Evaluating the Adverse Effects of COVID-19 Vaccination in Medical Students: Insights from a Private Medical College

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ABSTRACT

Introduction: Coronavirus infection (COVID-19) is a global pandemic spread across the world in March 2020 and was caused by the respiratory Virus SARS-COV-2. It affected more than 4.5 million people across the world. The affected people presented with various clinical manifestations. Many researches were conducted and after a lot of experimentation, the scientists were able to develop vaccines to fight this viral pandemic. Some of the people who were injected with these vaccines developed various adverse effects.

Objectives: This study aims to investigate the incidence of various side effects experienced by medical students after receiving COVID-19 vaccination ,to explore gender-based differences in the frequency of side effects among male and female students,to assess the relationship between types of vaccine and side effects following vaccination, and to compare the frequency of side effects reported after the first and second doses of vaccination.

Study Design: Cross-sectional study design.

Place and Duration: The study was conducted at Wah Medical College, from November 22, 2021, to June 22, 2022. A convenient sampling technique was used.

Methodology: A questionnaire was administered to medical students in all five MBBS classes. The students were briefed about the research purpose and were allowed to fill it out after obtaining informed consent. They were also told that their information would remain confidential. SPSS version 23 was used for data analysis.Categorical data were summarized using frequency and percentage calculations. Frequency and percentages were calculated for categorical data. The chi-square test was employed to examine the relationships between gender, vaccine type, and adverse effects, with a p-value of <0.05 indicating statistical significance.

Result: Fever, headache, and body aches are the most common adverse effects following COVID-19 vaccination. Fever was reported in 32.3%, Headache in 28.1% Body aches in 26.8% of students after 1st dose. Fever was reported in 25.5%, Headache in 22.6% Body aches in 7.1% of students after 2nd dose.Further analysis revealed significant associations between vaccine types and specific adverse effects. Students receiving mRNA vaccines (Pfizer, Moderna) were more likely to experience fever, cough, and sore throat. In contrast, those receiving viral vector vaccines (AstraZeneca) were more likely to report loss of taste and smell.Additionally, significant associations were found between vaccine types and cardiovascular symptoms, with

chest pain and hypertension reported more frequently among students receiving both mRNA and viral vector vaccines. Interestingly, gender-based differences emerged, with males more commonly reporting loss of taste and females more frequently experiencing swelling and tenderness at the injection site.

Conclusion: The analysis revealed that side effects were more commonly reported after the first dose and among recipients of mRNA (Pfizer, Moderna) and viral vector (AstraZeneca) vaccines. These findings have important implications for researchers and healthcare professionals, and may help alleviate concerns about the safety of inactivated vaccines (Sinopharm, Sinovac) in the Pakistani population, which were found to have a relatively mild side effect profile.

Keywords: Types of COVID vaccines, side effects, medical students, cross-sectional study

INTRODUCTION:

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a profound impact on global health since its declaration by the World Health Organization (WHO) on March 12, 2020. Since then,the virus has spread rapidly, resulting in millions of confirmed cases and approximately 4.5 million reported deaths worldwide. The clinical spectrum of COVID-19 is diverse, ranging from asymptomatic infections to severe and potentially fatal outcomes, including multi-organ failure and acute respiratory distress [1]. Since its start, many non-pharmaceutical measures like social distancing, wearing face masks, hand washing, and other personal protective measures were applied and these measures proved to be very helpful but these caused very negative impacts like psychological issues, depression, anxiety fear, etc. [2.] As the COVID-19 infection had posted a severe social, economic, and healthcare crisis, so there was a need for a vaccine to decrease this global devastation. According to the FDA, the wide-spectrum definition of an effective vaccine includes the ability of a vaccine to prevent the transmission of a virus from an infected person to a viable person. Moreover, retaining measures of progression of disease along with minimizing the utilization of intensive care resources[3]. As with the successful production and development of vaccines against this viral disease, the governments decided to vaccinate a maximum number of their citizens as this is the only important solution for the control of the pandemic[4].

The COVID-19 pandemic prompted a global response, with extensive preventive measures implemented to mitigate its impact. Although COVID-19 vaccines have shown outstanding efficacy and safety, continued monitoring in real-world settings is vital due to the reported side effects. Nine prominent vaccines have been developed, namely Pfizer-BioNTech, Moderna, Gamaleya, Novavax, Oxford-AstraZeneca, Sinopharm, Johnson & Johnson, Sinovac, and Bharat Biotech, all of which utilize the viral S-Glycoprotein of wild-type strains as antigens in their formulation [2,5]. The FDA has approved using Pfizer/BioNtech and Moderna in emergencies as these vaccines have proven to provide immunity via humoral and cell-mediated pathways. Although the COVID-19 vaccines have demonstrated high efficacy, they can cause various side effects. Common side effects include local reactions at the injection site (like pain, redness, and swelling), fever, fatigue, headache, muscle pain, nausea, vomiting, itching, chills, and muscle and joint pain. In rare cases, anaphylactic shock can occur. It's worth noting that the Moderna vaccine seems to be more commonly linked to these side effects compared to other vaccines.But as Moderna is less temperature sensitive comparatively, it can be transported and stored more

easily[6]. Certain cutaneous events following Covid 19 vaccination were quite common and include erythema, swelling, itching, pernio like lesions and generalized rashes[7].

This research aims to investigate the prevalence of various side effects experienced by medical students after receiving COVID-19 vaccination. It explores the relationship between vaccine types and side effects, comparing mRNA, viral vector, and inactivated vaccines. It also compares the frequency of side effects after the first and second doses, providing a comprehensive understanding of the vaccine's safety profile in this population. To evaluate the side effects emerging among post-vaccinated individuals with demographic characteristics including age, gender, comorbidities, history of past infection, and symptoms at the time of vaccination, recent research was conducted on 205 participants with a mean age 32.96~7.7 years, age range 23-55 years. The research comprised of 88 males (42.9%) and 117 females (57.1%). Among then 23(11.2%) were diabetic, 25(12.2%) were hypertensive, 2(1.0%) were asthmatic. Around 19.5% (40/205) were Covid Positive, whereas 60 (29.3%) were symptomatic at the time of vaccination. The side effects recorded by the research after vaccination include: fatigue/malaise 45.4% (93/205), headache/migraine 39.5% (81/205), fever 33.7% (69/205, chills and rigors 20.5% (42/205), GI disturbances 26.8% (55/205) and flu-like symptoms 13.7% (28/205)). Redness, soreness, and swelling 27.3% (56/205) were reported by participants at the site of injection[8].

METHODOLOGY

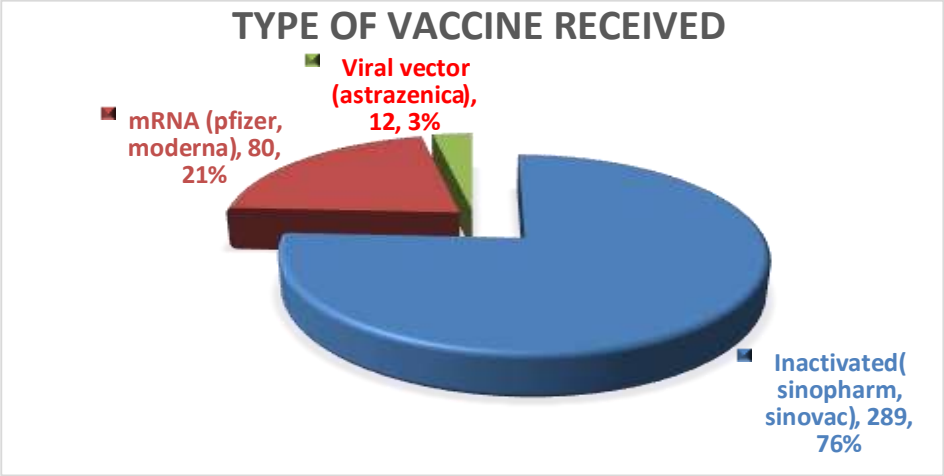
This cross-sectional study was conducted at Wah Medical College over six months, from November 22, 2021, to June 22, 2022. Using the Statulator sample size calculator, we determined the required sample size based on a prior study at the Foundation University of Dentistry, which reported fatigue and malaise as the most common side effects (45% prevalence). We employed a non-probability convenient sampling technique to select participants. With a 5% margin of error and a 95% confidence interval, our calculated sample size was 381 participants.

This study included students who had received two doses of the COVID-19 vaccine as eligible participants. Those who were unvaccinated, had received only one dose, or were under 18 years old were excluded. Data were collected via a structured questionnaire designed to gather information on participants' age, gender, weight, height, pre-existing co-morbid conditions, type of vaccine received, and the side effects experienced after both the first and second doses. The questionnaire was distributed among the students of all five MBBS classes, and informed consent was obtained before participation. Confidentiality was assured, and participants were informed that their responses would be used exclusively for research purposes.

Descriptive statistics, including frequencies and percentages, were used to summarize categorical variables. The Chi-square test was applied to assess the association between gender, type of vaccine, and the occurrence of adverse effects. Statistical significance was set at a p-value of less than 0.05.Data analysis was conducted using SPSS software version 23. Categorical variables were summarized using descriptive statistics such as frequencies and percentages. The Chi-square test was used to investigate the associations between gender, vaccine type, and the occurrence of adverse effects. A p-value of less than 0.05 was considered statistically significant.

RESULTS:

Figure 1: Type of Vaccination received



The frequency of inactivated (Sinopharm, Sinovac) received the vaccine was 289 (75.9%), mRNA (Pfizer, Moderna) received vaccine was 80 (21%) and viral vector (AstraZeneca) received vaccine was 12 (3.1%)**.**

Table 1: Frequency of comorbidities among students

Serial No.	Comorbid conditions	Frequency	Percentage
1	Hypertension	10	2.6%
2	Chronic Respiratory Disease	3	0.8%
3	Heart Disease	2	0.5%
4	Allergic Reaction	26	6.8%
5	Cancer	1	0.3%
6	Kidney Disease	3	0.8%
7	Liver Disease	1	0.3%
8	Endocrine Disease	1	0.3%
9	Auto Immune Disease	2	0.5%

The frequency of Hypertension was 10 (2.6%), chronic respiratory disease was 3 (0.8%), Heart disease was 2 (0.5%), Allergic reactions were 26 (6.8%), Cancer was 1 (0.3%), Kidney disease was 3 (0.8%), Liver disease was 1 (0.3%), Endocrine disease was 1 (0.3%), autoimmune disease was 2 (0.5%).

Table 2: Reported adverse effects following first and second doses of vaccination

	Side effects	After 1st dose		After 2nd dose	
		Frequency	Percentage	Frequency	Percentage
1	Fever	123	32.3%	97	25.5%
2	Headache	107	28.1%	86	22.6%
3	Body ache	102	26.8%	27	7.1%
4	Tenderness and swelling at injection site	81	21.3%	54	14.2%
5	Loss of taste	21	5.5%	13	3.4%
6	Loss of smell	18	4.7%	15	3.9%
7	Shortness of Breath	20	5.2%	16	4.2%
8	Sore throat and dry cough	24	6.3%	27	7.1%
9	Dizziness	47	12.3%	42	11%
10	Chest pain	12	3.1%	9	2.4%
11	Hypertension	16	4.2%	9	2.4%
12	No side effects	144	37.8%	210	55.1%

Following first dose of vaccination Fever was reported in 123 (32.3%)students, Headache in107 (28.1%), Body ache in 102 (26.8%), Tenderness and swelling at injection site in 81 (21.3%), loss of taste in 21 (5.5%), loss of smell in 18 (4.7%), shortness of breath in 20 (5.25%), sore throat and dry cough in 24 (6.3%), dizziness in 47 (12.3%), chest pain in 12 (3.1%), Hypertension in 16 (4.2%) and no side effects in 144 (37.8%) students. Following second dose of vaccination Fever was reported in 97 (25.5%) students, Headache in 86 (22.6%), Body ache in 27 (7.1%), Tenderness and swelling at injection site in 54 (14.2%), loss of taste in 13 (3.4%), loss of smell in 15 (3.9%), shortness of breath in 16 (4.2%), sore throat and dry cough in 27 (7.1%), Dizziness in 42 (11%), Chest pain in 9 (2.4%), Hypertension in 9 (2.4%) and no side effects in 210 (55.1%) students.

Table 3: Type of vaccine and fever

Type of vaccine	Fever				
	Yes	Percentage	No	Percentage	P Value
Inactivated (Sinopharm, Sinovac)	79	27.3%	210	72.7%	
mRNA (Pfizer, Moderna)	39	48.8%	41	51.2%	
Viral vector (Astrazenica)	5	41.7%	7	58.3%	0.001

There was a significant association between the type of vaccine and fever. The findings show that among those who received inactivated vaccines, such as Sinopharm and Sinovac, 27.3% (79 students) reported experiencing fever, while 72.7% (210 students) did not. For students who received mRNA vaccines, such as Pfizer and Moderna, a higher percentage of 48.8% (39

students) reported fever, while 51.2% (41 students) did not. Among those who received the viral vector vaccine, AstraZeneca, 41.7% (5 students) reported fever, while 58.3% (7 students) did not. The observed P-value of 0.001 suggests a strong statistically significant relationship between the vaccine type and the incidence of fever, indicating that the type of vaccine is significantly associated with the occurrence of fever. This means that the likelihood of experiencing fever varies significantly based on the vaccine type. Fever was more frequently reported among students who received mRNA vaccines (Pfizer and Moderna) compared to those who received inactivated vaccines or the viral vector vaccine.

Table 4: Type of vaccine and loss of taste

Type of vaccine	**Loss of taste**				
	Yes	Percentage	No	Percentage	P Value
Inactivated (Sinopharm, sinovac)	11	3.8%	278	96.2%	
mRNA (Pfizer, Moderna)	7	8.8%	73	91.3%	0.003
Viral vector (Astrazenica)	3	25%	9	75%	

The analysis revealed a significant correlation between the vaccine type and the incidence of loss of taste, with a P-value of 0.003, indicating that the type of vaccine is significantly linked to the occurrence of this particular side effect.The results show that among those who received inactivated vaccines, such as Sinopharm and Sinovac, 3.8% (11 students) reported experiencing a loss of taste, while 96.2% (278 students) did not. In contrast, for those who received mRNA vaccines, like Pfizer and Moderna, 8.8% (7 students) reported a loss of taste, whereas 91.3% (73 students) did not. The most notable finding was observed in students who received the viral vector vaccine, AstraZeneca, where 25% (3 students) reported experiencing a loss of taste compared to 75% (9 students) who did not.

Loss of smell was more frequently linked to viral vector vaccines, particularly AstraZeneca. Similarly, shortness of breath was also more commonly observed in those who received viral vector vaccines. Conversely, students who received mRNA vaccines, such as Pfizer and Moderna, reported sore throat and dry cough more often. Additionally, chest pain was a commonly reported side effect among students who had received both mRNA (Pfizer and Moderna) and viral vector (AstraZeneca) vaccines. The occurrence of acute hypertension was also significantly associated with both types of vaccines. Gender differences were noted in the occurrence of certain side effects. Females experienced tenderness and swelling at the injection site more frequently than males, while males were more likely to report a loss of taste after vaccination. Interestingly, no significant link was found between the type of vaccine and the occurrence of symptoms like headache or body aches. This study underscores how both the type

of vaccine and gender may influence the prevalence of specific side effects following vaccination.

DISCUSSION:

The swift development and emergency approval of COVID-19 vaccines have sparked concerns among some groups, leading to vaccination hesitancy and anxiety. Recent reports of rare yet serious side effects, including thrombosis[13,18] and myocarditis[19,20], have added to these worries. To alleviate these concerns and enhance public trust in COVID-19 vaccines, ongoing monitoring and evaluation of their safety are essential. To explore the safety profile of COVID-19 vaccines, we conducted a cross-sectional study at Wah Medical College, Pakistan, focusing on the adverse events experienced by students following immunization with inactivated (Sinopharm, Sinovac), mRNA (Pfizer, Moderna), and viral vector (AstraZeneca) vaccines.

The most common post-vaccination side effect after the first dose was fever as reported by 32.3% (123/381) of the participants, followed by headache, which was reported by 28.1% (107/381) of the participants. A similar trend was observed after the second dose, with 25.5% (97/381) of the participants reporting fever and 22.6% (86/381) of the participants reporting headache post-vaccination. Fever, sore throat, and dry cough are significantly associated with mRNA vaccines while loss of taste, loss of smell, and shortness of breath are associated with viral vector vaccine, AstraZeneca. Chest pain and hypertension are more reported by individuals who received mRNA and viral vector vaccines as compared to inactivated vaccines. The results are comparable with the research carried out in China where one of the inactivated vaccines (Sinopharm), was tested. The results showed that fatigue, headache, and body aches were not reported by any of the participants. Nevertheless, a portion of participants experienced injection-site reactions, with tenderness and swelling affecting 14.3% and fever affecting 2.4% of the participants, respectively.

[21]. On the contrary, when one of the mRNA vaccines (Pfizer) was tested in Slovakia, not only did the participants, report tenderness at the injection site (85.2%) but they also presented with fatigue (54.2%), headache (34.3%), myalgias (28.4%) and shivering (26.4%) [17]. A similar study, conducted in the United Kingdom, showed that individuals inoculated with the viral vector vaccine (AstraZeneca) mostly reported tenderness at the injection site (49.3%), headache (22.8%), fatigue (22.1%) and chills (14.7%) in addition to arthralgias (11.5%) [11].The differences in post-vaccination side effects could be related to population-specific factors. As vaccination trials were mainly conducted in a few select countries, including Europe, the United States, Australia, and China, additional studies are needed to assess the safety of COVID-19 vaccines in other regions and populations.

A separate clinical trial conducted in the United Kingdom investigated the safety profile of AstraZeneca's COVID-19 vaccine. The results showed that a significant proportion of participants experienced post-vaccination side effects, including fatigue (70%), headache (68%), body aches (60%), and fever (51%)[22] . Similarly, a study conducted in the United States evaluated the safety of Pfizer's COVID-19 vaccine and found that all participants reported headache, tenderness, and swelling at the injection site, while a majority experienced fatigue (83.3%), fever (66.7%), and body aches (58.3%)[23] .

According to the literature, the AstraZeneca clinical trials were temporarily suspended twice due to safety issues, with reports of multiple sclerosis and amyotrophic lateral sclerosis as side effects [22]. On the other hand, although Sinovac's clinical trials were halted in Brazil, the literature suggests that Sinopharm has not been associated with any serious side effects [3,24].

Another study found that tender or swollen lymph nodes were more frequently noted with the Pfizer vaccine whereas sweating, dizziness, anxiety, shortness of breath, tachycardia, sore throat and dry cough, nasal discharge, and abdominal pain were more commonly associated with the AstraZeneca vaccine [9]. Our data suggests a significant relationship between the viral vector vaccine (AstraZeneca) and post-vaccination loss of taste ($p = 0.003$), loss of smell ($p = 0.045$), shortness of breath ($p = 0.003$), and chest pain ($p = 0.015$). Similarly, a significant trend was observed between the mRNA vaccines (Pfizer, Moderna) and fever ($p = 0.001$), sore throat and dry cough ($p = 0.007$), and chest pain ($p=0.015$). No significant association could be proven for the inactivated vaccines (Sinopharm, Sinovac). Hence, our results are also suggestive of a relatively better safety profile for the inactivated vaccines when compared with the other vaccines. Any inference drawn from these comparisons, however, needs further consideration due to the limitations of some of the studies; these include a minimal sample size [23], and reports of serious adverse effects [25].

Research has consistently shown that women and younger individuals are more likely to experience side effects from COVID-19 vaccines compared to men[1,11] and older adults[17,30] . A study on Sinopharm vaccines found that side effects were more common in participants under 49 years old than in those over 49 [10]. Similarly, another study revealed that younger individuals were more prone to gastrointestinal disturbances and flu-like symptoms after receiving the Sinopharm vaccine, while females experienced more tenderness and headaches, and males experienced more gastrointestinal disturbances[8] . Additionally, a study on Pfizer and Moderna vaccines found that younger individuals (under 39) reported more headache, fatigue, and joint pain than older individuals (over 39)[14] . Our study found similar results, with females reporting more tenderness and swelling at the injection site ($p = 0.000$) and males reporting more loss of taste ($p = 0.006$). These differences may be related to biological differences between genders[31] . We also found a significant association between side effects and the number of doses received, which contrasts with previous reports of more side effects after the second dose[16,32] . However, our study's observational nature limits our ability to comment on vaccine effectiveness.

This study has some limitations. The use of self-reported data may introduce variability in the accuracy of the reports, as some participants may be more likely to report adverse effects than others. Additionally, the survey's distribution was limited to students at the authors' institution, which may not be representative of the broader population. To improve generalizability, future studies should consider conducting community-based surveys. Moreover, future research should investigate rare adverse events following COVID-19 vaccination, such as thromboembolic profiles and myocarditis, which were not examined in this study[19].

CONCLUSION:

In conclusion, the study indicates that side effects were more commonly reported following the first dose of mRNA (Pfizer, Moderna) or viral vector (AstraZeneca) vaccines, whereas inactivated vaccines (Sinopharm, Sinovac) demonstrated fewer side effects in the Pakistani population. These findings may provide reassurance regarding the safety of inactivated vaccines. The recommendations emphasize prioritizing inactivated vaccines where available, minimizing the use of vaccines associated with more side effects, and assessing the individual's immune status before vaccination.

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