Original Article

Investigation of the Side Effects of COVID-19 Vaccines in Southern Iran: A Cross-Sectional Study

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ABSTRACT

The COVID-19 disease is a newly emerging disease, and the COVID-19 vaccine is one of the necessities to prevent this disease. The present study aimed to investigate the side effects of COVID-19 vaccines in southern Iran. We used convenience sampling to conduct this cross-sectional study on 647 people living in cities under coverage in Kerman province, southern Iran. The data collection tool was a researcher-made questionnaire of vaccine symptoms and signs. The results were analyzed using ANOVA and Chi-squared tests by SPSS software (version 24). The mean age of the participants was 40.19±15.20. The results indicated that 431 people (66.6%) reported post-vaccination side effects, with 18.23% of them having severe side effects. We noticed the most severe side effects in AstraZeneca, Sinopharm, Sputnik, and Bharat. Fever, headache, and pain at the injection site were the most common side effects after vaccination in descending order, which had a statistically significant relationship with all types of vaccines (*P*=0.001). The side effects differed in the types of vaccines, and most of the vaccines had mild to moderate side effects. People with the B blood type showed the most severe side effects, while those with the AB showed the lowest rate of side effects. Therefore, the injection of the AstraZeneca vaccine in blood group B should be done with more caution. More attention should also be paid to blood groups B and A in the injection of COVID-19 vaccines. Moreover, health officials and the government should plan appropriate educational strategies to increase public awareness of the importance of vaccines in eradicating viral infections.

Keywords: COVID-19, Iran, Side effects, Vaccines

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1. Introduction

In December 2019, the coronavirus disease 2019 (COVID-19) outbreak was first identified in Wuhan, China, and then rapidly became a global pandemic. On August 26, 2020, more than 24 million people worldwide were infected. Sweden recommended herd immunity to protect vulnerable groups because 60% of the population was expected to be infected by COVID-19 (1). However, it failed, and the number of people killed in Sweden was at least five times that of Germany. Therefore, the development of an effective vaccine was the only practical way to achieve herd immunity (1). Researchers around the world were working around the clock to develop a COVID-19 vaccine. In late August 2020, researchers investigated more than 200 vaccines, with 30 vaccines under clinical trials, so they began vaccinating humans (2). Safe and effective vaccines limited the spread of COVID-19. We expected there to be an effective vaccine to prevent severe COVID-19. We witnessed in the past that vaccines prevented diseases and reduced their severe complications (3). For example, many vaccines were effective against severe diseases, including dengue, influenza, whooping cough, and rotavirus (4). Goss (2021) reported dizziness, headache, pain, muscle spasm, myalgia, and paresthesia, as well as tremors, double vision, tinnitus, dysphonia, and seizures in rare cases, as the most common symptoms of vaccines. The Centers for Disease Control and Prevention (CDC) analyzed the first month of vaccination and found no safety concerns (5). Soiza and Johnson found no serious or unexpected side effects in almost 100% of the participants in all age groups after 28 days. According to Johnson, older people had minor side effects immediately after vaccination. One report suggested that AstraZeneca was 70% effective, while Sputnik was 92% effective (6). These vaccines had no side effects in infants (7). Mothers receiving the mRNA vaccine had increased milk antibodies against SARS-CoV-2. Healthcare organizations and governments recommended these COVID-19 vaccines for breastfeeding mothers (8). Mehrotra reported fever, chills, cough, shortness of breath, fatigue, muscle or body aches, headache, a net loss of taste or smell, a sore throat, stuffy or runny nose, nausea or vomiting, and diarrhea. He also mentioned severe complications that indicated severe disease, such as respiratory failure, acute kidney disease, and nerve dysfunction (9). As older people may be hospitalized and die due to their weak immune systems, and since COVID-19 imposes a heavy burden on the population, vaccination is necessary to improve the body's immunity. We assume that the side effects of vaccines are different and related to the blood group. However, we need further studies to identify the vaccine side effects and promote the quality, effectiveness, and efficiency of vaccines. Therefore, the present study aimed to investigate the side effects of COVID-19 vaccines in southern Iran.

2. Materials and Methods

2.1. Study Design and Participants

We conducted this cross-sectional study on all people living in southern Iran. Individuals who had injected at least one dose of vaccines available in Iran and gave their informed consent were included in the study. On the other hand, the exclusion criteria were participants' illness and non-cooperation. We used convenience sampling by referring to the COVID-19 vaccination centers in each city until the desired sample size was reached. A researcher-made questionnaire was given to and completed by a health expert. The method of selecting the samples according to the vaccinated population of each city was as follows: 120 people were selected from Jiroft city, 95 from Kohnouj, 105 from Manojan, 90 from Qalehganj, 72 from Anbarabad, 100 from South Rudbar, and 65 from Faryab.

2.2. Data Collection

The data collection tool consisted of two parts. The first part was demographic information, and the second part included 34 signs and symptoms of the vaccine based on a four-point Likert scale ranging from zero (no symptoms) to three (high symptoms). We used available articles and books, as well as the CDC, to make the questionnaire. We sent the questionnaire to infectious diseases specialists, managers, and experts, who confirmed its validity. They rated all items based on relevance, clarity, and simplicity. For example, they checked the relevance of the options (not relevant, relatively relevant, relevant, and fully relevant). Finally, the content validity index score for all questions was higher than 90%. Ten health workers determined that the questionnaire's reliability was higher than 0.85 using Cronbach's alpha.

2.3. Sample Size

According to a study in the United States (10), 11% of people had post-vaccination pain. Therefore, we considered an 11% prevalence and an error level of 5% to determine the sample size (161 individuals). Finally, the sample size was 647 individuals due to the existence of four types of vaccines.

2.4. Data Analysis

Descriptive and inferential statistics were used to describe and analyze the data. The data were expressed as mean (standard deviation) for quantitative data and as frequency (percentage) for qualitative data. The data from the

researcher-made questionnaire were entered into SPSS software (version 24) and analyzed using ANOVA and Chi-squared tests.

3. Results

We invited 647 individuals to participate in this study. The mean age of the participants was 40.19±15.20. A total of 41% of them were men, and 59.5% had a postgraduate degree. Overall, 78.5% were married, 21.9% were rural, and 52.1% had an O blood type. Regarding the type of vaccine, 45.3% selected Sinopharm, while only 7% selected Baharat (Table 1). According to figure 1, the Sinopharm vaccine had the highest injection rate (45%). The severity of side effects varied among participants depending on the type of COVID-19 vaccine. AstraZeneca (54%), Sinopharm (34%), Sputnik (25%), and Bharat (5%) had the most severe side effects, in descending order (Table 2) (Figure 2). Although all the COVID-19 vaccines caused adverse events after vaccination, the severity and number of these events were significantly related to the type of vaccine. There was a statistically significant relationship between all side effects and the type of vaccine (P=0.0001). AstraZeneca had the highest intensity of fever, headache, injection site pain, chills, fatigue, and chest pain (P=0.001). On the other hand, Sinopharm had the lowest intensity of fever, headache, injection site pain, dizziness, and chest pain (P=0.0001). Bharat had the highest intensity of dizziness and the lowest intensity of shivering among the vaccines (P=0.001). Sputnik also had the lowest intensity of fatigue among the vaccines (P=0.001) (Table 3). In the present study, 431 (66.6%) participants reported post-vaccination side effects. Most of them reported mild (30%) to moderate (5%) side effects. Only 4% suffered from severe side effects (Figure 3). Fever was the most common side effect after vaccination, and we observed a significant difference in the severity of fever among blood groups (P=0.035). The intensity of fever was higher in those with the B blood type than in those with other blood types, and we noticed the lowest rate of fever in the O blood type group. Headache severity was also significantly different among blood groups (P=0.005). The intensity of headaches was higher in the B blood type group than in other groups, with the lowest rate of headaches in the AB blood type group. There was a statistically significant difference in the severity of shivering among blood groups (P=0.013). The intensity of shivering was higher in the B blood type group than in other blood groups, with the lowest rate of shivering observed in the AB blood type group. There was a statistically significant difference in the severity of dizziness among blood groups (P=0.003). The intensity of chest pain was higher in the AB blood type group than in other blood groups, and we noticed the lowest rate of fatigue in the A and B blood type groups (Table 4). Figure 4 shows the frequency of all side effects, regardless of the type of COVID-19 vaccine received. The most common side effects were fever (66.46%), headache (59.19%), pain and swelling at the injection site (52.85%), chills (51.31%), dizziness (48.99%), fatigue (47.49%), and chest pain (42.81%). Other side effects were less common among vaccinated participants.

Table 1. Classification of participants involved in the study based on their demographic data

Variable		N	%
Gender	Male	265	41
	Female	382	59
Education			
	High school or less	153	23.6
	Diploma/Bachelor's degree	109	16.8
	Postgraduate studies	385	59.5
Marital status			
	Married	508	78.5
	Single	139	21.5
Places of residence	City	505	78.1
	Village	142	21.9
blood type			
	AB	69	10.7
	A	113	17.5
	B	128	19.8
	O	337	52.1
Vaccine name			
	Sputnik	158	24.4
	Sinopharm	293	45.3
	Baharat	45	7
	AstraZeneca	151	23.4
Total		647	100

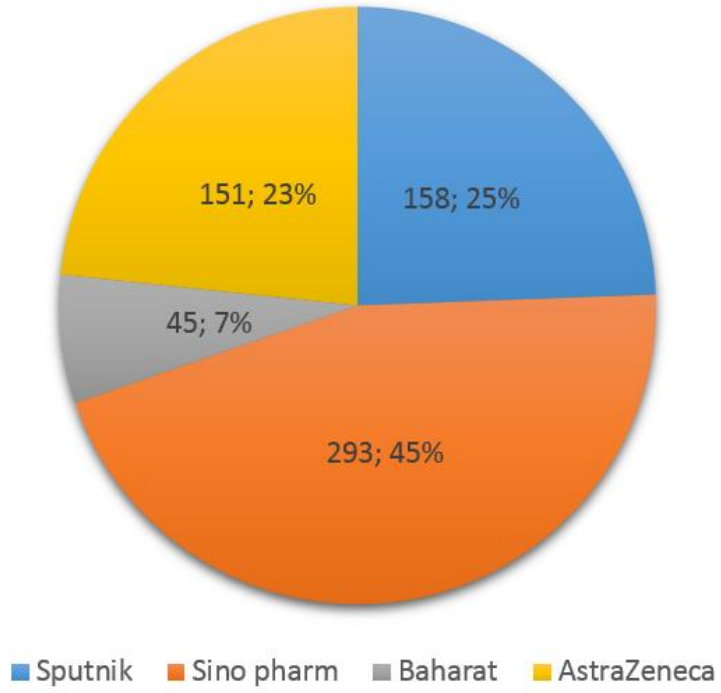

Figure 1. Frequencies of vaccines preferred by participants.

Table 2. Association of the side effects with the type of vaccine received

		Name of Vaccine				Total	P-value
		Sputnik(n%)	Sino pharm(n%)	Baharat(n%)	AstraZeneca(n%)		
Severity of side effect	No Side effects	41(25.94)	129(44.02)	17(37.77)	29(19.20)	216	
	Mild	42(26.58)	75(25.59)	14(31.11)	25(16.55)	156	
	Moderate	50(31.64)	55(18.77)	9(20)	43(28.47)	157	0.001
	Severe	25(15.82)	34(11.60)	5(11.11)	54(35.76)	118	
Total		158(100%)	293(100%)	45(100%)	151(100%)	647	

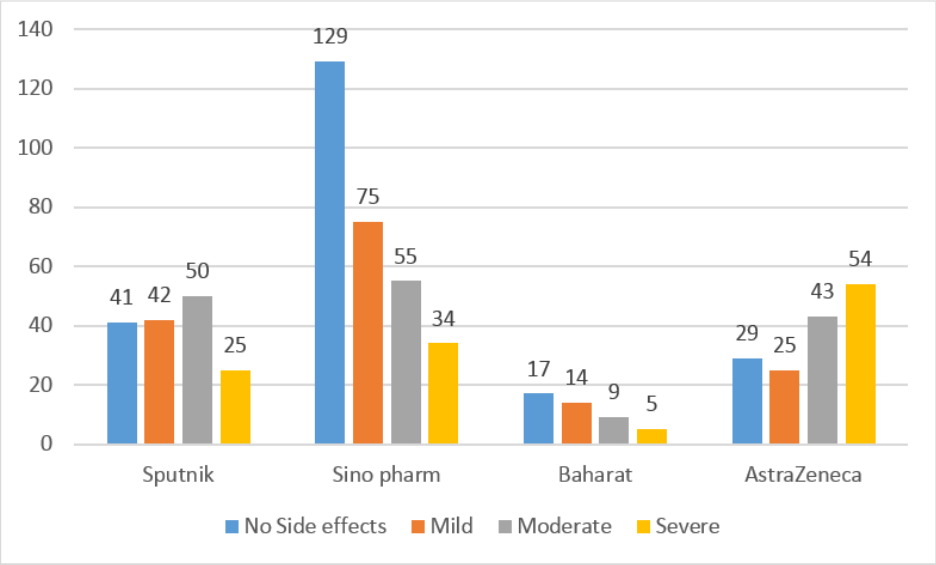

Figure 2. Severity of side effects based on the types of COVID-19 vaccine

Table 3. Correlation between complications of corona vaccines (Sputnik, Bharat, Sinopharm and Astraznica) and severity of symptoms

Side effects	Severity of the complication	AstraZeneca	Baharat	Sino pharm	Sputnik	P-Value
Fever	No Side effects	29	17	129	41	0.001
	Mild	25	14	75	42	
	Moderate	43	9	55	50	
	Severe	54	5	34	25	
Headache	No Side effects	45	16	151	52	0.001
	Mild	34	17	83	45	
	Moderate	20	6	32	37	
	Severe	52	6	27	24	
Injection site pain and swelling	No Side effects	53	18	174	60	0.001
	Mild	49	15	91	55	
	Moderate	19	8	17	15	
	Severe	30	4	11	28	
Chills	No Side effects	49	27	180	59	0.001
	Mild	37	11	80	52	
	Moderate	29	7	24	26	
	Severe	36	0	9	21	
Diziness	No Side effects	58	20	187	65	0.001
	Mild	49	16	74	64	
	Moderate	27	2	18	21	
	Severe	17	7	14	8	
Fatigue	No Side effects	55	22	190	73	0.001
	Mild	48	15	75	57	
	Moderate	25	5	20	26	
	Severe	23	3	8	2	
Chest pain	No Side effects	77	29	221	94	0.001
	Mild	56	15	64	54	
	Moderate	16	0	7	8	
	Severe	2	1	1	2	
	Total	158	293	45	146	

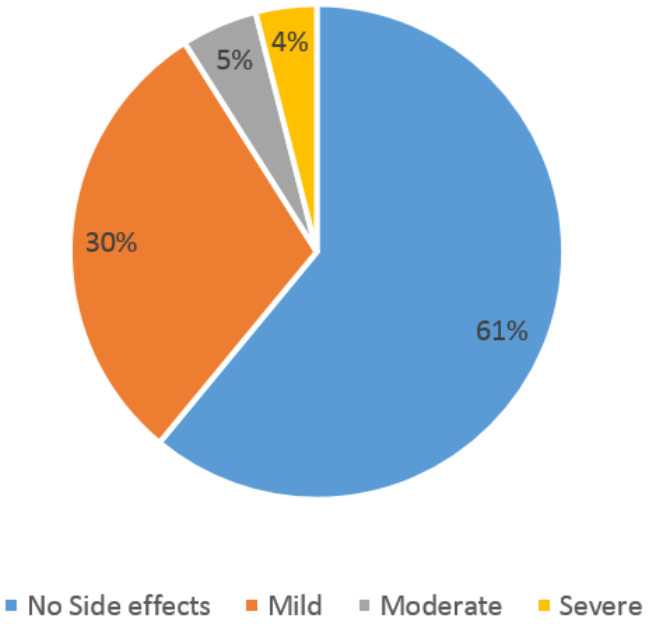

Figure 3. Severity of side effects after vaccination.

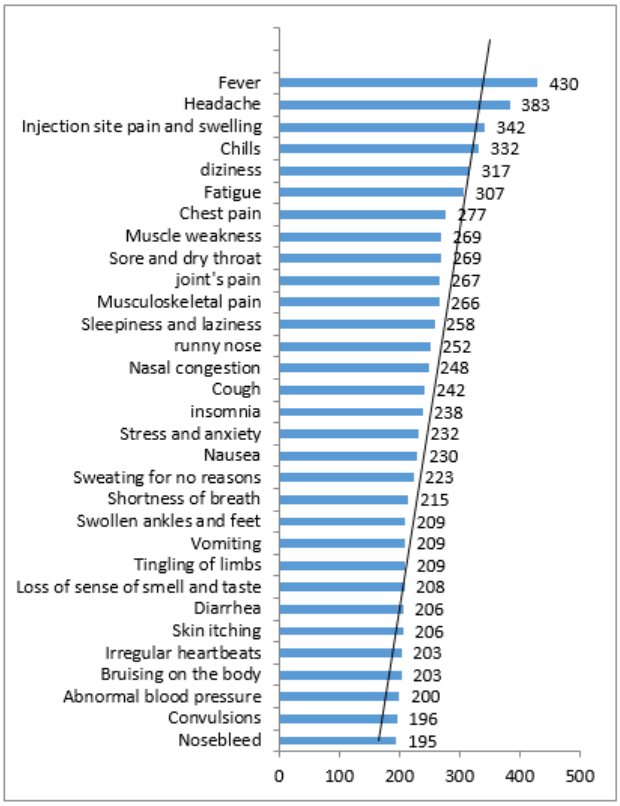

Figure 4. Frequencies of side effects that appeared after receiving COVID-19 vaccines

should be done with more caution. Furthermore, the Sinopharm vaccine is recommended as the least complicated vaccine for injection, and more attention should be paid to blood groups B and A in the injection of severe side effects, especially fever and chills. In addition, people with blood type B were more exposed to fever and chills. The severity of complications was higher in blood group B and lower in blood group AB. Therefore, the injection of the AstraZeneca vaccine in blood group B COVID-19 vaccines. In the present study, 431 people (66.6%) reported post-vaccination side effects, with most of them having mild (24.1%) to moderate (24.2%) side effects. Only 10.23% had severe side effects. Alessa (2022) reported post-vaccination side effects in 74.7% of the individuals (11). However, Hatmal et al. found that 39, 21, and 10% of the participants had mild, moderate, and severe post-vaccination side effects, respectively (12). The severity of side effects in our study was higher than that in Hatmal's study. In both studies, women constituted more than half of the participants, and more than 60% of the participants had a bachelor's degree. However, we conducted this study in the tropical regions of Iran, with half of the participants having the O blood type. The severity of side effects varied among participants depending on the type of COVID-19 vaccine and blood group. Aliberti et al. revealed only mild and moderate side

Table 4. The relationship between the most common side effects of vaccines and blood groups

Blood type / Side effects		AB	A	B	O	P-Value
Fever	No Side effects	26	33	37	120	0.035
	Mild	18	33	21	84	
	Moderate	14	26	41	93	
	Severe	11(15.9)	21(18.6)	29(22.7)	40(11.9)	
	Total	69	113	128	337	
Headache	No Side effects	27	36	44	157	0.005
	Mild	27	42	33	77	
	Moderate	10	20	33	59	
	Severe	5(7.2)	15(13.3)	18(14.1)	44(13.1)	
	Total	69	113	128	337	
Injection site pain and swelling	No Side effects	37	47	47	174	0.097
	Mild	22	43	54	91	
	Moderate	7	11	11	34	
	Severe	3(4.3)	12(10.6)	16(12.5)	38(11.3)	
	Total	69	113	128	337	
Chills	No Side effects	36	45	49	185	0.013
	Mild	17	41	45	77	
	Moderate	12	19	21	50	
	Severe	4(5.8)	8(7.1)	13(10.2)	25(7.4)	
	Total	69	113	128	337	
Diziness	No Side effects	34	47	51	198	0.003
	Mild	24	46	53	80	
	Moderate	9	12	16	36	
	Severe	2(2.9)	8(7.1)	8(6.3)	23(6.8)	
	Total	69	113	128	337	
Fatigue	No Side effects	37	51	54	198	0.094
	Mild	21	41	49	84	
	Moderate	7	13	18	42	
	Severe	4(5.8)	8(7.1)	7(5.5)	13(3.9)	
	Total	69	113	128	337	
Chest pain	No Side effects	46	67	69	239	0.058
	Mild	19	38	51	81	
	Moderate	3	8	8	13	
	Severe	1(1.4)	0	0	4(1.2)	
	Total	69	113	128	337	

4. Discussion

The Sinopharm vaccine had the fewest side effects among the COVID-19 vaccines, while AstraZeneca had the most

effects (13). They studied Vaxzervria, which was different from our study. The adverse effects of Vaxzervria depended on various variables, such as gender, blood types A, B, and O, and chronic pathologies. Overall, 60% of the participants were healthcare workers with a bachelor's or higher degree. Before the vaccine was available, several studies evaluated the acceptance of the COVID-19 vaccine among healthcare workers. Of the 2,213 individuals in a Jordanian study, 32% were healthcare workers (14). Another study in the Asia-Pacific region found that about 95% of healthcare workers (1,720) supported vaccination against COVID-19 (14). Amit et al. reported that only healthcare workers received the vaccine (15). They had higher education and took measures to prevent infection with COVID-19. Various factors increased doubt and a negative understanding related to vaccine effectiveness, safety, and convenience (16). The most common side effects after vaccination in this study were fever, headache, pain and swelling at the injection site, chills, dizziness, fatigue, and chest pain, whereas the most common side effects after vaccination in other studies were fatigue, pain and swelling at the injection site, headache, drowsiness, laziness, chills, myalgia, joint pain, and fever. However, most of these studies evaluated the side effects of Pfizer-BioNTech and Moderna vaccines (11, 17), and only two studies focused on AstraZeneca (12, 16). In addition, previous studies had large sample sizes with good reliability. We noticed that those who received AstraZeneca had the most side effects. The frequency of some side effects was also dependent on the type of vaccine, but the study in Jordan (2021) indicated that Sinopharm had the highest rate of adverse effects, followed by Pfizer, AstraZeneca, and Sputnik (12). These differences may be due to the nature of each vaccine and its mechanism of action. Alessa et al. found a significant relationship between the type of vaccine and the severity of side effects. Participants who received the Pfizer vaccine had more adverse effects (11). Available vaccine platforms are virus-based (live attenuated, inactivated), DNA-based, RNA-based, and protein-based. Vaccines produced by each of these strategies have various advantages and disadvantages related to efficacy, safety, immunogenicity, and ease of use (18, 19). Concerns about their safety and immunogenicity still require further research. Wang and Van (2020) demonstrated that both AstraZeneca and Sinopharm vaccines prevented viral interstitial pneumonia (20, 21). AstraZeneca revealed serious side effects due to blood clots in several people. Several reports from different European countries confirmed the rare risk of thrombocytopenia and abnormal blood clotting associated with the AstraZeneca vaccine (22). It is important to avoid the misidentification of other causes of post-vaccination side effects. Therefore, we should study a complete health history of patients who develop serious symptoms after vaccination to confirm whether these are vaccination-related adverse effects. However, the benefits of these vaccines are much greater than their risks, especially death from COVID-19 (23). The vaccines most commonly received by the participants were Sinopharm, Sputnik, AstraZeneca, and Baharat, in descending order. Although the first vaccine in Iran was Sputnik, only health workers welcomed it. Fear and suspicion, as well as a lack of information about clinical trials, were factors in avoiding COVID-19 vaccines. In addition, the epidemiological situation of COVID-19 in Iran also affected the use of vaccines (24). The low rate of the Sputnik vaccine in the present study indicated that most of the participants were afraid of receiving it. However, after the vaccination, participants felt more confident and recommended others be vaccinated. Therefore, the arrival of a large number of Sinopharm vaccines increased the number of people who received this vaccine. If researchers in each country conducted local studies on the safety of COVID-19 vaccines, the number of vaccinated people would increase. Our results suggested that individuals with the B blood type had the most serious side effects, while those with the AB blood type had the lowest rate of side effects. However, Aliberti (2022) reported that urban female respondents with A positive and B negative blood types, as well as chronic pathologies, suggested a higher rate of side effects, while those with O positive and A negative blood types showed no side effects (13). However, a cross-sectional retrospective study on 33,000 healthcare workers, students, and volunteers found no statistically significant relationship between the incidence of side effects, gender, and the A, B, and O blood types (11, 25). Another study indicated that women had more side effects than men (13). Therefore, the type of vaccine could be effective in the occurrence of side effects. Enguita-German noticed that those with the O blood type had a lower risk of COVID-19 or death than those with other blood types (26). Other studies reported that the A blood type increased the risk of infection with SARS-CoV-2 and admission to the intensive care unit. Individuals with the O blood type reduced the rate of infection and increased their immunity, compared to those with other blood types (11, 25). The Sinopharm vaccine had the fewest side effects among other vaccines, while the AstraZeneca vaccine had the most severe side effects, especially fever and chills. People with blood group B were more exposed to fever and chills. The severity of complications was higher in blood group B and lower in blood group AB. Therefore, the injection of the AstraZeneca vaccine in

blood group B should be done with more caution. Furthermore, the Sinopharm vaccine is recommended as the least complicated vaccine for injection, and more attention should be paid to blood groups B and A in the injection of COVID-19 vaccines. Health officials and the government should plan appropriate educational strategies to increase public awareness of the importance of vaccines in eradicating viral infections.

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Authors' Contribution

Study concept and design:
Acquisition of data:
Analysis and interpretation of data:
Drafting of the manuscript:
Critical revision of the manuscript for important intellectual content:
Statistical analysis:
Administrative, technical, and material support:

Ethics

The Ethics Committee of Jiroft University of Medical Sciences approved this study (IR.JMU.REC.1400.038). Then, we explained the study objectives to the participants, gained their consent, and assured them that their information would be kept confidential.

Conflict of Interest

The authors declare no conflict of interest in this study

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