

# Potential Adverse Effects of COVID-19 Vaccines on Iranian Healthcare Workers: Comparison of Four Available Vaccines in Tehran: A Retrospective Cross-sectional Study

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## ABSTRACT

**Objectives:** This study aimed to compare four COVID-19 vaccines for their potential extensive side effects and the relationship between the side effects and age, body mass index (BMI), and history of COVID-19 infection. **Methods:** This cross-sectional study was conducted from June to August 2021 among 1474 healthcare workers of seven selected hospitals in Tehran, Iran. All the subjects were vaccinated (91.7% received two doses and 8.3% received one dose) with one of four vaccines, Sputnik, Covaxin, AstraZeneca, and Sinopharm, at least 10 days before the study. The incidence of 47 side effects was measured after vaccination. **Results:** Over half of the participants (59.4%; n = 876) were 20–29 years of age, with the mean and average BMI being 26.1±9.0 and 23.5±3.4, respectively; 36.0% (n = 530) were previously diagnosed with COVID-19. There was no significant relationship between age and the incidence of side effects for AstraZeneca, Sputnik, and Covaxin; however, the occurrence of side effects of Sinopharm was significantly higher ( $p < 0.001$ ) among younger healthcare workers. There was no significant relationship between BMI and the incidence of side effects for all four vaccines. However, in the group with a history of COVID-19 disease, health care workers vaccinated with the Sinopharm vaccine showed significantly ( $p < 0.001$ ) more complications. The occurrence rate of at least one adverse effect and referral to medical centers for AstraZeneca, Sputnik, Covaxin, and Sinopharm vaccines were 24.9–93.9%, 18.2–86.0%, 14.8–77.0%, and 3.5–37.2%, respectively. The highest and lowest rates were found for AstraZeneca and Sinopharm showing a significant ( $p < 0.001$ ) difference. The most commonly observed side effects for the AstraZeneca vaccine included fever (64.4%), fatigue (62.5%), and muscle pain (59.9%); for Sputnik muscle pain (59.8%), fever (49.5%), and fatigue (49.5%); for Covaxin fever (49.2%), topical reaction (41.0), and fatigue (34.4%); and for Sinopharm fever (18.7%), topical reaction (17.9%), and fatigue (16.6%). Inactivated virus vaccines (Sinopharm and Covaxin) showed a lower (39.7%) occurrence rate of side effects compared to viral vector vaccines (AstraZeneca and Sputnik; 90.6%). The most likely time for the vaccines to exert side effects was the first 24 hours after vaccination. **Conclusions:** We found no significant relationship between age, BMI, history of COVID-19 disease, and the incidence of side effects in healthcare workers vaccinated with any of the four vaccines. All four vaccines are safe and have controlled side effects.

Since the onset of the COVID-19 pandemic in China in late 2019, millions of healthcare workers have died, and hundreds of millions of health personnel have been affected.<sup>1</sup> SARS-CoV-2 mainly causes a severe respiratory disease;<sup>2</sup> however, it has been reported to affect other systems such as the heart,<sup>3</sup> kidneys,<sup>4</sup> and gastrointestinal system.<sup>5</sup> Vaccination is the best way to control and end this pandemic.<sup>6</sup> Fortunately, several vaccines have been developed to prevent the further spread of this disease.<sup>7</sup> The available vaccines are classified into four basic categories related to their production technologies: 1) inactivated virus, 2) viral vector, 3) protein-based, and 4) nucleic acid-based.<sup>8</sup> The first dose of the Sputnik viral vaccine contains adenovirus 26. The second dose contains adenovirus 5 as a vector. These vectors carry the gene encoding spike protein, a coronavirus gene, to stimulate the host's immune system against the virus.<sup>9</sup> All four vaccines are new. Despite their safety test results and government approval, people around the globe, especially healthcare workers are hesitant toward COVID-19 vaccination.<sup>10,11</sup> Therefore, further assessment on greater scales of time and population is needed for public reassurance. Also, side effect monitoring helps the healthcare system and manufacturers ensure the quality of vaccines and follow subjects in the post-vaccination period. Scientists in different countries were sensitive and did their evaluations.<sup>12,13</sup> Because the outbreak of vaccine side effects plays a critical role in public perception, especially the Iranian population, about vaccination programs in Iran, different studies have given different assessments on post-vaccination side effects.<sup>14,15</sup> Covaxin and Sinopharm contain inactivated viruses to stimulate the immune system but do not cause disease.<sup>16</sup> Studies have shown that vaccination effectively reduces the risk of severe disease, hospitalization, and mortality from COVID-19.<sup>9</sup> However, post-vaccination side effects include fever, fatigue, muscle pain, skin rash and swelling,<sup>7</sup> headache,<sup>17</sup> restlessness, injection site pain and joint pain,<sup>18</sup> purpura and erythematous,<sup>19</sup> and nausea and chills<sup>20</sup> have been reported.

The objective of this study was to investigate the potential side effects of Sinopharm, AstraZeneca, Sputnik, and Covaxin vaccination and the relationship between the side effects and age, BMI, a previous history of COVID-19 infection, and allergies.

## METHODS

A descriptive-analytical cross-sectional study was conducted among 1474 healthcare workers working at seven selected hospitals in Tehran from June to August 2021. A healthcare worker was considered anyone who works in the studied hospitals, including healthcare students on clinical placement, and frontline healthcare workers (e.g., doctors, nurses, paramedics, medical technicians, laboratory technicians, etc.). Those employed as healthcare workers in one of the seven studied hospitals and had a history of at least one dose of the COVID-19 vaccine were included in the study. The exclusion criteria were no history of COVID-19 vaccination or employment in non-healthcare jobs. Data were collected by a researcher-made questionnaire using the complete enumeration method. The questionnaire consisted of 54 two-choice questions, five multiple-choice questions, and three open-ended questions. This study was approved by Aja university medical science (IR.AJAUMS.REC.1400.163). The study was performed by the principles of the Declaration of Helsinki.

Demographic data included gender, age, height, weight, marital status, underlying diseases such as hypertension, hyper- or hypothyroidism, kidney, heart, lung, and skin disease, diabetes, a history of allergic reaction to the influenza vaccine, a history of COVID-19 disease, the time from previous COVID-19 disease, the type of vaccine, and the number of doses received by the subjects. The side effects asked in the questionnaire included topical reactions (pain, swelling, and itching at the site of injection), fever, itchy skin, shortness of breath, numbness in the face, body, arms, and legs, swelling in the face, mouth or whole body, anaphylactic shock, fatigue, cold-like symptoms, muscle pain, chills, swelling in legs, nausea, vomiting, abdominal pain, diarrhea, sore throat, severe decrease in platelet count and coagulation problems, joint pain, excessive sweating, dizziness, nasal congestion, pain when swallowing, poor sleep quality, purpura, palpitation, hot flashes, severe drowsiness, extreme hunger and thirst, feeling energized, restlessness (malaise), hives, hair loss, eye soreness, runny nose, chest tightness, lip swelling, cough, balance problems, hematuria (blood in the urine), anorexia, delirium, olfactory, visual, hearing, and sexual dysfunctions. Also, the average time of the incidence of side effects, the need to go to an emergency department or medical center due

**Table 1:** Demographic characteristics of participants (N = 1474).

Variables	Vaccines			
	Sputnik n (%)	Covaxin n (%)	AstraZeneca n (%)	Sinopharm n (%)
<b>Sex</b>				
Male	132(61.7)	27 (44.3)	192 (62.1)	688 (77.3)
Female	82 (38.3)	34 (55.7)	117 (37.9)	202 (22.7)
<b>Marital status</b>				
Single	80 (37.4)	20 (32.8)	128 (41.4)	802 (90.1)
Married	134 (62.6)	41 (67.2)	181 (58.6)	88 (9.9)
<b>Position</b>				
Doctor	34 (15.9)	11 (18.0)	53 (17.2)	102 (11.5)
Nurse	71 (33.2)	22 (36.1)	118 (38.2)	305 (34.3)
Technician	109 (51.0)	28 (45.9)	138 (44.7)	483 (54.3)
<b>Number of received dose</b>				
One	22 (10.3)	1 (1.6)	85 (27.5)	15 (1.7)
Two	192 (89.7)	60 (98.4)	224 (72.5)	875 (98.3)
<b>History of underlying disease</b>				
No disease	191 (89.3)	53 (86.9)	271 (87.8)	837 (94.0)
Hypertension	1 (0.5)	3 (4.9)	6(1.9)	11 (1.2)
Hypo- or hyperthyroidism	3 (1.4)	1 (1.6)	9 (2.9)	14 (1.6)
Allergy	4 (1.9)	1 (1.6)	6 (1.9)	5 (0.6)
Neurological disease	2 (0.9)	0 (0.0)	0 (0.0)	1 (0.1)
Kidney disease	2 (0.9)	0 (0.0)	0 (0.0)	2 (0.2)
Lung disease	0 (0.0)	0 (0.0)	3 (1.0)	0 (0.0)
Diabetes	4 (1.9)	0 (0.0)	6 (1.9)	3 (0.3)
Skin disease	1 (0.5)	1 (1.6)	1 (0.3)	5 (0.6)
Heart disease	1 (0.5)	0 (0.0)	2 (0.6)	1 (0.1)
Liver disease	0 (0.0)	0 (0.0)	1 (0.3)	2 (0.2)
Addiction	2 (0.9)	1 (1.6)	1 (0.3)	3 (0.3)
Others	3 (1.4)	1 (1.6)	3 (1.0)	6 (0.7)
<b>History of allergy to influenza vaccine</b>	12 (5.6)	3 (9.4)	6 (1.9)	7 (0.8)
<b>Previous COVID-19 Infection</b>	95 (44.4)	18 (29.5)	106 (34.3)	311 (34.9)
<b>Date of previous COVID-19 infection</b>				
No previous COVID-19 infection	119 (55.6)	43 (70.5)	204 (66.0)	561 (63.0)
1 month before vaccination	9 (4.2)	0 (0.0)	5 (1.6)	12 (1.3)
2–3 months before vaccination	14 (6.5)	1 (1.6)	13 (4.2)	71 (8.0)
4–6 months before vaccination	29 (13.6)	7 (11.5)	33 (10.7)	90 (10.1)
> 6 months before vaccination	43 (20.1)	10 (16.4)	54 (17.5)	156 (17.5)
<b>Age, years</b>				
< 20	16 (7.5)	0 (0.0)	2 (0.6)	137 (15.4)
20–29	64 (29.9)	23 (37.7)	121 (39.2)	668 (75.1)
30–39	76 (35.5)	19 (31.1)	80 (25.9)	39 (4.4)
40–49	44 (20.6)	6 (9.8)	85 (27.5)	28 (3.1)
50–59	12 (5.6)	13 (21.3)	13 (4.2)	10 (1.1)
> 50	2 (0.9)	0 (0.0)	8 (2.6)	8 (0.9)
<b>Body Mass Index</b>				
Underweight (< 18.5)	8 (3.7)	2 (3.3)	8 (2.6)	27 (3.0)
Normal (18.5–25)	110 (51.4)	41 (67.2)	169 (54.7)	663 (74.5)
Overweight (25–29.9)	79 (36.9)	16 (25.8)	92 (29.8)	163 (18.3)
Obese (> 30)	17 (7.9)	2 (3.3)	40 (12.9)	27 (3.0)

**Table 2:** Frequency of at least one side effect and referral to medical centers among subjects receiving AstraZeneca, Sputnik, Covaxin, and Sinopharm vaccines.

Variables	Type of vaccine				Total n (%)	p-value
	AstraZeneca	Sputnik	Covaxin	Sinopharm		
	n (%)	n (%)	n (%)	n (%)		
<b>Occurrence of at least one side effect</b>						
Yes	290 (93.9)	184 (86.0)	47 (77.0)	331 (37.2)	852 (57.8)	< 0.001
No	19 (6.1)	30 (14.0)	14 (23.0)	559 (62.8)	622 (42.2)	
<b>Referral to the medical center</b>						
Yes	77 (24.9)	39 (18.2)	9 (14.8)	31 (3.5)	156 (10.6)	< 0.001
no	232 (75.1)	175 (81.8)	52 (85.2)	859 (96.5)	1318 (89.4)	
<b>Total</b>	309 (100)	214 (100)	61 (100)	890 (100)	1474 (100)	

to the vaccine's side effects, as well as the duration of maximum inefficiency or difficulty in performing daily tasks after vaccination, and getting back to feel healthy enough after vaccination to be able to perform his/her healthcare activities in the hospital properly without any problems were assessed.

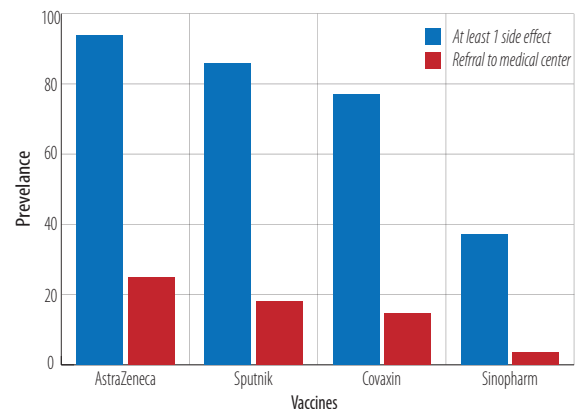
The questionnaire questions were prepared based on valid documents from the World Health Organization and Centers for Disease Control and Prevention.<sup>21,22</sup> Then, the instrument was carefully examined by 10 faculty members, clinical infections, and allergy immunity specialists, and the necessary changes were made. For the validity of the questionnaire, the questions were evaluated using the content validity index (CVI), the questions with CVI < 0.7 were omitted, and with CVI between 0.7–0.79 were reviewed. To confirm the reliability, the internal consistency was examined using Cronbach's alpha ( $\alpha$ ) coefficient, and good reliability ( $\alpha = 0.89$ ) was found.

The researcher obtained the ethical approval (approval ID: IR.AJAUMS.REC.1400.163), entered the medical centers, and distributed the questionnaire among healthcare workers who met the inclusion criteria. Before distributing the questionnaires, the study's objectives were explained, the confidentiality of the subjects was ensured, and the issues were signed on a consent form. The collected data were analyzed using SPSS (SPSS Inc. Released 2007. SPSS for Windows, Version 16.0. Chicago, SPSS Inc.). To analyze the data, central tendency and dispersion indicators including mean, SD, tables and diagrams, and the chi-squared, Fisher's exact, one-sample Kolmogorov-Smirnov, Mann-Whitney U, and *t*-tests were used. The level of significance was considered < 0.05.

## RESULTS

The mean age of the participants was  $26.2 \pm 9.0$  years. There were 1039 men (70.5%) and 435 women (29.5%), of whom 123 received one dose, and 1351 (91.7%) received two doses of the COVID-19 vaccine. The majority (91.7%) had no underlying disease; 36.0% ( $n = 530$ ) had COVID-19 infection. Eight hundred seventy-six healthcare workers (59.4%) were aged 20–29 years old. The mean BMI of the subjects was  $33.6 \pm 3.4$ , with 983 (66.7%) health personnel showing normal BMI and 86 (5.8%) were obese, 350 (23.7%) participants were overweight, and 45 (3.1%) participants were under weight. Of 1474 health personnel, 890 (60.4%) received the Sinopharm, 309 (21.0%) received the AstraZeneca, 214 (14.5%) received the Sputnik, and 61 (4.1%) received Covaxin vaccines [Table 1].

The results showed no side effects in 622 subjects (42.2%) after vaccination for all four vaccines [Table 2]. It was found that 93.9% of the subjects received



**Figure 1:** Frequency of at least one side effect and referral to medical centers among subjects receiving AstraZeneca, Sputnik, Covaxin, and Sinopharm.

**Table 3:** Frequency of side effects of four studied vaccines. Data are given as n (%).

Side effects of the vaccines	AstraZeneca®	Sputnik®	Covaxin®	Sinopharm®
Fever	199 (64.4)	106 (49.5)	30 (49.2)	166 (18.7)
Fatigue	193 (62.5)	100 (46.7)	21 (34.4)	148 (16.6)
Muscle pain	185 (59.9)	128 (59.8)	19 (31.1)	91 (10.2)
Topical reaction	113 (36.6)	57 (26.6)	25 (41.0)	159 (17.9)
Chills	161 (52.1)	89 (41.6)	14 (23.0)	37 (4.2)
Dizziness or headache	80 (25.9)	47 (22.0)	11 (18.0)	85 (9.6)
Cold-like symptoms	113 (36.6)	49 (22.9)	10 (16.4)	39 (4.4)
Poor sleep quality	39 (12.6)	22 (10.3)	3 (4.9)	24 (2.7)
Excessive sweating	42 (13.6)	22 (10.3)	5 (8.2)	12 (1.3)
Joint pain	38 (12.3)	24 (11.2)	3 (4.9)	10 (1.1)
Shortness of breath	25 (8.1)	7 (3.3)	2 (3.3)	14 (1.6)
Nasal congestion	20 (6.5)	10 (4.7)	0 (0.0)	18 (2.0)
Palpitation	15 (4.9)	13 (6.1)	2 (3.3)	10 (1.3)
Itchy skin	14 (4.5)	6 (2.8)	3 (4.9)	19 (2.1)
Nausea	19 (6.1)	4 (1.9)	6 (9.8)	8 (0.9)
Numbness (face and extremities)	9 (2.9)	6 (2.8)	3 (4.9)	15 (1.7)
Sore throat	12 (3.9)	12 (5.6)	1 (1.6)	8 (0.9)
Diarrhea	14 (4.5)	4 (1.9)	2 (3.3)	9 (1.0)
Abdominal pain	11 (3.6)	4 (1.9)	1 (1.6)	7 (0.8)
Olfactory and taste dysfunction	6 (1.9)	4 (1.9)	2 (3.3)	8 (0.9)
Pain when swallowing	9 (2.9)	8 (3.7)	0 (0.0)	2 (0.2)
Purpura	10 (3.2)	0 (0.0)	1 (1.6)	3 (0.3)
Anaphylactic shock	6 (1.9)	1 (0.5)	0 (0.0)	6 (0.7)
Vomiting	6 (1.9)	1 (0.5)	3 (4.9)	2 (0.2)
Coagulation problems and a decrease in platelet count	7 (2.3)	4 (1.9)	0 (0.0)	0 (0.0)
Hot flashes	2 (0.6)	4 (1.9)	0 (0.0)	5 (0.6)
Visual dysfunction	2 (0.6)	5 (2.3)	0 (0.0)	3 (0.3)
Severe drowsiness	1 (0.3)	1 (0.5)	0 (0.0)	7 (0.8)
Feeling energized	6 (1.9)	1 (0.5)	0 (0.0)	0 (0.0)
Restlessness (malaise)	1 (0.3)	0 (0.0)	1 (1.6)	4 (0.4)
Swelling (face)	2 (0.6)	2 (0.9)	0 (0.0)	1 (0.1)
Constant hunger and thirst	1 (0.3)	0 (0.0)	0 (0.0)	4 (0.4)
Hives	1 (0.3)	0 (0.0)	0 (0.0)	3 (0.3)
Hearing dysfunction	2 (0.6)	2 (0.9)	0 (0.0)	0 (0.0)
Hair loss	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.2)
Eye soreness	1 (0.3)	1 (0.5)	0 (0.0)	1 (0.1)
Runny nose	1 (0.3)	0 (0.0)	2 (3.3)	0 (0.0)
Chest tightness	0 (0.0)	1 (0.5)	1 (1.6)	1 (0.1)
Lip swelling	1 (0.3)	0 (0.0)	2 (3.3)	0 (0.0)
Cough	0 (0.0)	1 (0.5)	0 (0.0)	2 (0.2)
Swelling (legs)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)
Balance problems	2 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
Hematuria	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.1)
Anorexia	1 (0.3)	1 (0.5)	0 (0.0)	0 (0.0)
Sexual dysfunction	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.1)
Hallucination	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Other	8 (2.6)	4 (1.9)	2 (3.3)	8 (0.9)

AstraZeneca, 86.0% received Sputnik, 77.0% received Covaxin, and 37.2% received Sinopharm showed at least one complication after vaccination. The lowest and highest occurrence rates of side effects were observed for Sinopharm and AstraZeneca vaccines, respectively. There was a significant ( $p < 0.001$ ) difference in the occurrence of at least one side effect among the vaccines [Figure 1].

The need to refer to medical centers was also investigated. It was shown that 24.9% of healthcare workers receiving the AstraZeneca vaccine had a complication that required referral to a medical center or a hospital for services such as intravenous therapy. The rates of referral to a medical center for Sputnik, Covaxin, and Sinopharm were 18.2%, 14.8%, and 3.5%, respectively, showing a significant ( $p < 0.001$ ) difference [Table 2].

Fever was the most common complication after vaccination, with the complication rates for AstraZeneca, Sputnik, Covaxin, and Sinopharm being 64.4%, 49.5%, 49.2%, and 18.7%, respectively. The second most common complication was fatigue, with the complication rates for AstraZeneca, Sputnik, Covaxin, and Sinopharm being 62.5%, 46.7%, 34.4%, and 16.6%, respectively. The most common post-vaccination side effect was muscle pain followed by topical reaction, chills, dizziness, headache, and cold-like symptoms. The rate of other complications, including poor sleep quality, shortness of breath, palpitation, runny nose, etc., was less than 1.5% for all four vaccines. Sinopharm and AstraZeneca had the least and the most side effects among the four studied vaccines [Table 3 and Figure 2].

The seven most common post-vaccination side effects were reported in the following order:

1. AstraZeneca: fever, fatigue, muscle pain, chills, topical reaction, cold-like symptoms, and dizziness or headache.
2. Sputnik: muscle pain, fever, fatigue, chills, topical reaction, cold-like symptoms, and dizziness or headache.
3. Covaxin: fever, topical reaction, fatigue, muscle pain, chills, cold-like symptoms, and dizziness or headache.
4. Sinopharm: fever, topical reaction, fatigue, muscle pain, dizziness or headache, cold-like symptoms, and chills.

Side effects happened within the first 24 hours after vaccination among 72.5% receiving AstraZeneca, 72.9% of those receiving Sputnik,

57.4% receiving Covaxin, and 26.6% receiving Sinopharm [Table 4 and Figure 3].

The ability of the subjects to perform daily tasks after vaccination with the four studied vaccines was investigated: 58.3% of those receiving AstraZeneca, 40.7% receiving Sputnik, 29.5% receiving Covaxin, and 13.5% receiving Sinopharm reported that they could not perform their daily tasks within 24 hours after vaccination and needed to rest [Figure 4 and Table 5].

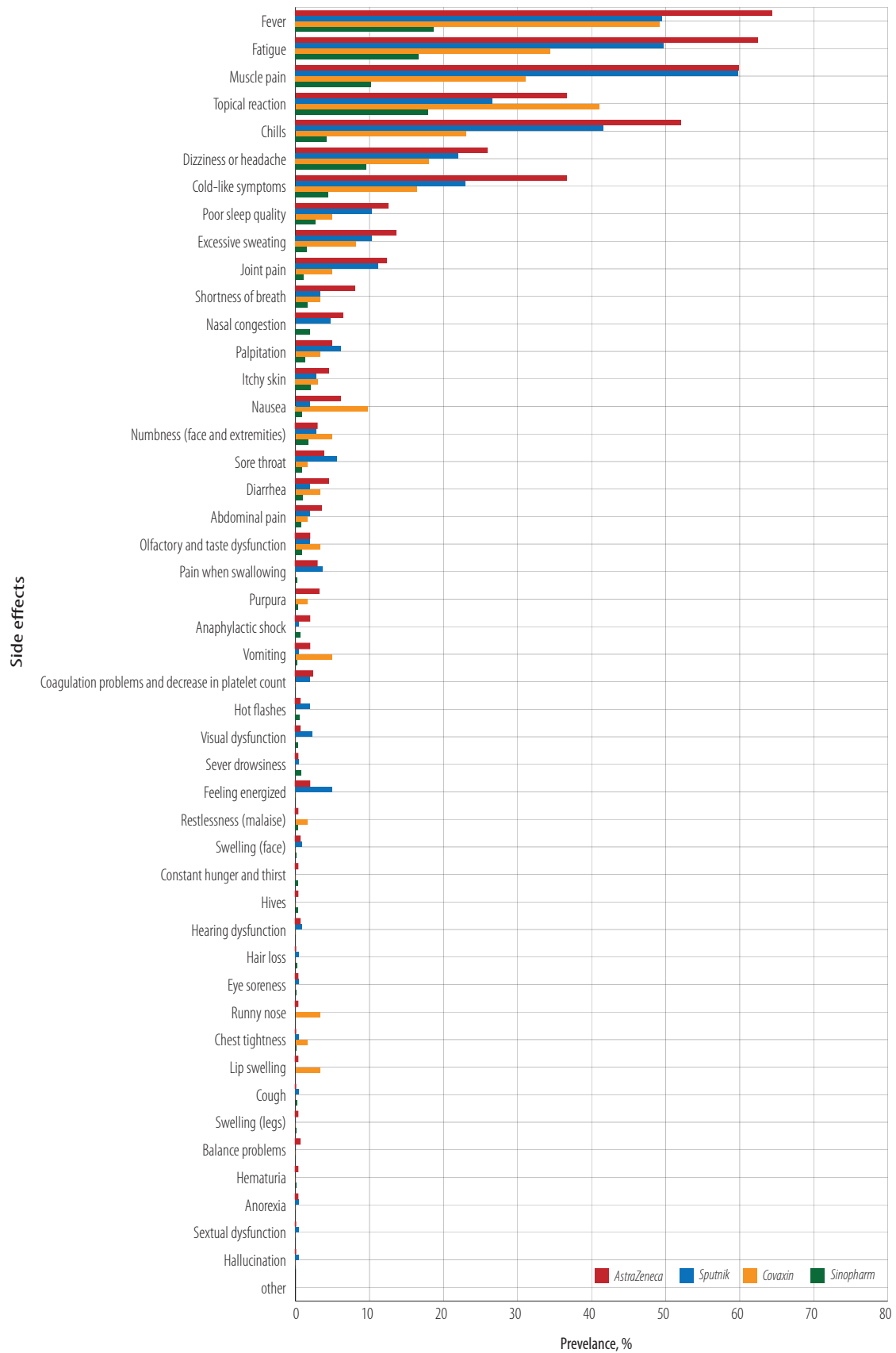
The relationship between the subjects' age and BMI and post-vaccination side effects was studied, and no significant relationship was observed for Sputnik, Covaxin, and AstraZeneca. The side effects of the Sinopharm vaccine were significantly higher among younger healthcare workers [Table 6]. There was no significant relationship between BMI and the occurrence of side effects for the four studied vaccines.

The frequency of side effects was higher among subjects with a previous history of COVID-19 disease for all the four studied vaccines; however, there was no significant relationship between the prior history of COVID-19 and the frequency of side effects for Sputnik, Covaxin, and AstraZeneca vaccines [Table 7]. However, side effects were significantly higher among those receiving Sinopharm with a history of COVID-19.

We found no significant relationship between a history of COVID-19 and the need to refer to medical centers. Also, the results showed no significant relationship between a previous history of allergy to the influenza vaccine and the occurrence of side effects among those receiving Sputnik, Covaxin, and AstraZeneca vaccines. Only among the subjects receiving Sinopharm had a significant relationship between a history of allergy and the occurrence of side effects ( $p = 0.012$ ) [Table 7].

The studied vaccines were divided into viral vector vaccines (Sputnik and AstraZeneca) and inactivated virus vaccines (Covaxin and Sinopharm); 90.6% of those receiving viral vector vaccines and 39.7% of those receiving inactivated virus vaccines reported the occurrence of side effects [Table 8].

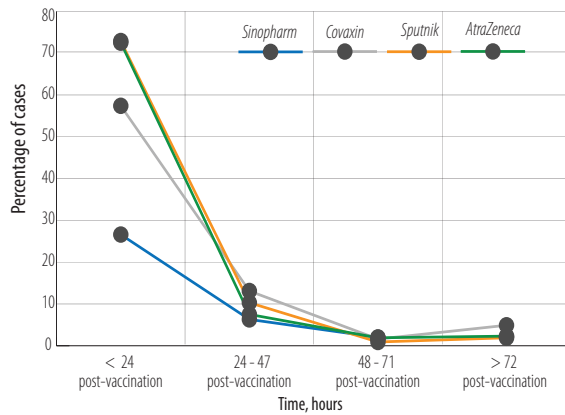
In addition, 22.2% of subjects vaccinated with viral vector vaccines and 4.2% of those immunized with inactivated virus vaccines needed a referral to medical centers. The occurrence of at least one side effect and referral to medical centers for the viral vector group was significantly ( $p < 0.001$ ) higher than those for inactivated virus vaccines [Figure 5].



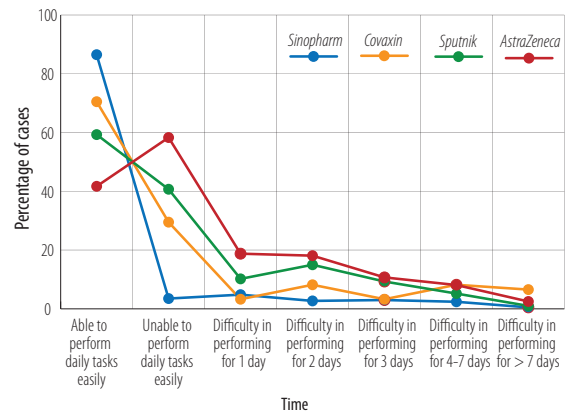
**Figure 2:** Frequency of 47 adverse effects following Sinopharm, Covaxin, Sputnik, and AstraZeneca vaccination.

**Table 4:** Time of occurrence of side effects.

Time of occurrence of side effects, hours	AstraZeneca	Sputnik	Covaxin	Sinopharm	Total
	n (%)	n (%)	n (%)	n (%)	n (%)
No side effects	19 (6.1)	30 (14.0)	14 (23.0)	559 (62.8)	622 (42.2)
< 24	223 (72.5)	156 (72.9)	35 (57.4)	237 (26.6)	651 (44.2)
24–47	54 (17.5)	22 (10.3)	8 (13.1)	56 (6.3)	140 (9.5)
48–71	6 (1.9)	2 (0.9)	1 (1.6)	18 (2.0)	27 (1.8)
> 72	7 (2.3)	4 (1.9)	3 (4.9)	20 (2.2)	34 (2.3)
Total	309 (100)	214 (100)	61 (100)	890 (100)	1474 (100)



**Figure 3:** Time of occurrence of side effects.



**Figure 4:** The rate of inefficiency after vaccination.

**Table 5:** The rate of inefficiency after vaccination.

Maximum inefficiency	AstraZeneca	Sputnik	Covaxin	Sinopharm
	n (%)	n (%)	n (%)	n (%)
Able to perform daily tasks easily	129 (41.7)	127 (59.3)	43 (70.5)	720 (80.9)
Unable to perform daily tasks easily	180 (58.3)	87 (40.7)	18 (29.5)	120 (13.5)
Difficulty in performing for one day	8 (2.6)	23 (10.7)	2 (3.3)	43 (4.8)
Difficulty in performing for two days	56 (18.1)	32 (15.0)	5 (8.2)	24 (2.7)
Difficulty in performing for three days	33 (10.7)	20 (9.3)	2 (3.27)	27 (3.0)
Difficulty in performing for 4–7 days	25 (8.1)	11 (5.1)	5 (8.2)	21 (2.4)
Difficulty in performing for > 7 days	8 (2.6)	2 (0.9)	4 (6.6)	5 (0.6)

**Table 6:** Age of subjects with or without post-vaccination side effects.

Type of vaccine	Side effects	Age, years		Body mass index		
		Mean ± SD	p-value	Side effects	Mean ± SD	p-value
AstraZeneca	Positive	36.5 ± 5.9	0.474	Positive	25.1 ± 4.4	0.955
	Negative	34.4 ± 9.9		Negative	25.0 ± 3.7	
Sputnik	Positive	34.7 ± 5.5	0.474	Positive	24.4 ± 2.5	0.629
	Negative	34.1 ± 9.6		Negative	24.9 ± 3.7	
Covaxin	Positive	29.7 ± 6.1	0.188	Positive	21.3 ± 2.2	0.166
	Negative	35.7 ± 9.8		Negative	24.3 ± 3.2	
Sinopharm	Positive	21.7 ± 4.4	< 0.001	Positive	22.9 ± 2.8	0.388
	Negative	24.8 ± 4.1		Negative	23.4 ± 3.8	

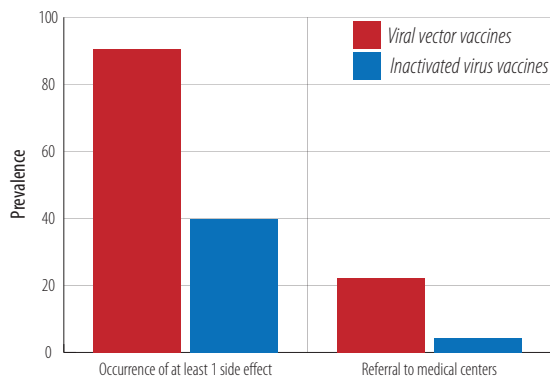


**Table 7:** Frequency of side effects among subjects with or without a history of COVID-19 and allergy to influenza vaccine. Data are given as n (%).

Variables	AstraZeneca			Sputnik			Covaxin			Sinopharm		
	At least on side effect	No side effects	Total	At least on side effect	No side effects	Total	At least on side effect	No side effects	Total	At least on side effect	No side effects	Total
<b>Previous COVID-19 disease</b>												
Yes	102 (96.2)	4 (3.8)	106 (100)	85 (89.5)	10 (10.5)	95 (100)	16 (88.9)	2 (11.1)	18 (100)	142 (45.7)	169 (54.3)	311 (100)
No	188 (92.6)	15 (7.4)	203 (100)	99 (83.2)	20 (16.8)	119 (100)	31 (72.1)	12 (27.9)	43 (100)	189 (32.6)	390 (67.4)	579 (100)
<i>p</i> -value	0.209			0.189			0.197			< 0.001		
<b>Allergy to influenza vaccine</b>												
Yes	6 (100)	0 (0.0)	6 (100)	9 (75.0)	3 (25.0)	12 (100)	3 (100)	0 (0.0)	3 (100)	6 (85.7)	1 (14.3)	7 (100)
No	283 (93.7)	19 (6.3)	302 (100)	175 (86.6)	27 (13.4)	202 (100)	44 (77.2)	13 (22.8)	57 (100)	325 (36.8)	558 (63.2)	883 (100)
<i>p</i> -value	1.000			0.382			1.000			0.012		

**Table 8:** Comparison of occurrence of side effects and referral to medical centers for inactivated virus vaccines (Sinopharm and Covaxin) and viral vector vaccines (Sputnik and AstraZeneca).

Variables	Viral vector vaccines (AstraZeneca + Sputnik)		Inactivated virus vaccines (Sinopharm + Covaxin)		Total		<i>p</i> -value
	n (%)	Total	n (%)	Total	n (%)	Total	
<b>Occurrence of at least one side effect</b>							
Yes	474 (90.6)	523 (100)	378 (39.7)	951 (100)	852 (57.8)	1474 (100)	< 0.001
No	49 (9.4)		573 (60.3)		622 (42.4)		
<b>Referral to medical centers</b>							
Yes	116 (22.2)	523 (100)	40 (4.2)	951 (100)	156 (10.6)	1474 (100)	< 0.001
No	407 (77.8)		911 (95.8)		1318 (89.4)		

**Figure 5:** Comparison of occurrence of side effects and referral to medical centers for inactivated virus vaccines (Sinopharm and Covaxin) and viral vector vaccines (Sputnik and AstraZeneca).

## DISCUSSION

We investigated the post-vaccination side effects of four vaccines among the medical care team members of seven selected hospitals in Tehran, Iran.

The results showed that 57.5% of the subjects experienced at least one side effect. The healthcare workers who received AstraZeneca and Sinopharm

vaccines showed the most and the most minor frequency side effects, respectively. Our results are consistent with the results obtained in Iraq and Jordan.<sup>17,23</sup>

In a study on the side effects of the Sinopharm vaccine in the UAE, only 24.5% and 37.5% of Turkish healthcare staff did not report any side effects.<sup>15,16</sup> However, our study showed that 62.8% of subjects reported no side effects. The need to refer to medical centers due to the side effects (generally temporary) they have faced after receiving the vaccine commonly fever and restlessness, or side effects that cause weakness and lethargy, and pressure reduction such as diarrhea, anorexia, and digestive side effects. We should also keep in mind that health personnel have better access to medical therapies (e.g., serious therapy) due to their profession. Frequent use of serum therapy might relate to the ease of access. This number for AstraZeneca, Sputnik, Covaxin, and Sinopharm vaccines was 24.9%, 18.2%, 14.8%, and 3.5%, respectively. However, these percentages were 3.2% and 0% for those who received the AstraZeneca vaccine in Germany and Ethiopia, respectively.<sup>24,25</sup>

Also, in a study conducted in the UAE, there was no post-vaccination complication among the subjects vaccinated with Sinopharm requiring hospitalization.<sup>26</sup> Half of the Turkish healthcare staff receiving the Sinopharm vaccine needed to be referred to the hospital.<sup>27</sup> The results showed that the most likely time for complications was the first 24 hours. On the second day for the AstraZeneca, Covaxin, and Sinopharm vaccines, this probability was about one-fourth of the chance on the first day and one-seventh for the Sinopharm vaccine, and then decreased significantly. A previous study showed that most complications such as fatigue, headache, and topical reaction occurred within the first 24 hours.<sup>27</sup> About 60% of healthcare workers receiving the AstraZeneca vaccine in Ethiopia reported that topical reaction occurred 12 hours after vaccination and continued for another 24–72 hours.<sup>24</sup>

There was no significant relationship between age and occurrence of side effects for AstraZeneca, Sputnik, and Covaxin. However, the occurrence rate of side effects of Sinopharm was significantly higher among younger healthcare workers. Previous studies on the AstraZeneca vaccine in Germany<sup>25</sup> and the Sinopharm vaccine in the UAE<sup>26</sup> revealed that topical side effects were higher among younger healthcare workers. In contrast, systemic complications were higher among older healthcare workers. A study conducted in Iraq showed that the occurrence rate of side effects was higher among healthcare workers under 50 years old.<sup>23</sup> A survey of the safety of the AstraZeneca vaccine in Brazil, Africa, and England showed a lower occurrence rate of side effects among older health personnel.<sup>28</sup> Some studies on the AstraZeneca vaccine and the current study showed no significant relationship between the age and occurrence of post-vaccination side effects.<sup>7,29</sup> There was no meaningful relationship between BMI and the occurrence of side effects in agreement with a study conducted in the UK.<sup>27</sup> The occurrence rate of complications for Sputnik, Covaxin, and AstraZeneca was higher among those with a previous history of COVID-19 disease; however, they showed no significant relationship. Our result is consistent with the findings of a study conducted in Poland.<sup>30</sup> However, the occurrence rate of side effects was significantly higher among those receiving the Sinopharm vaccine. A previous history of COVID-19 was consistent with a study conducted in Turkey.<sup>31</sup> In a survey of the vaccines

used in Iraq, the occurrence rate of complications was higher among healthcare workers with a history of COVID-19.<sup>23</sup>

The most common complication found among healthcare workers vaccinated with Sinopharm was fever, followed by fatigue, topical reaction, muscle pain, dizziness or headache, cold-like symptoms, and chills. In studies performed in Turkey and the UAE,<sup>26,31</sup> injection site pain was the most common topical side effect. The most common systemic complications were fatigue, headache, and muscle and joint pain.

Previous studies showed that the most common side effects of the Sputnik vaccine were injection site pain followed by fever, fatigue, headache, lethargy, and muscle and joint pain.<sup>32,33</sup> Our results revealed that the most common complication of Sputnik was muscle pain followed by fever, fatigue, chills, topical reaction, cold-like symptoms, and dizziness or headache. The most common side effects of the Covaxin vaccine were fever, topical reaction, fatigue, muscle pain, chills, cold-like symptoms, and dizziness or headache. Previous studies reported that the most common complications of Covaxin vaccines were tenderness, injection site pain, headache, muscle pain, nausea, and fatigue.<sup>29</sup> The adverse effects of AstraZeneca were fever, fatigue, muscle pain, chills, topical reaction, cold-like symptoms, and dizziness or headache. Previous studies found that the most common complication of the AstraZeneca vaccine was fatigue, followed by headache, body aches, muscle pain, topical reaction, fever, and joint pain.<sup>34</sup> In a study conducted in Iraq, the most common adverse effects of AstraZeneca were fever, fatigue, topical reaction, muscle pain, headache, and chills, and of Sinopharm were topical reaction, fatigue, fever, muscle pain, headache, and chills.<sup>23</sup>

Our results demonstrated that the occurrence rate of side effects of viral vector vaccines (AstraZeneca and Sputnik) was 90.6% and of inactivated virus vaccines (Sinopharm and Covaxin) was only 39.7%, which is in agreement with the results of studies conducted in Germany<sup>25</sup> and England,<sup>7</sup> which reported that the occurrence rate was higher for viral vector and messenger RNA vaccines. According to the European Medicines Agency report, the viral vector AstraZeneca vaccine leads to more side effects than inactivated virus Sinopharm vaccine.

The cause of such side effects trends in our study and the Iranian population is probably because the Iranian population is mainly vaccinated with four types of vaccines two of which are viral vectors. As previously mentioned, the most common side effects of viral-vector vaccines are inflammation-related and originate from factors such as tumor necrosis factor  $\alpha$ , interleukin-1, and interleukin-6. Studies have shown that this kind of vaccine can bind with receptors like coxsackie and adenovirus receptor and toll-like receptor, leading to the secretion of inflammation factors. As a result, the vaccinated subject may present inflammation signs like fever, fatigue, muscle pain, and skin reaction, similar to the observed subjects in our study.<sup>35</sup> The probable reason for fewer side effects of Sinopharm and Covaxin is because these vaccines are inactivated viruses, so they cause less inflammation and flu-like symptoms.<sup>8,16</sup>

Seven healthcare workers vaccinated with AstraZeneca (2.3%) and four vaccinated with Sputnik (1.9%) showed coagulation problems or decreased platelet count, previously found after viral vector vaccines.<sup>36,37</sup> Out of 20 million health personnel who received the AstraZeneca vaccine in the UK, 79 cases of a decrease in platelet count were observed.<sup>38</sup> However, a study conducted among 492 healthcare workers vaccinated with AstraZeneca observed no thrombocytopenia (low platelet count).<sup>39</sup>

Kadali et al,<sup>40</sup> performed a study among health personnel vaccinated with the Moderna vaccine. They found that 79.7% could do their daily activities on the first day after vaccination. The percentage found in our study was 41.7% for AstraZeneca, 59.3% for Sputnik, 70.5% for Covaxin, and 80.9% for Sinopharm vaccines.

The number of health personnel who received Covaxin and Sputnik vaccines was lower than those receiving other vaccines. The number of women was lower than that of men. It should be noted that since all of the subjects were healthcare workers, with the majority being hospital staff, they received different therapies, (e.g., intravenous drip therapy) simply because of the ease of access while not an urgent need.

As we know for the first time, a wide range of post-vaccination side effects ( $n = 47$ ) of Sinopharm, AstraZeneca, Sputnik, and Covaxin and the impact of various factors such as age, BMI, a previous history of COVID-19, and a previous history of allergy to influenza vaccine on the occurrence of

complications were investigated. The percentage of missing data was meager, and given that the side effects were evaluated among the healthcare workers, more accurate answers were obtained.

Literature has proved that vaccination side effects may originate from vaccines themselves. Yet, we have to consider healthcare workers were the first group of society vaccinated and as vaccination pioneers, may experience inefficiency in the vaccine supply chain and distribution system. Therefore, vaccination errors might have affected the outcome. Further evaluation of the vaccinated population and comparison with older results may help to distinguish occurred errors in initial systems.

## CONCLUSION

Our results showed the highest and the lowest occurrence rate of side effects for AstraZeneca and Sinopharm vaccines, respectively. The need to refer to medical centers after vaccination with AstraZeneca was more than that for Sinopharm. The side effects of inactivated virus vaccines such as Sinopharm and Covaxin were lower than that of viral vector vaccines. The negative impact of the Sinopharm vaccine on the ability to do daily routines was lower than other vaccines, and AstraZeneca had the highest effect. There was no significant relationship between a previous history of allergy to the influenza vaccine and the occurrence of side effects. However, such a relationship was observed for the Sinopharm vaccine. There was no significant relationship between BMI and the event of side effects. There was no significant relationship between age and side effects. However, the occurrence rate was significantly higher among younger healthcare workers vaccinated with Sinopharm. There was no significant relationship between a previous history of COVID-19 and the frequency of side effects among those receiving Sputnik, Covaxin, and AstraZeneca vaccines; however, it was significantly higher among those receiving Sinopharm vaccine with a previous history of COVID-19 disease. There was no significant relationship between the history of COVID-19 and referral to medical centers. The most likely time for the occurrence of complications was the first 24 hours, as the probability of the occurrence of side effects on the second day was one-fourth of the first day for AstraZeneca, Covaxin, and Sinopharm and about one-seventh of the first day

for Sputnik vaccine and then decreased significantly. Fever, fatigue, and muscle pain were the most common post-vaccination side effects. In order to confirm these findings, it is suggested to re-examine the results in more extensive clinical trials, especially for Covaxin and Sputnik, for whom a smaller statistical population was investigated.

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