

Research Paper

Examining Side Effects of the Sputnik V COVID-19 Vaccine



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ABSTRACT

Background: As a result of the COVID-19 pandemic, many vaccines were developed to counter the disease, including the vector-based Sputnik V vaccine. This study aims to identify the side effects of the Sputnik V COVID-19 vaccine in a medical center and compare the results with the previous reports.

Methods: A questionnaire-based study was performed after the injection of the first and second doses of the vaccine to assess the side effects experienced by the participants. It was performed by reviewing similar previous studies.

Results: Injection site pain, muscle pain, fever, fatigue, chills, and headache were the most common side effects of the vaccine. The incidence of major side effects decreased with age and was lower in men. In our study and others, the incidence of side effects was decreased in the second dose. In some studies, participants with a previous history of Severe Acute Respiratory Syndrome Coronavirus 2 (SARSCOV-2) infection developed more side effects, especially injection site pain, muscle pain, and fatigue.

Conclusion: Most studies agree with our reported results. Serious side effects of this vaccine are rare and may be considered tolerable in adults.

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1. Introduction

The outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection has been one of the most challenging public health issues during the past three years. As of April 29, 2022, more than 51000000 confirmed cases of COVID-19, including more than 6 200 000 deaths, were reported to the WHO. As of April 29, 2022, 11163040177 vaccine doses have been administered [1]. As of December 2020, over 200 vaccine candidates for COVID-19 are being developed. Of these, at least 52 candidate vaccines were in human trials [2].

Three main approaches exist to designing a vaccine. They differ in whether they use a whole virus or bacterium, the parts of the germ that triggers the immune system, or the genetic material that provides the instructions for making specific proteins, rather than the whole virus [2]. Sputnik V vaccine or Gam-COVID-Vac is a recombinant adenovirus (rAd) vector-based vaccine based on rAd type 26 (rAd26) and rAd type 5 (rAd5), both of which carry the gene for SARS-CoV-2 full-length glycoprotein S (rAd26-S and rAd5-S). rAd26-S and rAd5-S are administered intramuscularly separately with a 21-day interval [3].

Like any other vaccine, the COVID-19 vaccine can cause side effects, most of which are mild or moderate, and go away on their own within a few days [4]. Though several COVID-19 vaccines are available in Iran. Sputnik V COVID-19 vaccine was the first COVID-19 vaccine that has been used in Iran.

The present study was designed to identify the short-term side effects of the Sputnik V COVID-19 vaccine experienced by individuals receiving the first and second doses. The second part of the study is a thorough review of the article on the side effects of this vaccine and its comparison with our results.

2. Materials and Methods

A prospective cross-section study was conducted among healthcare workers of a general hospital in Tehran City, Iran, who received their first and second dose of vaccination with the Sputnik V COVID-19 vaccine. A structured questionnaire was created to record the symptoms that developed after receiving their first and second doses. The questionnaire was designed after an extensive literature review on the side effects of various COVID-19 vaccines. An open section was also provided

for participants to report any unlisted symptoms experienced by the participants.

Ethical approval was obtained from the Research Ethics Committee of our institute (Code: IR.SBMU.RETECH.REC.1400.197). This study was performed according to the Helsinki Declaration, and all participants were given informed consent. The inclusion criteria were healthcare workers in Loghman Hospital who received the first and second doses of Sputnik V COVID-19 vaccines without any prior COVID-19 vaccination.

The statistics and epidemiology department examined the reliability of the questionnaire. The first question was asked at the time of the second dose of the vaccine to have better access to the recipients. Trained physicians completed the questionnaires in a face-to-face conversation. Two weeks after the injection of the second dose, the second dose's side effects were questioned by telephone. Figure 1 shows the questionnaire's translated sample.

The results of the questionnaire were entered to the international Business Machines Corporation (IBM) SPSS Statistics for Windows, v.26 (IBM Corp., Armonk, NY, USA) sheet and reexamined by a second person. The participants' data were analyzed using SPSS 26 and descriptive data analysis, paired and independent t tests, Chi-square test, and linear regression modeling. Tableau Software v.2019.4 was used for visualization. All results were reported. P value less than 0.05 was considered significant.

To identify the articles evaluating Sputnik V COVID-19 vaccine, PubMed/Medline, Embase, and Google scholar were screened for English-written articles. The manuscripts published up to March 10, 2022, were included.

3. Results

Three hundred and fifty-two questionnaires were filled out, seven of which were excluded due to distortion; for follow-up of the second dose, 20 patients were unreachable, and data were included only for the side effects of the first dose. Out of 345 patients, 179 people (51.9%) were male and 166 people (48.1%) were female. The mean age of the participants was 37.86 ± 9.88 years (SD), ranging from 22 to 80 years. Fifteen patients (4.3%) had high blood pressure, 6 people (1.7%) had diabetes, 5 people (1.4%) had chronic heart disease, 2 people (0.6%) had chronic respiratory disease, 2 people (0.6%) were treated with corticosteroid, 1 person (0.3%) had chronic renal disease, and none had chronic liver disease or cancer.

Table 1. Side effects according to participant's report and differences between the first and second dose

Variables	No.(%)			P
	First Dose	Second Dose	Total	
Pain at injection site	122(35.4)	76(23.4)	198(29.5)	<0.001
Muscle pain	155(44.9)	89(27.4)	244(36.6)	0.18
Fever	123(35.7)	70(21.5)	193(28.8)	<0.001
Fatigue	100(29)	68(20.9)	168(25.0)	0.003
Chills	83(24.1)	43(13.2)	126(18.8)	<0.001
Headache	62(18)	38(10.7)	100(14.9)	0.003
Nausea	17(4.9)	10(3.4)	28(4.1)	0.16
Dizziness	17(4.9)	10(3.1)	27(4.0)	0.22
Diarrhea	10(2.9)	2(0.6)	12(1.7)	0.05
Cough	7(2)	6(1.7)	13(1.9)	0.76
Abdominal pain	6(1.7)	6(1.8)	12(1.7)	1
Admission to hospital	4(1.2)	0(0)	4(0.05)	0.04
Vomiting	3(0.9)	1(0.3)	4(0.05)	0.32
Cutaneous reactions	0	0	0	-
Total	345	325	670	

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The most common side effect was pain at the injection site (29.5%), muscle pain (36.6%), fever (28.8%), fatigue (25%), chills (18.8%), and headache (14.9%) (Table 1). Other side effects occurred in less than 10% of

the participants, and our patients did not experience serious side effects, such as death or long admission. Four patients were hospitalized, all due to high fever and after the first dose injection. The hospitalized patients were

Table 2. Relation of age, gender, and previous SARSCOV-2 infection with the major side effects

Variables	No.				No. (%)					
	Age (y)			P	Gender		P	Previous Infection		
	20-30	31-40	≥41		Male	Female		Yes (81)	No (264)	P
Pain at injection site	40	28.90	21.94	0.015	18.91	38.76	<0.001	19(23.5)	103(39)	<0.001
Muscle pain	42.94	35.78	33.67	0.051	29.81	43.20	0.62	39(48.1)	106(43.9)	0.328
Fever	40	27.52	19.39	0.002	29.17	28.99	0.45	36(44.4)	87(33)	0.005
Fatigue	28.82	26.61	18.37	0.240	19.55	30.77	<0.001	30(37)	70(26.5)	0.002
Chills	30.59	18.35	8.67	<0.001	18.59	19.53	0.84	25(30.9)	58(22)	0.003
Headache	22.35	11.93	13.27	0.082	10.26	19.82	<0.001	19(23.5)	43(16.3)	0.006

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Table 3. Comparison of the Incidence of the Most Common Side Effects Among Studies

Variables	No. (%)							
	Number of Participants	Pain at Injection Site	Muscle Pain	Fever	Fatigue	Chills	Headache	Next Most Common Side Effect
Our study	325	29.5	36.6	28.8	25	18.8	14.9	Nausea 4.1
Logunov et al. [4]	76	58	24	50	28		42	Joint pain 24
Pagotto et al. [5]	683	57	58	40	NA	NA	33	Vomiting 2
Jarynowski et al. [6]	11,515	NA	46.57	46.57	33.54	23.02	24.79	Insomnia 5.21
Zare et al. [7]	238	~56(no exact value available)	41.6	37.4	~35(no exact value available)	NA	~30(no exact value available)	Joint pain ~20(no exact value available)
Montalti et al. [8]	First/ second dose 2558/1288	24.8/43.8	16/21.4	11.9/15.5	11.8/17.8	16.5/18.1	18.5/21	Joint pain 16.5/21.9
Zhu et al. [9]	108	54	17	46	44	NA	39	Impaired appetite 16
Babamahmoodi et al. [10]	3236	56.9	45.2	32.4	50.9	29.8	35.7	Joint pain 30.3
Houshmand et al. [11]	1205/453*	67.4	61.3	41.5	69	33.3	56	Arthralgia 36.4

NA: Not addressed.

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* In this study 1205 participants were vaccinated with three different vaccine brands of which, 453 persons received Sputnik V vaccine.

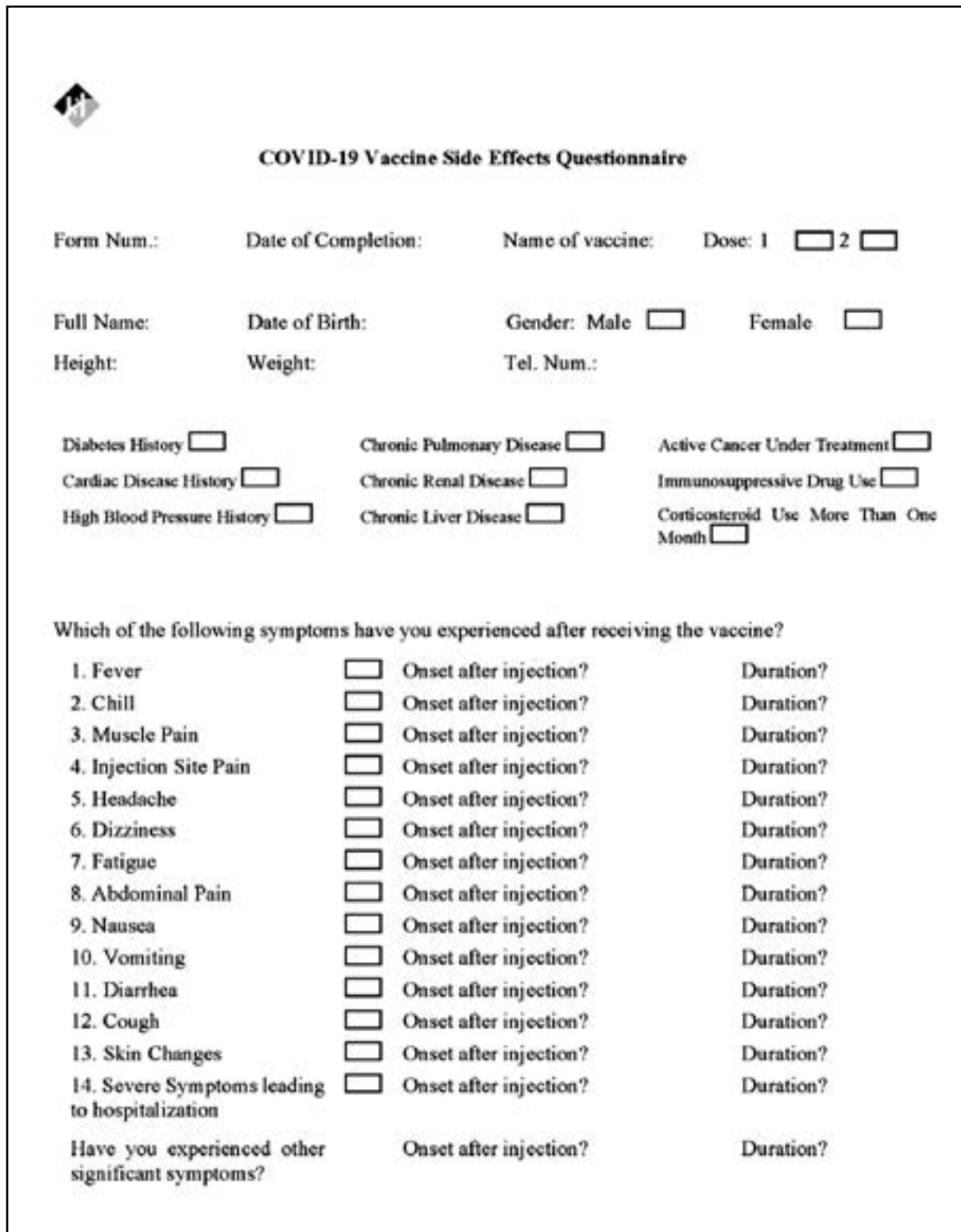
averagely admitted 24 hours after the first dose injection and were discharged 18 hours after admission. Rare side effects were dyspnea (3 patients, 0.08%), sore throat (2 patients, 0.6%), increased heart rate (2 patients, 0.6%), flushing, blurred vision, and chest pain (each in only one patient). All side effects were decreased in the second dose. The decrease was statistically significant for pain at the injection site, fever, chills, headache, fatigue, and hospitalization due to severe symptoms (Table 1).

Figure 2 shows the onset and duration of the three most common side effects after the first and second dose. As can be seen, the duration of side effects decreased in the second dose. Concerning the onset of symptoms, the beginning of fever and pain at the injection site was later for the second dose, but the muscle pain started sooner at the second dose. The incidence of the major side effects decreased with age, which was statistically significant for some (Table 2). The six main side effects, except fever, were more common in women, which were statistically significant for some of them (Table 2).

Individuals with a positive history of SARSCOV-2 infection (all confirmed with a previous positive polymerase reactive chain test for SARSCOV-2 experienced a higher rate of main side effects, which were statistically significant for all six main side effects except muscle pain (Table 2). The average Body Mass Index (BMI) of our study population was 25.63 ± 3.94 . A significant relationship was observed between injection site pain and BMI ($P=0.012$). The linear regression model was significant ($P=0.009$), R^2 was 0.15, and $B=0.014$. The model shows that an increase in BMI may result in a decrease in injection site pain.

4. Discussion

The six most common side effects of the vaccine in our study population were muscle pain, pain at the injection site, fever, fatigue, chills, and headache. As shown in Table 3, these side effects were similar to the most common ones in the other studies with different strengths [4-11]. In all studies except the case, pain at the injection site and muscle pain were the most common, and muscle



COVID-19 Vaccine Side Effects Questionnaire

Form Num.: Date of Completion: Name of vaccine: Dose: 1 2

Full Name: Date of Birth: Gender: Male Female

Height: Weight: Tel. Num.:

Diabetes History Chronic Pulmonary Disease Active Cancer Under Treatment

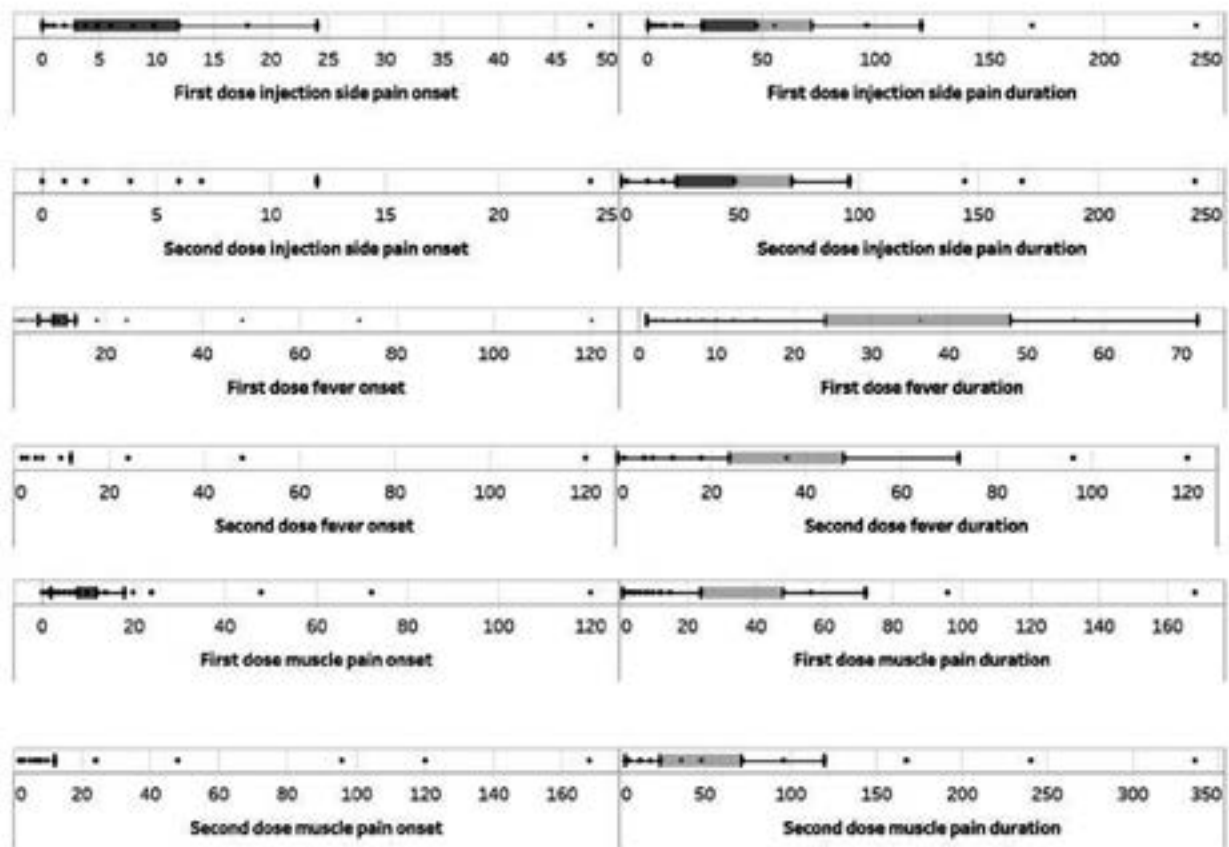
Cardiac Disease History Chronic Renal Disease Immunosuppressive Drug Use

High Blood Pressure History Chronic Liver Disease Corticosteroid Use More Than One Month

Which of the following symptoms have you experienced after receiving the vaccine?

1. Fever	<input type="checkbox"/>	Onset after injection?	Duration?
2. Chill	<input type="checkbox"/>	Onset after injection?	Duration?
3. Muscle Pain	<input type="checkbox"/>	Onset after injection?	Duration?
4. Injection Site Pain	<input type="checkbox"/>	Onset after injection?	Duration?
5. Headache	<input type="checkbox"/>	Onset after injection?	Duration?
6. Dizziness	<input type="checkbox"/>	Onset after injection?	Duration?
7. Fatigue	<input type="checkbox"/>	Onset after injection?	Duration?
8. Abdominal Pain	<input type="checkbox"/>	Onset after injection?	Duration?
9. Nausea	<input type="checkbox"/>	Onset after injection?	Duration?
10. Vomiting	<input type="checkbox"/>	Onset after injection?	Duration?
11. Diarrhea	<input type="checkbox"/>	Onset after injection?	Duration?
12. Cough	<input type="checkbox"/>	Onset after injection?	Duration?
13. Skin Changes	<input type="checkbox"/>	Onset after injection?	Duration?
14. Severe Symptoms leading to hospitalization	<input type="checkbox"/>	Onset after injection?	Duration?
Have you experienced other significant symptoms?		Onset after injection?	Duration?

Figure 1. Vaccine Questionnaire Translated Sample



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Figure 2. The onset and duration of three major side effects in hours. box plot with 95% intervals

pain and fever were the highest among systemic reactions.

In our study, all side effects decreased at the second dose and were statistically significant for injection site pain, fever, chills, headache, and fatigue (Table 1). Houshmand et al. [11] did not work on this difference. Pagotto [5], Zare [7], Zhu [9], and their colleagues reported only the side effects after the first dose. Jarynowski et al. [6] and Babamahmoodi et al. [10], like our study, found more side effects after the first dose. However, Montalti and colleagues [8] and Logunov et al. [4] reported more local and systemic reactions after the second dose.

As can be seen in Table 2, the incidence of the major side effects seems to decrease with age. This decrease was statistically significant for injection site pain, fever, and chills. In Logunov [4], Zhu [9], and Houshmand [11] et al.'s study, the age difference was not specified. In agreement with ours, other studies found fewer events for younger individuals [5-8, 10]. The difference in age-related side effects was statistically significant for those younger than 55 years in Pagotto et al. [5] and younger than 38 years in Babamahmoodi et al. [10] studies.

As shown in Table 2, the incidence of the major side effects, except fever, seems to be higher in females. This difference was statistically significant for injection site pain, fatigue, and headache. Pagotto [5], Jarynowski [6], and Babamahmoodi et al. [10], in concordance with our study, reported more side effects in women. Other available papers have not worked on the gender difference [4, 7-9, 11].

Cutaneous adverse reaction outside the injection site is not common for Covid-19 vaccines and has been reported mostly for Pfizer-BioNTech and Moderna's mRNA-1273 vaccines [12]. No cutaneous adverse reaction was seen in our studied population (Table 1). It was a rare event in the other articles concerning the Sputnik V vaccine. Babamahmoodi et al. [10] reported 2.3% rash in their study. Houshmand and colleagues [11] reported mild allergic reactions in 0.93% of their cases without further description. Logunov and colleagues [4] reported mild hives in 1.3% of their cases.

We had four hospitalizations (0.05%), all due to high fever, and no other serious side effects were observed in our study population. Pagotto et al. [5] reported that 5.1%

of the cases needed medical assessment, one was hospitalized (0.1%) due to an acute abdomen that resolved favorably without surgery, and the other ones' problems were unexplained. Babamahmoodi and colleagues [10] reported anaphylactic shock in 0.1% of their cases immediately after the first dose of the vaccine. The other reviewed articles reported no serious event, hospitalization, or death. Based on our findings and the literature results, the incidence of serious side effects of this vaccine was very low.

In our study, participants with a history of PCR-positive SARSCOV-2 infection had a higher rate of major side effects, which were statistically significant for all six main side effects except muscle pain (Table 2). Babamahmoodi and colleagues [10] stated that their participants with previous SARSCOV-2 infection experienced a significantly higher rate of pain at the injection site and some systemic side effects, such as body pain, fatigue, and weakness. However, some systemic side effects, such as fever, headache, and joint pain were significantly less common in the participants with previous SARSCOV-2 infection. Houshmand and colleagues [11] reported that individuals with a history of COVID-19 infection were more likely to report chills, shivers, and fainting than those without a history of SARSCOV-2 infection. Zare et al. [7] reported that side effects were significantly higher in the cases with a history of SARSCOV-2 infection ($P=0.048$). The other reviewed articles did not compare these two groups [4-6, 8-10].

BMI only had a significant relationship with injection site pain in our study. The experienced pain decreased in higher BMIs. Zare and colleagues [7] stated that the mean BMI among their participants was 23.45 ± 4.1 . In their study, the incidence of side effects was higher in people with a BMI above 25 for those vaccinated with AZD-1222 or the Covaxin vaccine but not for those who received the Sputnik V vaccine. The other reviewed articles did not assess the influence of BMI on the vaccine's side effects [4-6, 8-11].

Our questioning had the shortcoming that it was restricted to one vaccination center and the memory-based nature of the questionnaire. However, the study was improved by a literature review. To better understand side effects, we propose national surveys with a larger number of participants.

5. Conclusion

This study demonstrated that injection site pain, muscle pain, fever, fatigue, chills, and headache were the most

common side effects of the Sputnik V vaccine. The incidence of major side effects decreased with age and was lower in men. In our study and some others, the incidence of side effects was decreased in the second dose.

Most studies agreed with our findings. The reported severe side effects of this vaccine were few and may be considered a tolerable vaccine in adults.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Human Research Ethics Committee of the Shahid Beheshti University of Medical Sciences (Code: IR.SBMU.RETECH.REC.1400.197). It was performed according to Helsinki Declaration, and all participants were given informed consent.

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Authors' contributions

Conceptualization and Supervision: Ali Eftekharian and Kouros Eftekharian. Methodology: Kouros Eftekharian and Ilad Alavi Darazam. Investigation: Farzin Davoodi, Zahra Babamohamadi, Esfand Abadi, Mohsen Fazli. Data analysis: Kouros Eftekharian, Latif Gachkar and Sajjad Panahi; Participated in writing-original draft, review & editing: All authors

Conflict of interest

The authors declared no conflict of interest.

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