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COVID-19 Vaccination in Adolescents: Side Effects and Symptomatic Reinfections

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Abstract

Background: Although the COVID-19 pandemic is over, the disease remains a public health threat. Contracting and transmitting SARS-COV-2 among individuals under 18 is significant.

Objectives: This study aims to identify potential side effects and symptomatic reinfections among 12-18-year-olds after receiving COVID-19 vaccines.

Methods: In this longitudinal study conducted in 2021 - 2022 in Dezful, Iran, 1,000 vaccinated individuals were followed up for 6 months. Side effects and symptomatic reinfections of the first and second doses of PastoCovac and Sinopharm vaccines and a history of prior SARS-COV-2 infection were recorded.

Results: Only 7.6% received the PastoCovac vaccine, while 92.4% received the Sinopharm vaccine. The most common side effect for both vaccines was local pain at the injection site, while the least common was skin rash. Side effects were 1.9 times more prevalent with the PastoCovac vaccination. Women had a 2.3 times higher chance of experiencing side effects after the first dose and a 1.9 times higher chance after the second dose compared to men. Over the 6-month follow-up period, 11.6% and 14.3% of individuals experienced re-infection after the first and second vaccine doses, respectively. It seems with the passage of time and the decrease in the level of immunity, the possibility of re-infection increases.

Conclusions: Both vaccines were considered safe for 12-18-year-olds. However, receiving two doses does not guarantee protection against reinfection.

Keywords: PastoCovac Vaccine, Sinopharm Vaccine, SARS-COV-2 Reinfection, Side Effects, Symptomatic Reinfections

1. Background

There are various coronaviruses worldwide, and while there is no definitive treatment, prevention is crucial (1), with COVID-19 vaccines being a vital intervention (2). These vaccines are highly effective against symptomatic and severe diseases caused by the main variant of SARS-CoV-2, including the alpha variant (B.1.1.7) (3). However, due to limited and conflicting clinical evidence, the efficacy of the vaccines is still a subject of debate (4). The World Health Organization (WHO) emphasizes the importance of following health protocols despite ongoing research on vaccine protection against disease, infection, and transmission (5). Studies by the Centers for Disease Control and Prevention (CDC) in the United States show that, among 101 million vaccinated individuals, approximately 10,262 experienced COVID-19 reinfection, with 995 hospitalizations and 160 deaths, highlighting the effectiveness of vaccination despite not providing 100% immunity (6).

Vaccinating children is considered crucial in combating the epidemic, as achieving herd immunity is unlikely without vaccinating them, even if a large

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proportion of adults are vaccinated (7). Studies on vaccine side effects in children under 18 have reported issues such as myocarditis, myopericarditis, injection site swelling, and headache (8). In Iran, the vaccination of high school seniors with the Sinopharm vaccine began in September 2021 (8). The CDC recommends COVID-19 vaccination for individuals aged 12 and above as a crucial measure to protect against the disease and help curb the epidemic (9).

2. Objectives

Given the lack of sufficient evidence on available vaccines in Iran and the ongoing phase three research, data is needed to assess vaccine effectiveness among different populations and inform public health policies and recommendations. Therefore, considering the reopening of schools and the importance of the student's health, this study aimed to determine the potential side effects and symptomatic reinfection rates in the population aged 12-18.

3. Methods

3.1. Study Design and Population

This longitudinal study was carried out in Dezful, Iran, from 2021 to 2022, which is located 721 km southwest of Tehran. The study included individuals aged 12 - 18 years who received the first dose of COVID-19 vaccines (Sinopharm and PastoCovac) at comprehensive health service centers in 2021, as recommended by the Ministry of Health and Medical Education (MOHME). The study followed their vaccination feedback for 6 months to assess side effects and post-vaccination reinfections. The targeted population size for the studied age groups, as reported by Dezful Health Center in 2021, was 39,963. Sample size calculation determined a sample of n = 380.

In order to take into account the probable dropout of the subjects of the study during the six months of follow-up, a larger sample size (i.e., 1000 people) was considered. The samples were selected using random systematic sampling. After identifying all the people of the target group, which were about 40,000 people, and considering 1000 people, the size of the study sample and the interval between the samples were determined as follows:

The interval between samples = Number of samples ÷ number of people in the target group

 $40000 \div 1000 = 40$

Then, a random draw was made between the numbers 1 to 40. The first determined number was considered as the first person, and the next 999 people were selected at an

interval of 40 people. Given the national code extracted from the 'SIB system,' a code was allocated to each of the designated numbers. Based on the coordination made, 1000 specified codes were provided to all urban and rural comprehensive health service centers responsible for the COVID-19 vaccine (prior to the start of nationwide vaccination for those under 18 years of age in Iran). When referring to health centers, the researchers were provided with the mentioned codes to fill in the forms. Following interviewing the samples referring to the health centers and explaining to them the goals of the project, in case they met the required criteria for entering the study and if they were willing to cooperate, the consent form was presented to be filled in and signed by them, and their code was included in the study. In case the specified samples were not willing to participate in the study or if they did not visit the researcher, the necessary replacement was done by maintaining the sample interval.

The study was designed as a longitudinal study with the specific aim of following the conditions of individuals who had received the vaccine.

3.2. Inclusion and Exclusion Criteria

The inclusion criteria of this research were:

• Individuals between 12 and 18 years old (born in 2003 - 2009).

• Those referred to comprehensive health service centers and received shots of the COVID-19 vaccine.

• Participating in the study with consent while being fully informed.

• Cooperation and self-declaration of requested questions for 6 months.

The exclusion criteria of this research were:

- Not agreeing to participate in the study for 6 months.
- Failure to answer researchers' questions.
- Not responding to phone calls.
- Individuals' death for any reason.

• History of anaphylactic reaction after receiving any vaccine.

People who had an anaphylactic reaction following the injection of the vaccine were excluded from the study, but their information was recorded.

3.3. Data Collection

Interviewers visited comprehensive health service centers and collected data by filling out the demographic characteristics checklist (within the framework of an electronic questionnaire). Then, the samples were actively and passively traced for 6 months (according to the conducted studies) (10). Given the side effects caused by the vaccine and symptomatic reinfections (i.e., clinical or radiological evidence compatible with COVID-19 with the approval of a medical specialist or positive PCR test) following injection of the first and second dose of the vaccine were followed up, and their information was recorded in separate checklists. Participants with symptomatic reinfections were those who, after receiving the vaccine, experienced symptoms consistent with COVID-19, tested positive on a PCR test, or exhibited signs of the disease along with confirmed pathological findings by the relevant specialist and study focal point. It is noteworthy that their PCR test could also yield a negative result. In order to determine the side effects caused by the vaccine, active follow-up of samples was performed via phone calls and self-declaration, and all the information of this stage was entered in the checklists of side effects of the first and second doses. Finally, all recorded side effects and problems of the studied subjects were recorded, followed up, and analyzed, and the procedure continued until the symptoms were resolved. Also, the samples who were infected following the injection of the first and second doses of the vaccine were questioned every two weeks, and the results obtained were recorded in the relevant checklists. In addition, at the end of each day, after recording the data of the samples in the electronic questionnaire, the output of the data was determined. It is noteworthy that the research team gave the samples the necessary instructions to eliminate the side effects or diagnose and treat the reinfections after the injection of the vaccine. Six months later, the data obtained was analyzed. It should also be noted that symptomatic reinfections, rather than asymptomatic ones, were the focus of the study. Therefore, the study was conducted to identify symptomatic reinfections.

3.4. Data Analysis

Descriptive analyses were conducted to calculate the distribution of sociodemographic characteristics, clinical characteristics, and epidemiological factors of COVID-19 patients. The data related to continuous variables were reported as means and standard deviations, and categorical data were reported as frequency and percentages. The McNemar test has been used to compare post-vaccination side effects in the interval between the first and second doses.

Logistic regression models were used to determine the relationship between demographic characteristics, the type of vaccine received, the risk of experiencing vaccine-related side effects, and COVID-19 reinfections after vaccination. All statistical analyses were conducted using SPSS 24. The statistical significance was defined as a p-value less than 0.05.

4. Results

It is noteworthy that 1000 individuals were enrolled in the study and remained in the study until the end of the 6 months, and no participants dropped out.

4.1. Side Effects of COVID-19 Vaccination

Analysis of the obtained data indicated that 53.1% of vaccinated people were male and, 46.9% of them were female (n = 1000), 31.4% were between 12 and 15 years old, 23.3% were 16 years old, 25.9% were 17 years old, and 19.4% were 18 years old. Regarding the level of education, 40.5% had elementary and junior high school education, and 59.5% had senior high school education. As for vaccines used. 7.6% were vaccinated with the PastoCovac vaccine and 92.4% with the Sinopharm vaccine; 9.6% of the people had a history of chronic diseases, and 17.6% had a history of allergies. Based on the reports, 31.3% of the cases declared they had COVID-19 reinfections prior to vaccination, 11.6% cases reported COVID-19 reinfections after receiving the first dose of the vaccine, and 14.3% cases reported being infected following the injection of the second dose of the vaccine. The frequency of side effects after receiving the first and second doses of the vaccine is tabulated in Table 1. As shown in Table 1, pain at the injection site was the most common complication after receiving the first dose, with a frequency of 25.1%. Skin rash was the least frequent at 0.4%, and regarding complications after the second dose, pain at the injection site was the most frequent at 17.2%, and skin rashes at 0.1% have had the least frequency. In addition, 39.9% of people mentioned having at least one side effect after injection of the first dose and 27.2% after the injection of the second dose of the vaccine.

4.2. Chances of Side Effects After Vaccination

The results of the regression analysis indicated that the chance of having any complication emanating from the injection of the vaccine after the first and second doses in women was 2.34 and 1.91 times higher than in men, respectively. Also, people who had a history of allergy and underlying diseases had a 1.63- and 1.87-times higher chance of any complication caused by the vaccine after injection of the first dose, respectively. In addition, the chance of having any complication caused by the vaccine after the first dose was 1.99 times higher in those vaccinated with the PastoCovac vaccine than among people who had been vaccinated with the Sinopharm vaccine. It is worth noting that the chance of experiencing vaccine side effects after the first dose increases by 1.14 times with each additional year of age. Also, the chance of having any complication caused by the vaccine after injection of the second dose was 0.55 among people with

Side Effects of The Vaccine	No (%)		P-Value	
	First Dose Second Dose			
Headache	121 (12.1)	80 (8)	<0.001	
Body ache (myalgia)	114 (11.4)	94 (9.4)	0.02	
Gastrointestinal discomforts	17 (1.7)	11 (1.1)	0.14	
Fatigue	226 (22.6)	148 (14.8)	< 0.001	
Stiffness of injection site	133 (13.3)	94 (9.4)	< 0.001	
Pain in the injection site	251 (25.1)	172 (17.2)	< 0.001	
Losing sense of smell	23 (2.3)	13 (1.3)	0.05	
Losing sense of taste	22 (2.2)	9(0.9)	< 0.001	
Impaired consciousness	11 (1.1)	7 (0.7)	0.22	
Nasal congestion	36 (3.6)	20 (2)	< 0.001	
Runny nose	45 (4.5)	24 (2.4)	< 0.001	
Shortness of breath (dyspnea)	20(2)	13 (1.3)	0.09	
Allergic reactions	8(0.8)	4(0.4)	0.22	
Anxiety	28 (2.8)	20 (2)	0.07	
Phobia	20 (2)	16 (1.6)	0.42	
Appetite reduction	43 (4.3)	24 (2.4)	0.001	
Vertigo	74 (7.4)	52 (5.2)	0.002	
Sleepiness	129 (12.9)	82 (8.2)	< 0.001	
Cough	22 (2.2)	14 (1.4)	0.13	
Sneeze	35 (3.5)	17 (1.7)	0.001	
Sore throat	25 (2.5)	13 (1.3)	0.01	
Nausea and vomiting	21(2.1)	16 (1.6)	0.36	
Fever	79 (7.9)	40 (4)	< 0.001	
Chills	34 (3.4)	20 (2)	0.01	
Chest pain	12 (1.2)	7 (0.7)	0.22	
Backache	20 (2)	12 (1.2)	0.06	
Skin lesions/rash	4(0.4)	1(0.1)	0.25	
Having at least one complication after vaccination	399 (39.9)	272 (27.2)	< 0.001	

elementary and junior high school education levels (Table 2).

Also, the results of the regression analysis indicated that the chance of being infected by COVID-19 after receiving the first dose of the vaccine was 1.65 times higher among women than men. With an average increase of one year of age, the chance of contracting COVID-19 after receiving the first dose was 1.29 times higher. Moreover, there was no significant relationship between background variables and types of injected vaccines with the reinfections of COVID-19 after injection of the second dose (Table 3).

5. Discussion

Many studies on the effectiveness and side effects of COVID-19 vaccines in adults have already been conducted and published. However, few studies have focused on people under 18 years old due to ethical considerations and the delays in issuing the necessary licenses. Numerous studies have reported several side effects resulting from COVID-19 vaccination. The most common side effects include local side effects such as pain at the injection site, mild fever, headache, weakness, and myalgia. The results of our study are in agreement with those of previous reports (11-16). Most of these side effects emerged within

Characteristics	First Dose			Second Dose		
	OR	95% CI	P-Value	OR	95% CI	P-Value
Gender						
Male (Ref)	1			1		
Female	2.34	1.79 - 3.05	< 0.001	1.91	1.43 - 2.56	< 0.001
Education level						
Senior high school (Ref)	1			1		
Elementary and junior high school	0.84	0.56 - 1.24	0.37	0.55	0.35 - 0.85	0.007
History of allergy						
No (Ref)	1			1		
Yes	1.63	1.15 - 2.34	0.007	1.65	0.92 - 1.96	0.12
Presence of chronic disease						
No (Ref)	1			1		
Yes	1.87	1.18 - 2.97	0.008	1.51	0.94 - 2.41	0.08
Type of COVID-19 vaccine						
Sinopharm vaccine (Ref)	1			1		
PastoCovac vaccine	1.99	1.22 - 3.27	0.006	0.91	0.51 - 1.62	0.75
Age	1.14	1.01 - 1.29	0.04	1.07	0.93 - 1.22	0.35

Characteristics	First Dose			Second Dose		
	OR	95% CI	P-Value	OR	95% CI	P-Value
Gender						
Male (Ref)	1			1		
Female	1.65	1.12 - 2.46	0.01	1.18	0.83 - 1.70	0.36
Education level						
Senior high school (Ref)	1			1		
Elementary and junior high school	1.32	0.75 - 2.32	0.33	0.82	0.47-1.43	0.48
History of allergy						
No (Ref)	1			1		
Yes	1.51	0.92 - 2.46	0.10	1.21	0.76 - 1.91	0.43
Presence of chronic disease						
No (Ref)	1			1		
Yes	0.93	0.48 - 1.77	0.83	1.61	0.93 - 2.78	0.09
Type of COVID-19 vaccine						
Sinopharm vaccine (Ref)	1			1		
PastoCovac vaccine	1.32	0.64 - 1.70	0.44	0.43	0.17 - 1.08	0.07
Age	1.29	1.07 - 1.54	0.006	1.03	0.87 - 1.23	0.67

Table 2. Binomial Logistic Regression of the Impact of Demographic Characteristics and the Type of Received Vaccine on the Risk of Experiencing Vaccine-Related side Effects

the first 72 hours following the vaccination.

Fifty percent and 39% of people reported side effects after receiving the first dose of Soberana (PastoCovac) and Sinopharm vaccines, respectively, and 22% and 27% after receiving the second doses of the vaccines. According to the results of similar studies, side effects seem more common after the first dose of the vaccine due to immune response (1, 5).

It appears that the side effects experienced by adults are similar to those detected in people who are under 18 years old (17). Also, this paradigm does not depend on the type of vaccine (mRNA vaccines or non-mRNA vaccines) because the common side effects of all COVID-19 vaccines are almost the same (18). The majority of participants in the study received the Sinopharm vaccine, accounting for over 92% of the study group. This was due to the fact that at the time of the study, only two vaccines, Sinopharm and PastoCovac, had been granted a license by the Iran Food and Drug Administration (IFDA). This decision was based on the best available evidence, as well as the greater availability of the Sinopharm vaccine (19).

The results of the study showed that the emergence of severe side effects following injection of these two vaccines among people under 18 was rare. In a study conducted by Boshra et al., two vaccines (i.e., Sinopharm and AstraZeneca) were compared. The incidence of side effects was lower after injection of the Sinopharm vaccine, and it was declared as a safe vaccine, although all participants were above 18 (20). Also, in a study conducted in Pakistan on the Sinopharm vaccine, no severe or life-threatening side effect was reported (21).

We observed that the chances of side effects of these two vaccines among people aged 12-18 years are higher in women than in men (OR = 2.3, 95% CI: 1.79 - 3.05), and it was higher among people who had a history of allergies or underlying diseases (OR = 1.63, 1.87, respectively). In a study conducted by Babaee et al. in Iran on people above 18, it was reported that more than 54% of people who had side effects due to injection of the Sinopharm vaccine had at least one underlying disease. The most common underlying disease was diabetes. Interestingly, similar to our study, the incidence of side effects was higher in women (22). In another study in Bangladesh, it was reported that people with underlying diseases had a higher risk of developing side effects caused by the COVID-19 vaccines (23). It seems that following the injection of these vaccines, women and people with underlying diseases should receive more attention and follow-up.

Following the injection of the first dose of vaccines, 11.5% and 13.2% of vaccinated people (Sinopharm and PastoCovac, respectively), and up to six months after receiving the second dose, 14.9% and 6.6% of persons were re-infected. Also, 26.3% of them had a history of at least one episode of SARS-COV-2 infection prior to receiving both the Sinopharm and PastoCovac vaccines. The results of previous studies were different based on the study population and the type of vaccines used (24). In a study in Iran conducted by Tavakoli et al. on people under 18, only 1.8% of persons developed a COVID-19 infection after injection of two doses of the vaccine (i.e., PastoCovac or Sinopharm) (17). In our view, this difference can be attributed to various reasons. The first one is the time of follow-up. In the mentioned study, the follow-up period was three weeks, and in our study, it was 6 months. Secondly, the epidemic waves of the disease and exposure cases definitely affect the frequency of new or re-infected cases. At the time of the study, we were experiencing a new wave of COVID-19 epidemic peak. Thirdly, the genetic changes of the virus and the creation of new variants are effective in the number of infections (25, 26). Finally, over time and with the wane of vaccine immunity, the risk of the disease increases (20).

It seems that the previous immune status (naturally infected populations, infection-naïve, and vaccinated individuals) is also effective in the risk of re-infection (27, 28). We found that the reinfection rate within 6 months after vaccination was lower in naturally infected populations than in infection-naïve peoples (17.5% vs 20.8%). The risk of infection after vaccination is lower in naturally-infected populations, but this hypothesis should not be the basis for vaccination. Recent research has shown that severe and frequent infections with SARS-COV-2 may increase the risk of long-term complications (29, 30). Therefore, we should prevent people from getting infected with the SARS-COV-2 virus frequently, and one of the most effective ways is mass vaccination.

The mortality is higher among the elderly and adults with underlying diseases, but due to the delay in vaccination of those under 18, this probability has shifted towards children (31). Studies conducted on vaccinated children are limited. Taking into account various factors, parents' willingness to vaccinate their children is about 61.4% (21.6% to 91.4%), but it seems that the actual rate of child vaccination is smaller (32). Most studies emphasize the necessity of vaccinating children, especially those with underlying diseases. One of the main goals of vaccination in this group is to prevent serious complications such as multisystem inflammatory syndrome (MIS-C) (33).

In a study conducted by Yadegarynia et al. in Tehran, the impact of three COVID-19 vaccines (AstraZeneca, Sputnik V, and Sinopharm) was evaluated on 377 healthcare workers. The results indicated that the risk of side effects after injection of the first dose of the vaccine was higher than that of the second dose. Also, the most common side effect caused by the vaccines was local reactions. The least common side effects were seen with the Sinopharm vaccine. Although the participants in this study were not the same in our research, the results were similar. We assume that due to sensitization of the immune system after the injection of the first dose of vaccines, the chance of side effects will decrease with subsequent doses. This scenario seems to be the same for all COVID-19 vaccines. Based on the results of different studies, we figured out that the Sinopharm vaccine has the lowest probability of serious side effects compared to the other COVID-19 vaccines (34).

The keywords COVID-19, vaccine, and side effect, as well as the Google Scholar, Scopus, and PubMed databases, were searched, and the following studies were found. The most common side effects of COVID-19 vaccines in individuals under 18 are shown in Table 4.

Currently, due to a lack of evidence, the consequences of COVID-19 disease are not fully known, and further studies are needed. On the other hand, the pandemic of COVID-19 has changed to an endemic status, and it does not seem that this virus will eradicated in the near future, and it continues to be a public health threat. Therefore, it is necessary to improve vaccination coverage for children and develop potent vaccines for various virus variants (44).

5.1. Limitations of the Study

There existed a few limitations in this study:

- It was difficult to follow this number of people for six months, but we solved this problem by increasing the number of research team members and training them.

- Several factors have been influential in the results of studies conducted on vaccines. Because it was not possible to evaluate all factors in this research, more studies are needed to investigate various aspects of vaccination among people aged 12 - 18 years.

- We intended to evaluate more vaccines, but at the time of conducting this study in Iran, only two vaccines, PastoCovac and Sinopharm, were licensed for people aged 12 - 18 years. Therefore, it is our recommendation to use a control group in future studies, as one was not included for the reasons previously mentioned.

- Due to the limited resources (financial and human), despite the desire of the research team, it was not possible to increase the number of participants in the study.

- Another limitation of the study was the limited number of individuals vaccinated with the PastoCovac vaccine, which was unavoidable. Furthermore, due to the unavailability of specific samples, the vaccine was chosen, and as a result, we had to include the results and compare them with the Sinopharm vaccine. Ideally, it would have been preferable to have roughly the same number of vaccinated individuals in each group under similar conditions. However, we acknowledge that this was not feasible.

Due to the passive follow-up of the study, from the third day onwards and every two-week follow-up and the individual's self-report, even though the subjects were told to contact the researcher in case of the emergence of any symptoms, they might have missed such an opportunity.

5.2. Conclusions

The results of the study demonstrated that Sinopharm and PastoCovac vaccines are safe for people aged 12 - 18 years. The probability of re-infection after vaccination was lower among naturally infected populations than in infection-naïve individuals. However, injecting two doses of vaccine (PastoCovac or Sinopharm) in children does not mean complete immunity against re-infection. Considering the potential for future pandemics, particularly those caused by respiratory diseases such as COVID-19, it is imperative that we adhere to preventive protocols.

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Footnotes

Authors' Contribution: M. M. conceptualized and designed the study, designed the data collection instruments, carried out the initial analyses, supervised and reviewed data analysis, reviewed and revised the manuscript, made substantial contributions to the interpretation of the data, and critically reviewed the manuscript for important intellectual content. J. M. conceptualized and designed the study, designed the data collection instruments, carried out the initial analyses, prepared the initial article draft, reviewed and revised the manuscript, reviewed data analysis, made substantial contributions to the interpretation of the data, and critically reviewed the manuscript for important intellectual content. Z. R. designed the data collection instruments, carried out the initial analyses, reviewed data analysis, made substantial contributions to the interpretation of the data, and critically reviewed the manuscript for important intellectual content. H. A. B. designed the data collection instruments and reviewed

Author	Year	Country	The most Common Side Effects	COVID-19 Vaccine		
Frenck et al. (35)	2021	USA	Injection-site pain	Pfizer BioNTech		
Creech et al. (36)	2021	USA, Canada	Injection-site pain, headache, and fatigue	mRNA-1273 vaccine (Moderna)		
Thomas et al. (10)	2020	Argentina, Brazil, Germany, South Africa, Turkey, USA	Local reaction	Pfizer BioNTech		
Munoz et al. (37)	2022	USA, Brazil, Poland, Spain, Finland.	Local reaction	Pfizer BioNTech		
Tian et al. (38)	2022	China (systematic review)	Injection-site pain, fever, headache, cough, fatigue, and muscle pain	Inactivated virus vaccines, viral vector vaccines, RNA vaccines, DNA vaccines, recombinant vaccines, subunit vaccine		
Walter et al. (39)	2021	USA, Spain, Finland, Poland	Local reactions	Pfizer BioNTech		
Ali et al. (40)	2021	USA	Injection-site pain	mRNA-1273 vaccine (Moderna)		
Han et al. (41)	2021	China	Injection-site pain	CoronaVac inactivated vaccine		
Xia et al. (19)	2020	China	Local reaction	BBIBP-CorV Inactivated vaccine		
Zhu et al. (42)	2020	China	Injection-site pain, fever, headache, and fatigue	Ad5-nCoVAdenovirus vaccine		
Khobragade et al. (43)	2021	India	Injection-site pain, fever, headache	ZyCov-D DNA vaccine		

and revised the manuscript. L. M. helped in the acquisition of data. M. A. E. collected the data. M. N. collected data. A. SH. collected the data. Z. H. collected the data. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

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References

- Chung YH, Beiss V, Fiering SN, Steinmetz NF. COVID-19 Vaccine Frontrunners and Their Nanotechnology Design. ACS Nano. 2020;14(10):12522-37. [PubMed ID: 33034449]. https://doi.org/10. 1021/acsnano.0c07197.
- Tregoning JS, Brown ES, Cheeseman HM, Flight KE, Higham SL, Lemm NM, et al. Vaccines for COVID-19. *Clin Exp Immunol*. 2020;**202**(2):162–92. [PubMed ID: 32935331]. [PubMed Central ID: PMC7597597]. https://doi. org/10.1111/cei.13517.
- Andrews N, Stowe J, Kirsebom F, Toffa S, Rickeard T, Gallagher E, et al. Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. *N Engl J Med*. 2022;**386**(16):1532–46. [PubMed ID: 35249272]. [PubMed Central ID: PMC8908811]. https://doi.org/10.1056/NEJM0a2119451.

- Huang J, Tao G, Liu J, Cai J, Huang Z, Chen JX. Current Prevention of COVID-19: Natural Products and Herbal Medicine. *Front Pharmacol.* 2020;**11**:588508. [PubMed ID: 33178026]. [PubMed Central ID: PMC7597394]. https://doi.org/10.3389/fphar.2020.588508.
- World Health Organization. Covid 19 vaccines: World Health Organization (WHO). 2021. Available from: https://www.who.int/ emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines.
- World Health Organization. Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process. 2021. Available from: https://extranet.who.int/pqweb/sites/default/files/documents/ Status_COVID_VAX_15/uly2021.pdf.
- Berkeley LJ; CNBC. FDA Permits Use of the Pfizer-BioNTech COVID Vaccine in Kids Ages 12 to 15 2021. 2021. Available from: https://www. nbcchicago.com/news/business/money-report/fda-permits-use-ofthe-pfizer-biontech-covid-vaccine-in-kids-ages-12-to-15/2506643/.
- Staff MC. COVID-19 vaccines for kids: What you need to know 2021. 2021. Available from: https://www.mayoclinic.org/diseases-conditions/ coronavirus/in-depth/covid-19-vaccines-for-kids/art-20513332.
- Centers for Disease Control and Prevention. COVID-19 Vaccines for Children and Teens. 2021. Available from: https://www.cdc.gov/ coronavirus/2019-ncov/vaccines/vaccine-safety-children-teens.html.
- Thomas SJ, Moreira EJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months. *N Engl J Med.* 2021;**385**(19):1761-73. [PubMed ID: 34525277]. [PubMed Central ID: PMC8461570]. https://doi.org/10.1056/NEJM0a2110345.
- Omeish H, Najadat A, Al-Azzam S, Tarabin N, Abu Hameed A, Al-Gallab N, et al. Reported COVID-19 vaccines side effects among Jordanian population: a cross sectional study. *Hum Vaccin Immunother*. 2022;**18**(1):1981086. [PubMed ID: 34614383]. [PubMed Central ID: PMC8920252]. https://doi.org/10.1080/21645515.2021.1981086.
- Anderson EJ, Rouphael NG, Widge AT, Jackson LA, Roberts PC, Makhene M, et al. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. *NEngl J Med*. 2020;**383**(25):2427-38. [PubMed ID: 32991794]. [PubMed Central ID: PMC7556339]. https://doi.org/10.1056/NEJM0a2028436.
- 13. Mulligan MJ, Lyke KE, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in

adults. *Nature*. 2020;**586**(7830):589–93. [PubMed ID: 32785213]. https://doi.org/10.1038/s41586-020-2639-4.

- 14. Ghiasi N, Valizadeh R, Arabsorkhi M, Hoseyni TS, Esfandiari K, Sadighpour T, et al. Efficacy and side effects of Sputnik V, Sinopharm and AstraZeneca vaccines to stop COVID-19; a review and discussion. *Immunopathologia Persa*. 2021;7(2):e31.
- Saeed BQ, Al-Shahrabi R, Alhaj SS, Alkokhardi ZM, Adrees AO. Side effects and perceptions following Sinopharm COVID-19 vaccination. *Int J Infect Dis*. 2021;**111**:219–26. [PubMed ID: 34384899]. [PubMed Central ID: PMC8351310]. https://doi.org/10.1016/j.ijid.2021.08.013.
- Abu-Hammad O, Alduraidi H, Abu-Hammad S, Alnazzawi A, Babkair H, Abu-Hammad A, et al. Side Effects Reported by Jordanian Healthcare Workers Who Received COVID-19 Vaccines. *Vaccines (Basel)*. 2021;9(6). [PubMed ID: 34205917]. [PubMed Central ID: PMC8228820]. https:// doi.org/10.3390/vaccines9060577.
- Tavakoli N, Nafissi N, Shokri S, Fallahpour M, Soleimani S, Riahi T, et al. Pediatric and adolescent COVID-19 vaccination side effects: A retrospective cohort study of the Iranian teenage group in 2021. *J Med Virol*. 2022;**94**(10):4890–900. [PubMed ID: 35758760]. [PubMed Central ID: PMC9349687]. https://doi.org/10.1002/jmv.27962.
- Qamar N, Rukh G, Khan SN. Vaccines for Covid-19: An insight on their effectiveness and adverse effects. *JMed Virol*. 2022;94(8):3554–60. [PubMed ID: 35474583]. [PubMed Central ID: PMC9088412]. https:// doi.org/10.1002/jmv.27810.
- Xia S, Zhang Y, Wang Y, Wang H, Yang Y, Gao GF, et al. Safety and immunogenicity of an inactivated COVID-19 vaccine, BBIBP-CorV, in people younger than 18 years: a randomised, double-blind, controlled, phase 1/2 trial. *Lancet Infect Dis.* 2022;22(2):196–208. [PubMed ID: 34536349]. [PubMed Central ID: PMC8443232]. https:// doi.org/10.1016/S1473-3099(21)00462-X.
- Boshra MS, Hussein RRS, Mohsen M, Elberry AA, Altyar AE, Tammam M, et al. A Battle against COVID-19: Vaccine Hesitancy and Awareness with a Comparative Study between Sinopharm and AstraZeneca. *Vaccines (Basel)*. 2022;**10**(2). [PubMed ID: 35214750]. [PubMed Central ID: PMC8876757]. https://doi.org/10.3390/vaccines10020292.
- Rizwan W, Qureshi AU, Rana MN, Duggal MN, Sohaib M, Sadiq M. Safety profile of sinopharm COVID-19 vaccine and breakthrough infections in Pakistan. *medRxiv*. 2022;2022.01. 18.22268965.
- Babaee E, Amirkafi A, Tehrani-Banihashemi A, SoleimanvandiAzar N, Eshrati B, Rampisheh Z, et al. Adverse effects following COVID-19 vaccination in Iran. *BMC Infect Dis.* 2022;**22**(1):476. [PubMed ID: 35585518]. [PubMed Central ID: PMC9116064]. https://doi.org/10.1186/s12879-022-07411-5.
- 23. Mohsin M, Mahmud S, Mian AU, Hasan P, Muyeed A, Ali MT, et al. Side effects of COVID-19 vaccines and perceptions about COVID-19 and its vaccines in Bangladesh. *medRxiv*. 2022:2022.01. 31.22270172.
- Cohen-Stavi CJ, Magen O, Barda N, Yaron S, Peretz A, Netzer D, et al. BNT162b2 Vaccine Effectiveness against Omicron in Children 5 to 11 Years of Age. N Engl J Med. 2022;387(3):227-36. [PubMed ID: 35767475]. [PubMed Central ID: PMC9258754]. https://doi.org/10.1056/NEJM0a2205011.
- Khan NA, Al-Thani H, El-Menyar A. The emergence of new SARS-CoV-2 variant (Omicron) and increasing calls for COVID-19 vaccine boosters-The debate continues. *Travel Med Infect Dis.* 2022;**45**:102246. [PubMed ID: 34942376]. [PubMed Central ID: PMC8687713]. https://doi.org/10.1016/j.tmaid.2021.102246.
- El-Shabasy RM, Nayel MA, Taher MM, Abdelmonem R, Shoueir KR, Kenawy ER. Three waves changes, new variant strains, and vaccination effect against COVID-19 pandemic. *Int J Biol Macromol.* 2022;**204**:161–8. [PubMed ID: 35074332]. [PubMed Central ID: PMC8782737]. https://doi.org/10.1016/j.ijbiomac.2022.01.118.
- Rahman S, Rahman MM, Miah M, Begum MN, Sarmin M, Mahfuz M, et al. COVID-19 reinfections among naturally infected and vaccinated individuals. *Sci Rep.* 2022;**12**(1):1438. [PubMed ID: 35082344]. [PubMed Central ID: PMC8792012]. https://doi.org/10.1038/s41598-022-05325-5.
- 28. Nordstrom P, Ballin M, Nordstrom A. Risk of SARS-CoV-2 reinfection

Arch Clin Infect Dis. 2023; 18(6):e142060.

and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden. *Lancet Infect Dis.* 2022;**22**(6):781–90. [PubMed ID: 35366962]. [PubMed Central ID: PMC8971363]. https://doi.org/10.1016/S1473-3099(22)00143-8.

- Al-Jahdhami I, Khalid A, Al-Mawali A, Bennji SM. Respiratory Complications after COVID-19. Oman Med J. 2022;37(1). e343. [PubMed ID: 35282425]. [PubMed Central ID: PMC8907756]. https://doi.org/10.5001/omj.2022.52.
- d'Ettorre G, Gentilini Cacciola E, Santinelli L, De Girolamo G, Spagnolello O, Russo A, et al. Covid-19 sequelae in working age patients: A systematic review. J Med Virol. 2022;94(3):858–68. [PubMed ID: 34655247]. [PubMed Central ID: PMC8661973]. https://doi.org/10.1002/jmv.27399.
- Desai AD, Lavelle M, Boursiquot BC, Wan EY. Long-term complications of COVID-19. *Am J Physiol Cell Physiol*. 2022;**322**(1):C1-C11. [PubMed ID: 34817268]. [PubMed Central ID: PMC8721906]. https://doi.org/10.1152/ajpcell.00375.2021.
- Chen F, He Y, Shi Y. Parents' and Guardians' Willingness to Vaccinate Their Children against COVID-19: A Systematic Review and Meta-Analysis. Vaccines (Basel). 2022;10(2). [PubMed ID: 35214638]. [PubMed Central ID: PMC8880569]. https://doi.org/10.3390/ vaccines10020179.
- Ladhani SN. COVID-19 vaccination for children aged 5-11 years. *Lancet.* 2022;400(10346):74-6. [PubMed ID: 35780800]. [PubMed Central ID: PMC9246472]. https://doi.org/10.1016/S0140-6736(22)01245-4.
- 34. Yadegarynia D, Tehrani S, Hadavand F, Arshi S, Abtahian Z, Keyvanfar A, et al. Side Effects of COVID-19 Vaccination Among Healthcare Workers in Tehran, Iran: Side effects after COVID-19 vaccination. Int J Med Toxicol Forensic Med. 2023;13(3). https://doi.org/10.32598/ijmtfm. v13i3.40536.
- Frenck RJ, Klein NP, Kitchin N, Gurtman A, Absalon J, Lockhart S, et al. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. N Engl J Med. 2021;385(3):239-50. [PubMed ID: 34043894]. [PubMed Central ID: PMC8174030]. https:// doi.org/10.1056/NEJM0a2107456.
- Creech CB, Anderson E, Berthaud V, Yildirim I, Atz AM, Melendez Baez I, et al. Evaluation of mRNA-1273 Covid-19 Vaccine in Children 6 to 11 Years of Age. N Engl J Med. 2022;386(21):2011-23. [PubMed ID: 35544369]. [PubMed Central ID: PMC9127699]. https://doi.org/10.1056/NEJMoa2203315.
- Munoz FM, Sher LD, Sabharwal C, Gurtman A, Xu X, Kitchin N, et al. Evaluation of BNT162b2 Covid-19 Vaccine in Children Younger than 5 Years of Age. N Engl J Med. 2023;388(7):621–34. [PubMed ID: 36791162]. [PubMed Central ID: PMC9947923]. https://doi.org/10.1056/NEJM0a2211031.
- Tian F, Yang R, Chen Z. Safety and efficacy of COVID-19 vaccines in children and adolescents: A systematic review of randomized controlled trials. *J Med Virol*. 2022;94(10):4644–53. [PubMed ID: 35705969]. [PubMed Central ID: PMC9350282]. https://doi.org/10.1002/jmv.27940.
- Walter EB, Talaat KR, Sabharwal C, Gurtman A, Lockhart S, Paulsen GC, et al. Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5 to 11 Years of Age. N Engl J Med. 2022;386(1):35–46. [PubMed ID: 34752019]. [PubMed Central ID: PMC8609605]. https://doi.org/10.1056/NEJMoa2116298.
- Ali K, Berman G, Zhou H, Deng W, Faughnan V, Coronado-Voges M, et al. Evaluation of mRNA-1273 SARS-CoV-2 Vaccine in Adolescents. *N Engl J Med.* 2021;**385**(24):2241-51. [PubMed ID: 34379915]. [PubMed Central ID: PMC8385554]. https://doi.org/10.1056/NEJM0a2109522.
- Han B, Song Y, Li C, Yang W, Ma Q, Jiang Z, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy children and adolescents: a double-blind, randomised, controlled, phase 1/2 clinical trial. *Lancet Infect Dis*. 2021;21(12):1645–53. [PubMed ID: 34197764]. [PubMed Central ID: PMC8238449]. https://

doi.org/10.1016/S1473-3099(21)00319-4.

42. Zhu F, Jin P, Zhu T, Wang W, Ye H, Pan H, et al. Safety and Immunogenicity of a Recombinant Adenovirus Type-5-Vectored Coronavirus Disease 2019 (COVID-19) Vaccine With a Homologous Prime-Boost Regimen in Healthy Participants Aged >/=6 Years: A Randomized, Double-Blind, Placebo-Controlled, Phase 2b Trial. *Clin Infect Dis.* 2022;**75**(1):e783–91. [PubMed ID: 34551104]. [PubMed Central ID: PMC8522421]. https://doi.org/10.1093/cid/ciab845.

43. Khobragade A, Bhate S, Ramaiah V, Deshpande S, Giri K, Phophle H, et

al. Efficacy, safety, and immunogenicity of the DNA SARS-CoV-2 vaccine (ZyCoV-D): the interim efficacy results of a phase 3, randomised, double-blind, placebo-controlled study in India. *Lancet.* 2022;**399**(10332):1313–21. [PubMed ID: 35367003]. [PubMed Central ID: PMC8970574]. https://doi.org/10.1016/S0140-6736(22)00151-9.

 Chemaitelly H, Abu-Raddad LJ. Waning effectiveness of COVID-19 vaccines. *Lancet.* 2022;**399**(10327):771-3. [PubMed ID: 35219385]. [PubMed Central ID: PMC8871492]. https://doi.org/10.1016/S0140-6736(22)00277-X.