

**An investigation of post vaccination side-effects
experienced by the students of Punjabi University Patiala,
India: A gender based study**

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Abstract

The present study aimed to assess the post vaccination side-effects among the 484 university students (241 males and 243 females) of Punjabi University Patiala. The study used a stratified sampling method to collect the data by using a self-made pre-structured proforma. Among the subjects, the maximum number of participants received Covishield vaccine (75.4 %). The most common post vaccination side-effects were fever in 35.3 percent males and 51.3 percent females, body pain in 18.3 percent males and 37.1 percent females, tiredness in 15.4 percent males and 21.9 percent females and headache in 8.7 percent males and 20.1 percent females. The side-effects were more common in females and also few female subjects reported irregularities in the length of menstrual cycle.

Key words : Biological differences, Doses, Post-vaccination, SARS-CoV-2, Sexual dimorphism, Side-effects.

Viral infections such as influenza and measles have the potential to cause severe acute respiratory symptoms and have been responsible for many epidemics. In the spring of 2003, there was a global outbreak of severe acute respiratory infection (SARI). The World Health Organization (WHO) termed the acronym SARS for severe acute respiratory syndrome and subsequently named the causative coronavirus as SARS-CoV. After that in the summer of 2012, another SARI broke out in Saudi Arabia, the WHO named

this respiratory disease Middle East Respiratory Syndrome (MERS) and the causative coronavirus MERS-CoV. In the winter of 2019, another SARI outbreak occurred in Wuhan, China which spread globally so quickly and the culprit was identified as another novel coronavirus, which the WHO named SARS-CoV-2 due to its similarities with SARS-CoV and the disease was called coronavirus disease 2019, also termed as COVID-19⁷.

Coronaviruses (CoVs) are a highly diverse family containing encapsulated positive-sense single-stranded RNA viruses (+ssRNA). These viruses infect humans, other mammals and birds. The family Coronaviridae belongs to the order Nidovirales and the suborder Coronavirineae. The latter is further divided into the Orthocoronavirinae subfamily, which comprises of four genera: alphacoronavirus (α), betacoronavirus (β), gammacoronavirus (γ) and deltacoronavirus (δ). The alpha and beta coronaviruses exclusively infect mammalian species, whereas, gammacoronaviruses and delta coronaviruses have a wider host range that includes avian species. Human and animal coronavirus infections mainly result in respiratory and enteric diseases¹⁵.

The Coronavirus, SARS-CoV-2 spread quickly after it was first recorded in China. It eventually outspread around the world¹⁸ and was declared a global pandemic by the World Health Organization on 11th of March 2020. Due to the economic consequences, most of the middle-income countries surged to the top. Nine of the top 10 countries for new daily cases were middle income countries (MICs) rather than high-income countries (HICs) depicting that the economy of the country is the backbone for tackling the deadliest diseases like coronavirus⁸. Among the middle-income countries, India was at the first place and the number of instances thereafter increased sharply due to its trade link up with neighbouring countries like Bhutan, Pakistan, Bangladesh, Myanmar, China and Nepal¹⁰.

To combat the spread of coronavirus, the World Health Organization has initiated the

“Solidarity” clinical trial worldwide which is comparing four of the most promising treatment options viz. Remdesivir, lopinavir, lopinavir-ritonavir combined with interferon β -1a and hydroxychloroquine⁷. But the treatments mentioned were not in a way to mitigate the spread of the contagious disease. So, to halt the spread of this pandemic, vaccination was the only possible answer. Till December 2021, 334 vaccines had been approved, out of which 194 were in preclinical development, while the remaining 140 were being studied in clinical trials. Out of these vaccines, only 33 have been approved in at least one country for mitigating the effects of the COVID-19 pandemic⁹.

In India, three vaccines Covishield, Covaxin and Sputnik-V were approved. The Covishield vaccine was produced by the Serum Institute of India (SII), Oxford University and AstraZeneca under the code name AZD1222, but has been marketed as Covishield. For its formation, an adenovirus-ChAdOx1 (AZD1222) extracted from chimpanzees has been moulded to induce the COVID-19 spike protein into human cells. Once it is administered, the antibodies are produced against the SARS-CoV-2 spike protein and its effect remains upto the 56th day¹⁴. The first vaccine India formulated against COVID-19 was Covaxin, under the code name BBV152. Covaxin was manufactured jointly by Bharat Biotech, Hyderabad with the National Institute of Virology (NIV), Pune and the Indian Council of Medical Research (ICMR), Delhi. This vaccine was produced from a whole virus particle of inactivated virion. As the vaccine is in inactivated form, it was not able to infect people but could trigger their immune system to produce protective antibodies against various infections. The

vaccine produced by the Gamaleya Research Institute of Epidemiology and Microbiology, Russia was Sputnik-V, under the code names: rAd26-S and rAd5-S. Sputnik-V used a viral vector platform that was adenovirus for its formation. The first component of Sputnik-V was recombinant human adenovirus serotype number 26 (rAd26-S) while the other one was rAd5-S. Upon administration of Sputnik-V, light antigen-specific antibodies were produced, mainly IgG. Both rAd5-S and rAd26-S had verdict effective and well-tolerable results among the individuals¹⁴.

No doubt these vaccines helped in mitigating the spread of the pandemic and also prevented further infections, but individual reactions to immunization varied greatly. There were no studies in India that assessed the post vaccination side-effects based on gender. So, the current study aimed to assess the post vaccination side-effects among the University students based on sexual dimorphism, taking into account the two vaccines: Covishield and Covaxin.

A self-made pre-structured proforma was used to collect the data through stratified sampling from a total of 500 university students but, 16 subjects were excluded due to the insufficient information, reducing the sample size to 484 which comprised of 241 males and 243 females. The data was collected at Punjabi University Patiala, Punjab, India from 10th February to 2nd April 2023. The personal information that was required to be filled in the proforma included name, gender, contact number, blood group, place of residence and age. The other information that was to be filled included the status of Covid-19, comorbidities,

the vaccine type received, number of doses and the side effects experienced along with other information related to post vaccination side effects. The students selected for the study were between the age group of 17 to 35 years. A permission letter from the Head of the Department, Human Genetics, Punjabi University Patiala was provided for the collection of data from the students of the university. A consent form was also signed by each subject before filling the proforma. The subjects between the age group of 17-35 years, having received either one, two or three doses of the vaccination and who had filled the proforma properly by comprehending it were included in the present study. While the subjects with one or more comorbidities, who were not sure about the name of the vaccine administered and those who did not provide sufficient information related to the study were excluded. The data analysis was done by statistical package for social sciences version 27 (SPSS Inc.). The proportion of post vaccination side-effects by males and females was calculated. The χ^2 test was applied to find out the association between outcome and predictor variables among males and females, considering $p < 0.05$ as significant. Also, percentage was used to calculate the contribution of different side effects, number of doses received, vaccine type, COVID-19 status and the time required for post vaccination side effects to arise.

A total of 484 university students (241 males and 243 females) participated in the study through self-made pre structured proforma in the age group of 17-35 years. In the study, two types of vaccines viz. Covaxin and Covishield were taken into account for analysis among males and females. The number of doses were categorized as one, two

and three (booster), while the COVID-19 positive persons were categorized on the basis of whether they were Covid positive before vaccination or after vaccination or both (before and after vaccination). Also, the frequency of males and females was recorded on the basis of whether they had experienced post-vaccination side effects after taking 1st dose, after 2nd dose or both (after 1st and 2nd dose) or the ones who didn't remember (Table-1). Considering the type of vaccine administered, it had been observed that greater percentage

of both males and females received Covishield and in overall percentage also, 75.4 percent participants were administered with Covishield. Comparing the number of doses received, it has been reported that 83.67 percent of participants received two doses, irrespective of gender assuring the safety of the vaccines. Taking sexual dimorphism into account, it was contemplated that both males and females showed greater frequency in positive cases before vaccination. However, the percentage of COVID-19 positive cases was greater in

Table-1. Categorization of subjects on the basis of type of vaccine, number of doses, status of COVID-19 and the side-effects experienced

Variables	Males (n=241)		Females (n= 243)		Total frequency with the total percentage
	Frequency	Percentage (%)	Frequency	Percentage (%)	
Type of Vaccine					
Covaxin	58	24.06	61	25.11	119 (24.6%)
Covishield	183	75.94	182	74.89	365 (75.4%)
Number of doses received					
1	29	12.03	22	9.05	51 (10.53%)
2	199	82.58	206	84.77	405 (3.67%)
3	13	5.39	15	6.18	28 (5.79%)
Covid-19 positive					
Before	6	2.48	9	3.70	15 (3.10%)
After	5	2.07	5	2.05	10 (2.06%)
Before and After	1	0.41	2	0.82	3 (0.62%)
Side-effects experienced					
After Ist dose	78	32.36	121	49.79	199 (41.12%)
After 2 nd dose	15	6.23	15	6.18	30 (6.19%)
Both	24	9.96	40	16.46	64 (13.23%)
Don't remember	18	7.47	11	4.52	29 (6%)
Not experienced	106	43.98	56	23.05	162 (33.47%)

Table-2. Time interval required for post-vaccination side-effects to arise among males and females

Time interval	Frequency with percentage				Chi-square value (p-value) (< 0.05)
	Males (n=241)		Females (n= 243)		
	Frequ-ency	Percen-tage (%)	Frequ-ency	Percen-tage (%)	
1-10 hours	73	30.3	139	57.2	41.219 (<0.00001)****
10-20 hours	37	15.4	20	8.2	
20-30 hours	6	2.5	7	2.9	
Don't remember	19	7.9	21	8.7	
No side effects	106	44	56	23.1	

****Statistically significant (p-value ≤ 0.0001)

Table-3. Post-vaccination side effects experienced by males and females

Side-effect/ Symptom post- vaccination	Present/ Absent	Frequency with percentage		p-value (< 0.05)
		Males (n=241)	Females (n= 243)	
Tiredness	Present	37 (15.4 %)	53 (21.9 %)	(0.08)
	Absent	204	190	
Body Pain	Present	44 (18.3 %)	90 (37.1 %)	(<0.00001)****
	Absent	197	153	
Pain at the injection site	Present	6 (2.5 %)	14 (5.8 %)	(0.114)
	Absent	235	229	
Fever	Present	85 (35.3 %)	125 (51.5 %)	(0.00047)***
	Absent	156	118	
Headache	Present	21 (8.7 %)	49 (20.1 %)	(0.000557)***
	Absent	220	194	
Others	Present	5 (2.1 %)	5 (2 %)	(0.759)
	Absent	236	238	

Statistically significant (p-value ≤ 0.001)*Statistically significant (p-value ≤ 0.0001).

Among the female participants (n=243), 9.05 percent of subjects experienced changes in the length of the menstrual cycle, either increase (4.12%) or decrease (4.94%) (Table-4).

Table-4. Changes in the menstrual cycle post-vaccination

Changes in the length of menstrual cycle	Number of participants (n=243)	Percentage (%)
Increase	10	4.12
Decrease	12	4.94
No change	205	84.36
Don't know	16	6.58

females. It was also observed that a greater frequency of both male and female peers experienced post vaccination side effects after the administration of the 1st dose. But it was also noticed that the frequency of post vaccination side-effects was higher in females than in males (Table-1). Regarding the time taken for post-vaccination side effects to arise among males and females, a greater percentage of both males (30.3%) and females (57.2%) experienced the side-effects mostly within the first 10 hours. However, higher frequency of males had experienced these side effects within 10-20 hours in comparison to females. Out of the total number of respondents, 44 percent males and 23.1 percent females showed no post-vaccination side effects, indicating that females were more susceptible to develop the post vaccination side effects than males (Table-2). Some of the post vaccination side effects had been assessed in the present study in association with males and females, few of them have shown statistically significant results. The most common side effects were fever in 35.3 percent males and 51.3 percent females, body pain in 18.3 percent males and 37.1 percent females, tiredness in 15.4 percent males and 21.9 percent females and headache in 8.7 percent males and 20.1

percent females. Other side effects such as diarrhoea, nausea and faintness were less common among the vaccinated participants (Table-3).

In this study, the post vaccination side-effects were investigated among the university students on the basis of sexual dimorphism, taking into account the two vaccines: Covishield and Covaxin. From the analysis, it was observed that a greater percentage of both males and females received Covishield vaccine. In Vishakhapatnam, India, similar pattern was reported, in which 94 percent participants were administered Covishield while only 6 percent were administered Covaxin¹². While comparing males with females, it was reported that the frequency of COVID-19 positive cases was greater in females than in males. In contrast to this, (Bwire 2020) stated that men were more susceptible to COVID-19 infection than females due to the biological differences in the immune system and several other factors including sex hormones and lifestyle. The most important factor was the high expression of coronavirus receptor (ACE2) levels in males than in females (especially in the Asian population). Based on the number of doses received, it was reported that 82.58 percent males and 84.77 percent females had received two doses of the vaccines. Out of the total, 83.67 percent of the respondents received two doses, showing positive attitude towards taking the COVID-19 vaccination (Table-1). Cordina *et al.*⁴ also reported the same pattern in their study, hence removing the seed of hesitancy among the individuals from different occupational backgrounds and manifesting the safety of the vaccines.

The most common post vaccination side effects showing statistically significant results were fever (35.3% in males and 51.3% in females), body pain (18.3% in males and 37.1% in females), tiredness (15.4% in males and 21.9% in females) and headache (8.7% in males and 20.1% in females). While Monadhel *et al.*¹³ showed that injection site pain ranked highest in side effects, followed by tiredness. From the results, it can be also interpreted that the occurrence of these side effects was more common in females than in males. Keeping the gender into consideration, Qazaz *et al.*¹⁶ reported that only 65 percent males experienced post vaccination side effects compared to females (77%). Considering systematic symptoms such as headache, tiredness, fever, myalgia and chills; females had significantly greater rates of severe and moderate adverse effects ($p < 0.05$) than males. Hoffmann *et al.*,⁶ concluded that females were more likely to experience side effects associated with the vaccination than males. The most frequently reported vaccine side effects were pain at the injection site (more than 80%), fatigue (more than 60%), headache (more than 50%), muscle pain and chills (more than 30%), joint pain (more than 20%), fever and swelling at the injection site (more than 10%).

Other than the frequency of the post vaccination side-effects, the analysis was done on the basis of number of doses received by males and females and the side-effects thereafter. It was interpreted that a greater frequency of both males and females experienced post vaccination side effects after the administration of the 1st dose, rather than the 2nd dose or after the administration of both

the doses. However, the females showed higher frequency of post vaccination side effects as compared to males (Table-1). Among the findings of earlier studies, Parida *et al.*,¹⁵ Hatmal *et al.*,⁵ and Amer *et al.*,² also reported that post vaccination side effects were more prevalent after receiving the 1st dose of the vaccine than the 2nd dose. In connection with the time required for the post vaccination side effects to arise, it was observed that these side effects were experienced mostly within the first 10 hours, irrespective of the gender. However, in the time interval of 10-20 hours, males had reported more side-effects than females ($p < 0.00001$). Hatmal *et al.*,⁵ observed that 35 percent of participants experienced post vaccination side-effects within 9-12 hours after the injection and about 26 percent of the participants revealed that post vaccination side-effects started after 5-8 hours.

The present study demonstrated that the frequency of the post vaccination side-effects were more common in females and mostly appeared within the time interval of 1-10 hours, irrespective of gender. Females were more susceptible to get the infection due to the biological differences in the immune system, the reason for which is not yet fully understood and needs to be explored by doing more research with large sample sizes among different ethnicities. Also, the study observed fluctuations in the menstrual cycle of few females after the vaccination which could be due to psychological, nutritional or genetic factors, which is not fully comprehensible and requires to be elaborated to uncover the reasons for the same.

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