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Short-term Side Effects of COVID-19 Vaccines (Astrazeneca, Sputnik-V, and Sinopharm) in Health Care Workers: A Cross-Sectional Study in Iran

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Abstract

Background: The occurrence of side effects of vaccines plays an important role in their acceptance by people. Therefore, the aim of this study was to evaluate the side effects of COVID-19 vaccines
(Sputnik-V, AstraZeneca, and Sinopharm) in Neyshabur health care workers (HCWs).

Methods: A cross-sectional study was performed to evaluate the side effects of COVID-19 vaccines among the HCWs of the Neyshabur University of Medical Sciences from July 31, 2021, to September 6, 2021, by using a self-report checklist. We sent our checklist via an internet link to collect data such as demographic data of participants, previous COVID-19 infection (PCR+), vaccine information and side effects of vaccines. Mean, median and standard deviation were used to determine descriptive statistics and a logistic regression model was also used to determine the relationship between the type of vaccine and its side effects.

Results: 317 participants filled out the checklist; among them 47% (N= 149), 21.14% (N= 67), and 31.86% (N= 101) have been vaccinated with Sputnik-V, AstraZeneca, and Sinopharm, respectively. The percentage of side effects after the first dose was 62.15% (N= 197). The Percentage of local side effects was 76% (N= 241) and systemic side effects were 29.36% (N= 95). The most common side effects in all three vaccines were injection site pain (75.08%, N= 240), muscle pain (62.46%, N=198) and headache (52.05%, N=165). Also, the odds ratio of injection site pain, chill and sweating in those who received the AstraZeneca vaccine was 3.9(95% CI, 1.7-9.3), 3.7 (95% CI, 1.8-7.3), and 3.2 (95% CI, 1.7-63), of those who received the Sputnik V vaccine ($p \leq 0.001$).

Conclusion: The most common side effects among our participants were injection site pain, muscle pain, and headache. Most of the post-vaccination side effects are mild to moderate in severity and self-limited. Reported side effects were more common in recipients with AstraZeneca than in those with Sputnik-V and Sinopharm.

Keywords: COVID -19 Vaccine, Side effects, AstraZeneca, Sputnik-V, Sinopharm

Conflicts of Interest: None declared
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Introduction

Severe acute respiratory syndrome (SARS), which broke out in December 2019 in Wuhan Province, China, has spread rapidly around the world, challenging healthcare systems. Since November 30, 2021, more than 261 million cases have been confirmed, and more than five million deaths have been reported worldwide (1).

One of the methods of controlling infectious diseases is vaccination, the short-term goal of which is to control the

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↑What is "already known" in this topic:
COVID-19 is a highly infectious and, in some cases, highly dangerous disease. Getting vaccinated against COVID-19 can reduce risk of getting and spreading the virus that causes COVID-19.

→What this article adds:
Side effects which is reported in this survey were mild to moderate and self-limiting in Sputnik-V, AstraZeneca and Sinopharm vaccines. None life-threatening complications reported.

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disease in human societies, and its ultimate goal is to eradicate the disease. In order to respond appropriately to the COVID-19 pandemic, more than 200 vaccine production projects have been registered worldwide. Some of the vaccines that have been licensed by relevant organizations so far include BioNTech, Moderna, Pfizer, Johnson & Johnson, AstraZeneca, Bharat, Sputnik-V, Sinovac and Sinopharm (2). Since November 28, 2021, more than 7 billion COVID-19 vaccine doses have been injected worldwide (1).

The effectiveness and power of proper immunization and also absence of side effects are the most important components that affect vaccine acceptance. After the clinical trial and determination of the effectiveness of a vaccine and obtaining marketing authorization permission, there should be monitoring systems to evaluate its effectiveness in larger populations (2). Although some side effects of COVID-19 vaccines, such as injection site pain, fever, chills, muscle pain, headaches and vascular thrombosis, have been identified and reported during the clinical trials (3-6), there is limited information on side effects in larger populations.

One of the groups at risk of contracting infectious diseases is health care workers (HCWs), and in order to continue providing health services, maintaining their health should be a priority and they should be one of the first groups that undergo extensive vaccination (7). Although there are no accurate statistics on the number of COVID-19 cases and deaths among HCWs in different countries (8), according to reports released by the World Health Organization, HCWs account for 14% of COVID-19 patients, and this figure is as high as 35% in some developing countries (9). WHO estimated that at least 115,000 HCWs had died of COVID-19 by May 2021 (10).

Iran is one of the first countries to face the COVID-19 pandemic, and there have been more than 6 million confirmed cases by November 30, 2021, and 129711 COVID-19-related deaths(1). According to the data from the medical system of the Islamic Republic of Iran, 138 HCWs had died of COVID-19 infection by July 23, 2020 (11). In Iran, HCWs, like in other countries, have been among the first target groups of COVID-19 vaccination (12). Although some studies about the side effects of COVID-19 vaccines were published in Iran (13, 14), compare Sputnik- V, Sinopharm and AstraZeneca vaccines don't be done. HCWs at Neyshabur University of Medical Sciences received Sputnik- V, Sinopharm and AstraZeneca vaccines on February 11, 2021. By the time of the present study (August 20, 2021), out of 3500 staff of Neyshabur University of Medical Sciences, 2469 have been vaccinated against COVID-19.

Since having accurate information about vaccines' side effects can help to make a better decision to choose a suitable vaccine with fewer side effects, the present study aimed to investigate the short-term side effects of COVID-19 vaccines among HCWs at Neyshabur University of Medical Sciences.

Methods

This cross-sectional study was conducted on the staff of Neyshabur Medical University for six weeks, from July 31, 2021, to September 6, 2021. In order to investigate the short-term side effects of the COVID-19 vaccines, an anonymous checklist was designed online on Google. The link of checklist was sent via SMS to the mobile phones of all vaccinated staff of Neyshabur University of Medical Sciences. They were asked to participate in the study in case of any side effects after the COVID-19 vaccination. This checklist was designed based on the results of previous studies (15) and consisted of four sections: 1. Demographic information such as age, sex, education, underlying disease, and occupation 2. Information about the history of COVID-19 based on PCR test results 3. Information about the injected COVID-19 vaccine, including the type of vaccine and number of doses and 4. Vaccine-related short-term side effects, medications are taken to improve symptoms, time of onset of symptoms, and the history of hospitalization following the vaccination.

Inclusion/exclusion criteria

Inclusion criteria included receiving at least one dose of COVID-19 vaccines, including Sputnik- V, AstraZeneca, and Sinopharm. Exclusion criteria also included an incomplete checklist and a COVID-19 positive test during the study period.

Statistical analysis

The collected data were analyzed using Stata ver. 16. Mean, median, and standard deviation were used to determine descriptive statistics and a logistic regression model was also used to determine the relationship between the type of vaccine and its side effects. To determine the relationship among the variables, P-value<0.05 was considered as the statistically significant level.

Results

Demographic information

A total of 317 people participated in the present study. Table 1 shows the demographic characteristics, history of COVID-19, and type of vaccine. The majority of participants (53%, N=168) were female, and the mean age of the subjects was 34.08 ± 8.23 years. The majority of participants (59.62%, N=189) were also members of the clinical group (physicians, nurses, operating room specialists, anesthesiologists, and Emergency Medical staff).47% of people had received the sputnik-V vaccine, and nearly half of the participants (48.9%, N=155) reported a history of positive COVID-19 test results.

Frequency of side effects

Figure 1 shows the percentage of side effects of each vaccine. The highest percentage of side effects was reported after the first vaccine dose (62.15%, N=197). The most commonly reported side effects included injection site pain (75.08%, N=240), muscle pain (62.46%, N=198), and headache (52.05%, N=165).

Menstrual irregularities (N=15 women, 4.73%), chest pain (N = 11, 3.47%), swollen lymph nodes (N = 7, 2.2%), petechiae (N = 7, 2.2%), blurred vision (N = 4, 1.26%) and seizures (N = 2, 0.63%) were experienced less

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Table 1. Demographic Characteristics of participants (N=317)

Characteristic	Level	Frequency (Number & percentage)
Age (mean ±SD)		34.08± 8.23
Sex	Male	149 (47%)
	Female	168 (53%)
Employment	Clinical	189 (59.62%)
	Non-Clinical	128 (40.38%)
Vaccine	Sputnik-V	149 (47%)
	AstraZeneca	67 (21.14%)
	Sinopharm	101 (31.86%)
Previous infection	Yes	155 (48.9%)
with COVID 19 (PCR+)	No	162 (51.1%)
Time of Onset Side Effects	<12 h	129 (40.69%)
	12-<24h	150 (47.32%)
	24-<48h	22 (6.94%)
	48-<72h	11 (3.47%)
	72h<	5 (1.58%)

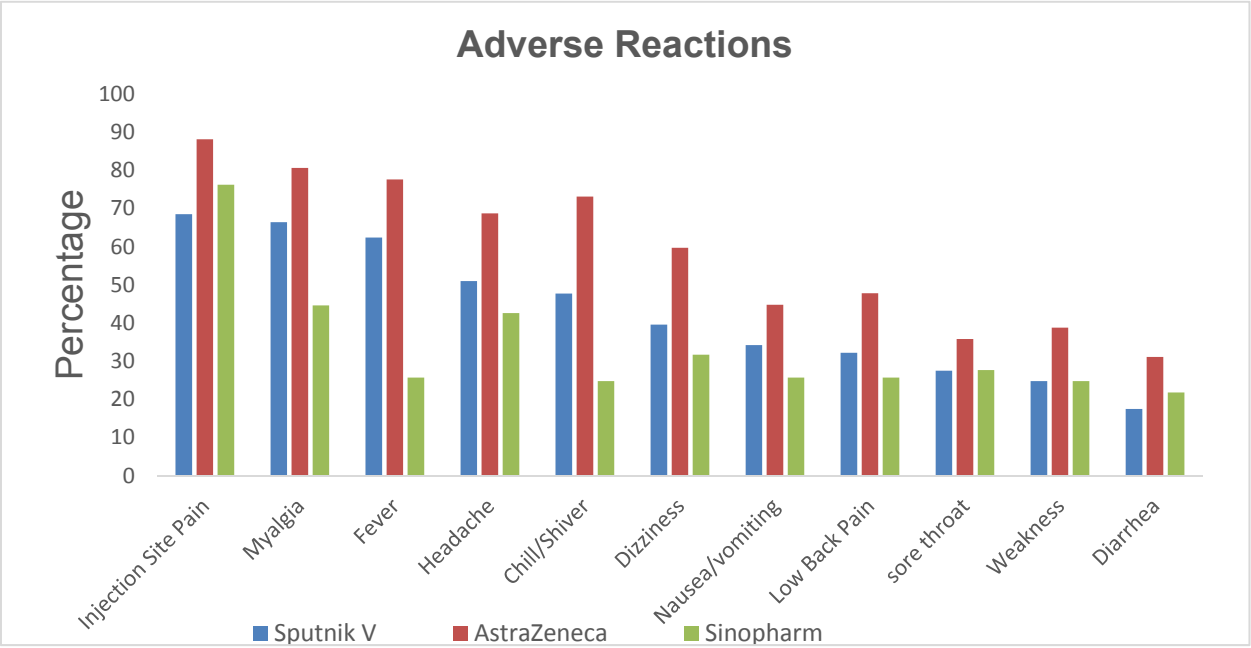

Fig. 1. Side effects reported by participants after vaccination (Percentage)

frequently by participants.

No vaccine-related deaths were reported, and approximately half of the reported side effects (46.69%, N=148) disappeared without any drugs, except for one case, in which patients were admitted to the hospital emergency department for six hours after AstraZeneca vaccination due to chest pain and shortness of breath. This patient was discharged after cardiac examinations and tests. The most common drugs used to limit vaccine-related side effects included acetaminophen (36.65%, N=116), non-steroidal anti-inflammatory drugs (NSAIDs) (15.14%, N=48) and other drugs (2.52%, N=8), respectively.

The results of univariable logistic regression showed no significant difference between the incidence of side effects such as nausea, sore throat, runny nose, cough, shortness of breath, abdominal pain, diarrhea, hypertension, petechiae, and visual disturbances with the type of vaccine ($p > 0.05$). On the other hand, there was a significant relationship between side effects such as injection site pain, headache, chills, fever, myalgia, dizziness, loss of appetite, sweating, having hot or cold sensations in the fingers, back pain and lethargy with the type of vaccine ($p \leq 0.05$) (Table 2).

The results of multivariable logistic regression showed a significant relationship between the vaccine type and side effects such as local pain at the injection site, headache, chills, myalgia, dizziness, fever, loss of appetite, sweating, warm and cold sensation in the limbs, back pain and weakness ($p \leq 0.05$). According to the adjusted risk ratios shown in Table 3, the odds ratio of local pain at the injection site, chills, and sweating were 3.9, 3.7, and 3.2 times higher in AstraZeneca recipients, respectively, than Sputnik-V recipients ($p \leq 0.001$).

Also, the odds ratio of fever, chills, and muscle pain in Sinopharm recipients were 0.1, 0.3 and 0.4 times more than in Sputnik-V recipients , respectively ($p \leq 0.003$)

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Table 2. Odds Ratio (OR) estimates of side effects based on the univariable logistic regression

Variable	Vaccine	OR	*P*-value	95% CI
Pain at the injection site	Sputnik - V	Ref		
	AstraZeneca	3.39	0.003	1.5 , 7.8
	Sinopharm	1.47	0.186	0.8 , 6.2
Headache	Sputnik - V	Ref		
	AstraZeneca	2.11	0.016	1.1 , 3.8
	Sinopharm	0.71	0.194	0.4 , 1.1
Chill	Sputnik - V	Ref		
	AstraZeneca	2.99	0.001	1.5 , 5.6
	Sinopharm	0.36	<0.001	0.2 , 0.6
Fever	Sputnik - V	Ref		
	AstraZeneca	2.08	0.030	1.0 , 4.0
	Sinopharm	0.20	<0.001	0.1 , 0.3
Myalgia	Sputnik - V	Ref		
	AstraZeneca	2.09	0.037	1.0 , 4.2
	Sinopharm	0.40	<0.001	0.2 , 0.6
Dizziness	Sputnik - V	Ref		
	AstraZeneca	2.25	0.007	1.2 , 4.0
	Sinopharm	0.70	0.233	0.4 , 1.2
Reduced Appetite	Sputnik - V	Ref		
	AstraZeneca	2.31	0.006	1.2 , 4.1
	Sinopharm	0.91	0.752	0.5 , 1.6
Sweating	Sputnik - V	Ref		
	AstraZeneca	2.08	0.001	1.5 , 5.1
	Sinopharm	0.65	0.121	0.3 , 1.1
Warm/Coolness of Extremities	Sputnik - V	Ref		
	AstraZeneca	2.51	0.002	1.3 , 4.5
	Sinopharm	1.59	0.117	0.3 , 1.1
LBP	Sputnik - V	Ref		
	AstraZeneca	1.92	0.030	1.0 , 3.4
	Sinopharm	0.72	0.275	0.3 , 1.2
Weakness	Sputnik - V	Ref		
	AstraZeneca	1.91	0.038	1.0 , 3.5
	Sinopharm	0.99	0.988	0.5 , 1.7

Table 3. Odds Ratio (OR) estimates of side effects based on the multivariable logistic regression

Variable	Vaccine	OR	P
Pain at the injection site	Sputnik - V	Ref	
	AstraZeneca	3.9	<0.001
	Sinopharm	1.5	0.185
Headache	Sputnik - V	Ref	
	AstraZeneca	2.2	0.015
	Sinopharm	0.6	0.141
Chill	Sputnik - V	Ref	
	AstraZeneca	3.7	<0.001
	Sinopharm	0.3	<0.001
Fever	Sputnik - V	Ref	
	AstraZeneca	2.1	0.030
	Sinopharm	0.1	<0.001
Myalgia	Sputnik - V	Ref	
	AstraZeneca	2.6	0.011
	Sinopharm	0.4	0.003
Dizziness	Sputnik - V	Ref	
	AstraZeneca	2.6	0.003
	Sinopharm	0.6	0.131
Reduced Appetite	Sputnik - V	Ref	
	AstraZeneca	2.7	0.003
	Sinopharm	0.8	0.676
Sweating	Sputnik - V	Ref	
	AstraZeneca	3.2	<0.001
	Sinopharm	0.6	0.086
Warm/Coolness of Extremities	Sputnik - V	Ref	
	AstraZeneca	2.9	<0.001
	Sinopharm	0.5	0.070
LBP	Sputnik - V	Ref	
	AstraZeneca	2.1	0.020
	Sinopharm	0.6	0.207
Weakness	Sputnik - V	Ref	
	AstraZeneca	2.0	0.031
	Sinopharm	0.9	0.817

(Table 3).

Discussion

The occurrence of post-vaccination side effects is not

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only rare but also indicates that the body is responding to it (16). Some concerns about the side effects of COVID-19 vaccines have cast doubt on people's perceptions of the benefits of vaccination (17). Factors such as knowledge about vaccines, cultural and religious beliefs, past experiences, the role of media and vaccine side effects affect vaccine acceptance (18, 19). The present study investigated the short-term side effects of three COVID-19 vaccines (Sputnik - V, AstraZeneca and Sinopharm) among HCWs in Iran.

The Sputnik-V vaccine has become the first registered COVID-19 vaccine, which has been used in 71 countries so far. A randomized controlled trial in Russia was the first study reporting that Sputnik-V safety and efficacy was 91.6% (20). The AstraZeneca vaccine, developed by a British company called AstraZeneca using the chimpanzee ChAdOx1 adenovirus as a viral vector, is better tolerated in older adults than in young people (19). The efficacy of this vaccine reaches 76% after 22 days of the first dose and 81% after the second dose (21). Sinopharm vaccine, which is one of the inactivated viral COVID-19 vaccines, is produced by China, and its efficacy has been reported to be 79.34% (22, 23).

The most commonly reported side effects for the three vaccines included injection site pain, muscle pain, headache, and chills, which are similar to those reported in other studies (13, 18, 24). However, compared to other studies, the frequency of the above side effects in our study was higher than other studies, which may be due to age differences. In the present study, 75% of the research samples were less than 40 years of age, and the maximum age of the research samples was 61 years, while in other studies, the mean age of the subjects was higher than in the present study (25). However, the percentage of these side effects was different in the three types of vaccines. The most frequently seen side effects for the AstraZeneca vaccine included muscle pain, chills, and headache, respectively, but muscle pain, headache, and chills in Sputnik-V and Sinopharm, respectively, which is consistent with the results of the study by Zare et al. (13). Hatmal et al. also found that the incidence of side effects in AstraZeneca vaccine is higher than that in Pfizer and Sinopharm vaccines (26). Although thrombosis has been reported occasionally in some people receiving the AstraZeneca recipients (26-29), the present study reported mostly local and systemic side effects that were not life-threatening and did not report any side effects such as thrombosis or anaphylactic shock. On the other hand, the incidence of side effects after the first vaccine dose was significantly higher than the second vaccine dose, so more than 62% of side effects occurred after the first dose, which is consistent with the results of other studies (3, 30, 31). Inconsistent with the results of the present study, results of a study by Menin et al. showed that the incidence of side effects increased after the second Pfizer dose (24). Because vaccines are available in different platforms, such as DNA-based, RNA-based, protein-based, or attenuated live inactivated or inactivated virus, such differences may be related to the vaccine nature.

The results of the present study also showed a statistically significant difference between the three types of vaccines in terms of the percentage of some side effects (Table 2), i.e. injection site pain, muscle pain, fever, chills, dizziness, headache, loss of appetite, sweating, and warm and cold sensation in the limbs were significantly higher in AstraZeneca recipients than the Sputnik-V and Sinopharm recipients, which is consistent with the findings of a study by Zare et al. (13).

In a study, Kim et al. found that AstraZeneca recipients experienced more side effects than Pfizer recipients (3). However, there was no significant difference between the three types of vaccines in terms of the percentage of other side effects such as nausea, sore throat, running nose, cough, shortness of breath, abdominal pain, diarrhea, hypertension, petechiae and visual disturbances.

The results of multivariable logistic regression (Table 3) indicate that the odd ratio of local pain at the injection site, chills, and sweating in AstraZeneca recipients was 3.9, 3.7, and 3.2 times higher than Sputnik-V recipients, respectively ($p \leq 0.001$).

Limitations

The present study had some limitations. First, since only 317 (12.8%) of the 2469 vaccinated individuals completed the side effects form in a self-reported manner, it's possible some vaccinated people who had side effects had not participated in the present study. Secondly, since our study population included people with a relatively high level of knowledge in the medical sciences, they may have information bias that required clinical evaluations, which were not possible for us to do so. Third: The present study investigated the short-term side effects of COVID-19 vaccines, and further studies should be performed to evaluate the long-term side effects of these vaccines. Fourth: There may be some confounding variables that have not been studied in this study and their effects on the incidence of side effects may be negligible.

To the best knowledge of the researcher, this is the first study that investigates and compares the side effects of COVID-19 vaccines, namely, Sputnik-V, AstraZeneca, and Sinopharm in Iran. Overall, side effects such as local pain at the injection site, fever, chills and sweating, headache, back pain, dizziness, muscle pain, loss of appetite, and warmth and coldness of the limbs were significantly higher in AstraZeneca recipients than Sputnik -V and Sinopharm recipients. But none of the people reported a life-threatening complication. Since COVID-19 disease is still spreading, in order to eliminate unnecessary fears of people, it is necessary to identify the side effects of different vaccines in future studies and present them to people to help increase vaccination and control the pandemic.

Conclusion

Although there was a statistically significant difference in the incidence of side effects such as injection site pain, chills, and sweating in AstraZeneca recipients, the findings showed that none of them reported life-threatening side effects. Most of the reported side effects were mild to moderate and self-limiting. Considering the prevalence of

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the current deadly pandemic, the benefits of vaccines seem to outweigh the mild to moderate short-term side effects. In the meantime, it is not yet possible to say with certainty that vaccines are completely safe because their long-term effects cannot be studied.

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Ethical Approval and Informed Consent

The study protocol was approved by the research and ethics committee of the Neyshabur University of Medical Sciences. All participants provided their consent prior to taking part in the study. Participation was completely voluntary, and participants were able to withdraw from the study at any time without any consequence.

Conflict of Interests

The authors declare that they have no competing interests.

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