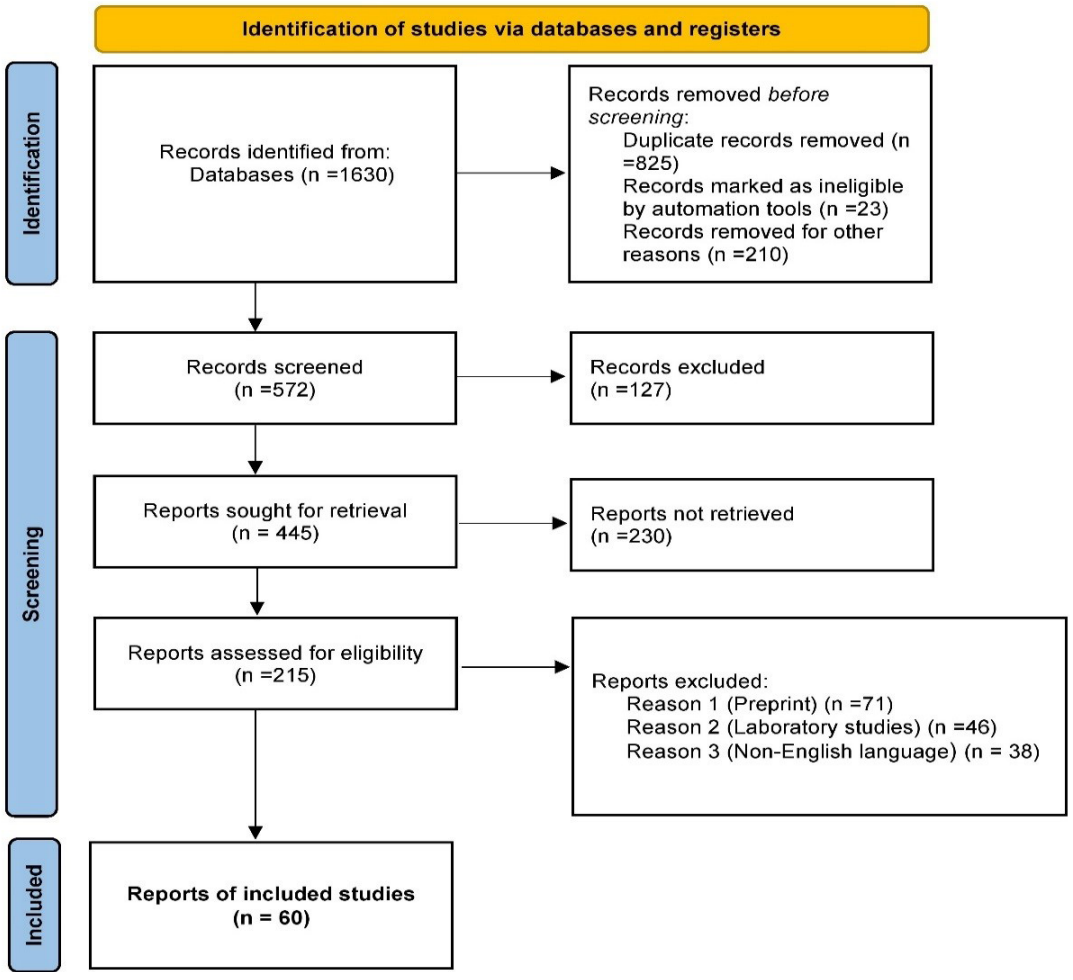

Figure 1. Study Protocol

Table 1. The Efficacy of COVID-19 Vaccines

Authors, Year [Ref].	Country /Region	Vaccine	Platform	Study Design	Sample Size	Population	Study Duration	Efficacy		Vaccines	
								Dose 1	Dose 2	Dose 3	Overall
Logunov et al[26]	Moscow, Russia.	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	A randomized, double-blind, placebo-controlled, phase 3 trial	21 977	≥18 years	7 September to 24 November, 2020	73.1%	91.1%	NR	91.6%
McKeigue et al[27]	Scotland	BNT162b2 mRNA-1273	mRNA	A case-control study	5645 cases 50 096 controls	NR	1 December 2020 to 8 September, 2021	NR	92%	NR	NR
Robert et al[25]	United States	BNT162b2	mRNA	A randomized, placebo-controlled, observer-blinded, phase 3 trial	2260	12-15 years	15 October 2020 to 12 January, 2021	NR	NR	NR	100%
Baden et al[28]	US	mRNA-1273	mRNA	Single-blind, randomized, controlled trial	30 420	≥18 years	27 July to 23 October, 2020	NR	NR	NR	94.1%
Baden et al[28]	US	mRNA-1273	mRNA	Single-blind, randomized, controlled trial	30 420	≥18 to<65 years	27 July to 23 October, 2020	NR	NR	NR	95.6%
Baden et al[28]	US	mRNA-1273	mRNA	Single-blind, randomized, controlled trial	30 420	≥65 years	27 July–23 October 2020	NR	NR	NR	86.4%
Emary et al[29]	UK	(ChAdOx1 nCoV-19/ AZD1222)	Adenovirus recombinant vector vaccine	Single-blind, randomized, controlled trial	8534	≥18 years	31 May 13 November, 2020	NR	NR	NR	B.1.1.7 variant 70.4%
Swift et al[30]	US	BNT162b2	mRNA	Observational study	76 000	Healthcare workers	1 January 31 March, 2021	78.1%	96.8%	NR	NR
Swift et al[30]	US	mRNA-1273	mRNA	Observational study	76 000	Healthcare workers	1 January 31 March, 2021	91.2%	98.6%	NR	NR
Pilishvili et al[31]	US	BNT162b2	mRNA	A test-negative case–control study	1482 case participants and 3449 control participants	Healthcare workers	28 December to 19 May, 2021	77.6%	88.8%	NR	NR
Pilishvili et al[31]	US	mRNA-1273	mRNA	A test-negative case-control study	1482 case participants and 3449 control participants	Healthcare workers	28 December to 19 May, 2021	88.9%	96.3%	NR	NR
Kyriakidis et al[5]	Argentina	Gam-COVID-Vac (Sputnik V)	recombinant adenovirus (rAd)-based vaccine	A retrospective cohort study	415 995	60-79 years	29 December 2020 to 21 March, 2021	NR	NR	NR	87.6%
Falsey et al[32]	United States, Chile, and Peru	(ChAdOx1 nCoV-19/ AZD1222)	Adenovirus recombinant vector vaccine	Double-blind, randomized, placebo-controlled, phase 3 clinical trial	32 451	≥18-64 years	NR	NR	NR	NR	72.8%
Falsey et al[32]	United States, Chile, and Peru	(ChAdOx1 nCoV-19/ AZD1222)	Adenovirus recombinant vector vaccine	Double-blind, randomized, placebo-controlled, phase 3 clinical trial	32 451	≥65 years	NR	NR	NR	NR	83.5%
Falsey et al[32]	United States, Chile, and Peru	(ChAdOx1 nCoV-19/ AZD1222)	Adenovirus recombinant vector vaccine	Double-blind, randomized, placebo-controlled, phase 3 clinical trial	32 451	≥18 years	NR	NR	NR	NR	74%
Bajema et al[23]	US	BNT162b2	mRNA	Test-negative case-control	1896	≥18-64 years	1 February 1 to 30September, 2021	NR	NR	NR	89.4%

Table 1. Continued

Authors, Year [Ref].	Country /Region	Vaccine	Platform	Study Design	Sample Size	Population	Study Duration	Efficacy		Vaccines	
								Dose 1	Dose 2	Dose 3	Overall
Bajema et al[23]	US	BNT162b2	mRNA	Test-negative case-control	1896	≥65 years	1 February to 30 September, 2021	NR	NR	NR	72.9%
Bajema et al[23]	US	mRNA-1273	mRNA	Test-negative case-control	1896	≥18-64 years	1 February to 30 September, 2021	NR	NR	NR	94.5%
Bajema et al[23]	US	mRNA-1273	mRNA	Test-negative case-control	1896	≥65 years	1 February to 30 September, 2021	NR	NR	NR	78.6%
Self et al[33]	US	BNT162b2	mRNA	A case-control analysis	3689	≥18 years	11 March to 15 August, 2021	NR	NR	NR	88%
Self et al[33]	US	mRNA-1273	mRNA	A case-control analysis	3689	≥18 years	11 March to 15 August, 2021	NR	NR	NR	93%
Moline et al[10]	US	BNT162b2	mRNA	COVID-19-associated hospitalization surveillance network (COVID-NET)	7280	65-74 years	1 February to 30 April, 2021	NR	NR	NR	96%
Moline et al[10]	US	mRNA-1273	mRNA	COVID-19-associated hospitalization surveillance network (COVID-NET)	7280	65-74 years	1 February to 30 April, 2021	NR	NR	NR	96%
Moline et al[10]	US	BNT162b2	mRNA	COVID-19-associated hospitalization surveillance network (COVID-NET)	7280	≥75 years	1 February to 30 April, 2021	NR	NR	NR	91%
Moline et al[10]	US	mRNA-1273	mRNA	COVID-19-associated hospitalization surveillance network (COVID-NET)	7280	≥75 years	1 February to 30 April, 2021	NR	NR	NR	96%
Lopez Bernal et al[34]	UK	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Test-negative case–control	Delta variant 4272	≥16 years	NR	Delta variant 30%	Delta variant 67%	NR	NR
Lopez Bernal et al[34]	UK	BNT162b2	mRNA	Test-negative case–control	Delta variant 4272	≥16 years	NR	Delta variant 35.6%	Delta variant 88%	NR	NR
Paris et al[35]	Western Europe	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	An observational study using surveillance data	NR	≥50 years	NR	86.2%	NR	NR	NR
Paris et al[35]	Western Europe	mRNA-1273	mRNA	An observational study using surveillance data	NR	≥50 years	NR	38.2%	100%	NR	NR
Paris et al[35]	Western Europe	BNT162b2	mRNA	An observational study using surveillance data	NR	≥50 years	NR	49.2%	94.6%	NR	NR
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	67 149	16-24 years	22 January to 10 June, 2021	NR	NR	NR	82.3%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	144 278	25-34 years	22 January to 10 June, 2021	NR	NR	NR	83.2%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	208 085	35-44 years	22 January to 10 June, 2021	NR	NR	NR	84.2%

Table 1. Continued

Authors, Year [Ref].	Country /Region	Vaccine	Platform	Study Design	Sample Size	Population	Study Duration	Efficacy		Vaccines	
								Dose 1	Dose 2	Dose 3	Overall
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	231 593	45-54 years	22 January to 10 June, 2021	NR	NR	NR	85.6%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	232 871	55-64 years	22 January to 10 June, 2021	NR	NR	NR	85%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	310 079	65-74 years	22 January to 10 June, 2021	NR	NR	NR	85.3%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	230 046	75-84 years	22 January to 10 June, 2021	NR	NR	NR	82.1%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	72 910	≥85 years	22 January to 10 June 2021	NR	NR	NR	74.3%
Vokó et al[24]	Hungary	BNT162b2	mRNA	Nationwide, retrospective, observational study	1 497 011	≥16 years	22 January to 10 June, 2021	NR	NR	NR	83.3%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	10 312	16-24 years	22 January to 10 June, 2021	NR	NR	NR	80.5%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	20 658	25-34 years	22 January to 10 June, 2021	NR	NR	NR	97.0%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	34 890	35-44 years	22 January to 10 June, 2021	NR	NR	NR	90.6%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	40 781	45-54 years	22 January to 10 June, 2021	NR	NR	NR	93.6%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	35 726	55-64 years	22 January to 10 June, 2021	NR	NR	NR	84.5%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	39 118	65-74 years	22 January to 10 June, 2021	NR	NR	NR	93.2%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	27 111	75-84 years	22 January to 10 June, 2021	NR	NR	NR	88.9%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	14 296	≥85 years	22 January to 10 June, 2021	NR	NR	NR	84.1%
Vokó et al[24]	Hungary	mRNA-1273	mRNA	Nationwide, retrospective, observational study	222 892	≥16 years	22 January to 10 June, 2021	NR	NR	NR	88.7%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	55 632	16-24 years	22 January to 10 June, 2021	NR	NR	NR	75.5%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	94 808	25-34 years	22 January to 10 June, 2021	NR	NR	NR	82.7%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	167 038	35-44 years	22 January to 10 June, 2021	NR	NR	NR	84.7%

Table 1. Continued

Authors, Year [Ref].	Country /Region	Vaccine	Platform	Study Design	Sample Size	Population	Study Duration	Efficacy		Vaccines	
								Dose 1	Dose 2	Dose 3	Overall
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	194 601	45-54 years	22 January to 10 June, 2021	NR	NR	NR	85.7%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	166 499	55-64 years	22 January to 10 June, 2021	NR	NR	NR	84.8%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	120 096	65-74 years	22 January to 10 June, 2021	NR	NR	NR	87.8%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	20 056	75-84 years	22 January to 10 June, 2021	NR	NR	NR	85.9%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	1830	≥85 years	22 January to 10 June, 2021	NR	NR	NR	90.9%
Vokó et al[24]	Hungary	Gam-COVID-Vac (Sputnik V)	Recombinant adenovirus (rAd)-based vaccine	Nationwide, retrospective, observational study	820 560	≥16 years	22 January to 10 June, 2021	NR	NR	NR	85.7%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	8995	16-24 years	22 January to 10 June, 2021	NR	NR	NR	68.5%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	15 313	25-34 years	22 January-June10 2021	NR	NR	NR	77.2%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	32 886	35-44 years	22 January to 10 June, 2021	NR	NR	NR	68.6%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	88 266	45-54 years	22 January to 10 June, 2021	NR	NR	NR	68.6%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	79 206	55-64 years	22 January to 10 June, 2021	NR	NR	NR	68.3%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	51 838	65-74 years	22 January to 10 June, 2021	NR	NR	NR	72.2%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	23 722	75-84 years	22 January to 10 June, 2021	NR	NR	NR	64.8%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	3912	≥85 years	22 January to 10 June, 2021	NR	NR	NR	38.7%
Vokó et al[24]	Hungary	ChAdOx1 nCoV-19	Adenovirus recombinant vector vaccine	Nationwide, retrospective, observational study	304 138	≥16 years	22 January to 10 June, 2021	NR	NR	NR	71.5%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	65 720	16-24 years	22 January to 10 June, 2021	NR	NR	NR	67.3%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	91 946	25-34 years	22 January to 10 June, 2021	NR	NR	NR	84.6%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	104 018	35-44 years	22 January to 10 June, 2021	NR	NR	NR	69.0%

Table 1. Continued

Authors, Year [Ref].	Country /Region	Vaccine	Platform	Study Design	Sample Size	Population	Study Duration	Efficacy		Vaccines	
								Dose 1	Dose 2	Dose 3	Overall
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	80960	45-54 years	22 January to 10 June, 2021	NR	NR	NR	78.6%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	126028	55-64 years	22 January to 10 June, 2021	NR	NR	NR	66.1%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	281725	65-74 years	22 January to10 June, 2021	NR	NR	NR	71.1%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	130323	75-84 years	22 January to 10 June, 2021	NR	NR	NR	66.4%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	14745	≥85 years	22 January to 10 June, 2021	NR	NR	NR	43.1%
Vokó et al[24]	Hungary	BBIBP-CorV	Inactivated vaccine	Nationwide, retrospective, observational study	895465	≥16 years	22 January to 10 June, 2021	NR	NR	NR	68.7%
Polack et al[36]	American, Argentinian, Brazilian, South African, German, Turkish/White	BNT162b2	mRNA	Randomized single-blind control	43448	>16 years	NR	82%	90.5%	NR	NR
Xia et al[9]	Henan Province, China	BBIBP-CorV	Inactivated vaccine	Randomized, double-blind, placebo controlled, phase 1/2 trial	44325	18-80 years	NR	NR	NR	NR	79-86%

Note. COVID-19: Coronavirus disease 19; NR, not reported.

Safety of COVID-19 Vaccine

Pfizer

Local and systemic reactions were more common in those who received the *Pfizer* vaccine than in those who received a placebo, and the most commonly reported local reaction was pain at the injection site that disappeared one or two days later, and fatigue and headache were more common in systemic reactions.[36,41] The second dose of the vaccination caused more systemic complications than the first dose, but local reactions were not different in persons with a history of COVID-19 infection vs. those who had never been infected with COVID-19 previously.[25] After the third dose, complications were greater in those receiving vaccination than in those who received a placebo, as in the first and second doses. Local and systemic reactions were mild to moderate in the third dose, although there were some significant adverse effects such as tachycardia and increased liver enzyme levels.[50] In general, the body's reactions to the *Pfizer* vaccine were mild to moderate and within a few days, but there were some serious complications such as myocarditis, lymphadenopathy, appendicitis, calculi, pericarditis, and the like.[51]

Moderna

Following the injection, the vaccinated group experienced greater systemic and local side effects than the group that was injected with a placebo, with severity levels of one and two, the effect of which disappeared two to three days after the injection. After 8 days, some persons experienced delayed symptoms at the injection site, including erythema, stiffness, and sensitivity, which disappeared after a period. Adverse reactions to the vaccination were more common in younger people than in older people, and those who had been infected with COVID-19 before the injection showed fewer adverse effects than those who had not been infected with this virus. The most prevalent side effects of the *Moderna* vaccine were headache and fatigue, and in this type of vaccine, more symptoms and complications were observed after the second dose. Overall, the side effects of this vaccine were mostly mild to moderate, and a few people suffered from severe complications.[28,52,53]

AstraZeneca

The *AstraZeneca* vaccine, similar to previous vaccines, caused higher systemic and local responses in the vaccine group than in the placebo group, and its most common adverse effects were flu-like illness, headache, and local reaction. It was an injection, thus the majority of the adverse effects were grades 1 and 2, and only a few people experienced grade 3 side effects; however, some people

Table 2. The Efficacy of the COVID-19 Vaccine Against SARS-CoV-2 Infection in Different Variants

Authors, Year [Ref].	Vaccine	Alpha	Beta	Gamma	Delta	Omicron
IHME[37]	(ChAdOx1 nCoV-19/ AZD1222)	63%	69%	69%	69%	36%
Chemaitelly et al[38]	mRNA-1273	Dose1 (88.1%) Dose2 (100%)	Dose1 (61.3%) Dose2 (96.4%)	NR	NR	NR
Skowronski et al[39]	BNT162b2 mRNA-1273	67%	NR	61%	NR	NR
Nasreen et al[40]	(ChAdOx1 nCoV-19/ AZD1222)	Dose 1 (63%) Dose 2 (87%)	Dose 1 (84%) Dose 2 (NR)	Dose 1 (41%) Dose 2 (NR)	Dose 1 (68%) Dose 2 (88%)	NR
Nasreen et al[40]	mRNA-1273	Dose 1 (82%) Dose 2 (92%)	NR	Dose 1 (89%) Dose 2 (NR)	Dose1 (70%) Dose 2 (94%)	NR
IHME[37]	Gam-COVID-Vac (Sputnik V)	86%	85%	85%	85%	44%
Nasreen et al[40]	BNT162b2	Dose 1 (67%) Dose 2 (88%)	Dose 1 (50%) Dose 2 (86%)	Dose 1 (63%) Dose 2 (90%)	Dose 1 (57%) Dose 2 (92%)	NR
Thomas et al[41]	BNT162b2	NR	100%	NR	NR	NR
Madhi et al[42]	ChAdOx1 nCoV-19	NR	First-outcome analysis (21.9%) Secondary-outcome analysis (10.4%)	NR	NR	NR
Lefèvre et al[43]	BNT162b2	NR	Infection (49%) Severe COVID (86%)	NR	NR	NR
Haas et al[44]	BNT162b2	Dose 2 (95.3%)	NR	NR	NR	NR
IHME[37]	BBIBP-CorV	68%	67%	67%	67%	35%
Hall et al[45]	BNT162b2	Dose 1 (70%) Dose 2 (85%)	NR	NR	NR	NR
Charmet et al[46]	BNT162b2, mRNA-1273	Dose 2 (86%)	NR	NR	NR	NR
Lopez Bernal et al[34]	ChAdOx1 nCoV-19	Dose 1 (48.7%) Dose 2 (74.5%)	NR	NR	Dose 1 (30%) Dose 2 (67%)	NR
Lopez Bernal et al[34]	BNT162b2	Dose 1 (47.5%) Dose 2 (93.7%)	NR	NR	Dose 1 (35.6%) Dose 2 (88%)	NR
IHME[37]	mRNA-1273	92%	91%	91%	91%	48%
Fowlkes et al[47]	BNT162b2 mRNA-1273	NR	NR	NR	66%	NR
Tang et al[48]	BNT162b2	NR	NR	NR	Dose 1 (64.2%) Dose 2 (53.5%)	NR
Bruxvoort et al[49]	mRNA-1273	98.4%	NR	NR	86.7	NR
IHME[37]	BNT162b2	86%	84%	84%	84%	44%
Tang et al[48]	mRNA-1273	NR	NR	NR	Dose 1 (79.0%) Dose 2 (84.8%)	NR

Note. SARS-CoV-2: Severe acute respiratory syndrome *coronavirus 2*; COVID-19: Coronavirus disease 19; NR, not reported.

also had muscular pain and diarrhea. The intensity of the reactions was at its peak one day after immunization, and the symptoms began to fade after two days. Reactivity was less prevalent in the second dose of *AstraZeneca* vaccination than in the first one.[54,55]

Sputnik V

As regards the *Sputnik* vaccine, the most common reactions were flu-like illness, reaction at the injection site, and headache, and most of the complications reported in this type of vaccine were grades 1 and 2, and a few had grade 3 complications. Some people also had muscle pains and diarrhea. In a few individuals who showed severe side effects to this vaccine, there was no correlation between the occurrence of serious side effects and the injection of the vaccine.[26,56,57]

Sinopharm

The most common adverse reaction to the *Sinopharm* vaccine was pain at the injection site, followed by swelling, itching, and other reactions, while the most common systemic reaction was fever, followed by fatigue, nausea, anorexia, and constipation. After 28 days, all vaccine-induced problems were mild to moderate, and no significant complications were reported in this regard.[9,58]

Discussion

Following the outbreak of COVID-19 and significant deaths worldwide, researchers sought to develop a vaccine as the best factor in preventing this disease, and several vaccines have so far completed their clinical trials and have been released worldwide.[59] Despite their short history, vaccines have contributed to dramatic improvements

in public health around the world. In current centuries, many humans have died from viral and infectious diseases, but many lives had been saved with the development of technology and the supply of vaccines. There had been many damaging results of the worldwide COVID-19 outbreak, and vaccination is the acceptable manner to save and conquer this pandemic. Therefore, the present study was designed as a systematic review to report the efficacy and safety of COVID-19 vaccines in different doses and variants.

By examining different studies, it was revealed that the efficacy of different COVID-19 vaccines was variable in different times, places, people, and age groups. A study in the United States reported a 78.6% efficacy for the *Moderna* vaccine in people over 65 years of age,[23] while in a study in Hungary, the efficacy of the *Moderna* vaccine in people aged 25-34 was about 97%.[24] The difference in the effectiveness of vaccines can be due to the difference among vaccinated people; for example, in the *Moderna* vaccine, people with cardiovascular diseases, kidney diseases, mental stress, and the like had a lower efficacy than other people.[60] Moreover, in the United States, older people with underlying diseases had lower antibody levels than healthy people, and less efficacy.[33]

By examining different studies, it was found that the effectiveness of the COVID-19 vaccines varied in different variants so that the most effective was observed in the alpha variant, while the least effective was detected in the omicron variant. This contradiction in the effectiveness of COVID-19 vaccines in different variants can be due to the fact that new strains have changed their structure with mutations and changes have occurred in the basic molecular components of the virus and the molecular weight, causing the vaccine to escape and thus reduce the efficacy of different COVID-19 vaccines in the newer variants.[61]

The vaccine efficacy of the Omicron variant was the lowest of all types; this finding broadly supports the work of another study. Accordingly to evidence, given that the omicron variant is extremely infectious, spreads quickly, and escapes vaccination immunity, current vaccines are less effective against the omicron variant than others.[62]

Limitations of the Study

The present study had several limitations. First, if the study was designed as a meta-analysis, the study could compare the results of different articles if it was a meta-analysis study, but due to the lack of criteria for entering data into the meta-analysis model, the study was designed as a systematic review. Further, it was impossible to access the full text of some articles, thus there is a possibility that the results of those studies could influence the general conclusion of the issue.

Conclusion

In general, the findings of the current study showed that the use of any type of COVID-19 vaccine during the pandemic can be effective in increasing the body's immunity and reducing the complications of the disease. Among different vaccine platforms, mRNA vaccines were the most effective than other platforms, and the *Moderna* vaccine was the best vaccine of this platform group. The results of various articles revealed that in all vaccines, the injection of two doses of vaccine is significantly more effective than the injection of one dose. Furthermore, it is important to give necessary training and advice to people in this field. Of course, it is essential to note that despite the good efficacy of most COVID-19 vaccines, due to the ambiguity of phase 4 clinical trials of these vaccines, further research on the long-term side effects of these vaccines is necessary.

Author Contributions

Conceptualization: Hamed Delam.
Data curation: Reza Zare.
Investigation: Sara Moghaddam.
Methodology: Hamed Delam.
Validation: Reza Zare.
Writing – original draft: Hamed Delam, Reza Zare.
Writing – review & editing: Hamed Delam, Reza Zare, Sara Moghaddam.

Availability of Data and Materials

The datasets and information supporting the conclusions of this article are available from the corresponding author upon reasonable request.

Conflict of Interest Disclosures

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