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Adverse Effects of Covid-19 Vaccines Among Medical Students: A Cross-Sectional Study

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Abstract

Purpose : To verify the frequency and severity of adverse effects of COVID-19 vaccines applied to Brazilian medical students.

Methods : This cross-sectional study was conducted at the Faculdade Pernambucana de Saúde (FPS, Brazil). Data were collected between September 2021 and April 2022. Sociodemographic and clinical data, vaccination schedule, and adverse effects were analyzed. Statistical analysis was performed on Jamovi 2.3 and R Core Team.

Results : A total of 300 medical students of the FPS from the first to the eighth semester (mean age of 21 years) were included ; most were females. The most used vaccine on the vaccination schedule was viral vector vaccine (AstraZeneca). A total of 246 medical students reported mild adverse effects on the first dose (fever, headache, and myalgia), mainly after the viral vector vaccine (AstraZeneca) ($p < 0.05$). The most used vaccine on the booster dose was vaccine mRNA (Pfizer), followed by viral vector vaccine (AstraZeneca).

Conclusion : The available vaccines in Brazil were safe and caused mild adverse effects ; the AstraZeneca vaccine had the most reactogenicity.

Keywords: Immunization; Infections; Young Adult; RNA Viruses; Disease Transmission, Infectious.

Introduction

On March 11, 2020, the World Health Organization (WHO) declared the coronavirus disease (COVID-19) pandemic due to the high number of infections and deaths [1]. Until September 2022, 603,932,387 cases were confirmed worldwide; 34,467,867 were in Brazil [2]. In this same period, the world had 64,938,670 deaths; 684,354 were in Brazil [2].

Health professionals on the frontline have been infected since the beginning of the COVID-19 pandemic, impacting personal and family life and health systems [3]. The COVID-19 pandemic also impacted health students because they attended the population and were exposed to the virus. The WHO estimated that 80 to 180 thousand health professionals worldwide died from COVID-19 from January 2020 to May 2021 [4]. Thereby, prevention measures against COVID-19 in this group are essential for maintaining public health policies.

In Brazil, the vaccination initiated in January 2020 and was important to contain the COVID-19. Until September 2022, 12.6 billion doses were applied to 4.93 billion people worldwide. In Brazil, 471 million doses were applied to 172 million people [5].

The first vaccines used in Brazil were inactivated vaccine (Coronavac), viral vector vaccine (AstraZeneca) , followed by vaccine mRNA (Pfizer) and viral vector vaccine (Janssen)[6]. The vaccination schedule comprises two first doses and one or two booster doses. Health professionals and students have been the priority groups since the beginning of the vaccination [7].

The safety of vaccines is a worldwide concern and a determining factor in the success of a vaccination schedule [8]. As COVID-19 vaccines were among the large-scale vaccinations, concerns arose about their possible adverse effects. Nevertheless, the risks of severe adverse effects caused by vaccines are lower than those caused by diseases [9, 10].

According to the Ministry of Health (MH), 134,184 adverse effects caused by COVID-19 vaccines were registered in Brazil. The most reported mild adverse effects were headaches, fever, and myalgia, and incidence varied among vaccines [6]. On the other hand, severe adverse effects were observed after inactivated vaccine (CoronaVac) and viral vector vaccine (AstraZeneca), mostly respiratory, thoracic, and related to mediastinal disorders.[6] Vaccine mRNA (Pfize)r and viral vector vaccine (Janssen) vaccines caused mainly nervous system adverse effects [6].

Thrombotic events after administering the viral vector vaccine (AstraZeneca) were an adverse effect that concerned the scientific community [6]. According to the MH, 4,675 deaths caused by severe adverse effects were registered in the first and second years of the pandemic, of which only 16 were caused by COVID-19 vaccines (12 related to viral vector vaccine (AstraZeneca) and 4 to viral vector vaccine (Janssen). All cases were thrombotic events with thrombocytopenia, which are rare [6].

The literature still lacks studies about the adverse effects of COVID-19 vaccines on specific populations, such as medical students. Therefore, more studies on this topic are needed because they may positively influence vaccination and demonstrate that most adverse effects are mild and transitory in younger populations. Moreover, understanding the effects of vaccines on this population may be important to improve adherence to the vaccination schedule, develop more effective public policies, and fight the "fake news" about COVID-19 vaccines. Thus, this study aimed to verify the frequency and severity of adverse effects of the COVID-19 vaccines applied to Brazilian medical students.

Methods

This cross-sectional study was conducted at the Faculdade Pernambucana de Saúde (FPS) (Recife, Pernambuco, Brazil). Data collection occurred from September 2021 to April 2022. A convenience sample of medical students from the first to the eighth semester of the FPS composed the study. The inclusion criterion was vaccination against COVID-19 regardless of the number of doses or vaccines applied. A total of 300 (34%) out of 871 medical students of the FPS adhered to the study.

Students were invited to participate in the research at the FPS campus after a brief explanation of the study. A specific form verified sociodemographic data (age, weight, height, gender, race, and semester of the course), clinical history of the disease (COVID-19), and the COVID-19 vaccination schedule (vaccine platform and number of doses). The form was delivered after signing the informed consent form. The adverse effects were evaluated and divided into local (pain at the vaccine application, erythema, swelling, and induration) and systemic effects (headache, fatigue, myalgia, fever, pruritus, diarrhea, nausea, vomiting, abdominal pain, dizziness, loss of appetite, allergic or immediate hypersensitivity, thrombotic events, and cardiac changes [e.g., myocarditis or pericarditis] [10].

Variables were categorized as age, sex, weight (kg), height (m), semester of the course, race, hospitalization by COVID-19 before and after vaccination, presence of comorbidities (i.e., cardiovascular diseases, diabetes, severe acute asthma, or coagulopathies), and vaccine applied inactivated vaccine (Coronavac), and viral vector vaccine AstraZeneca, vaccine mRNA (Pfizer) or viral vector vaccine (Janssen) in the first or booster dose. Post-vaccination adverse effects were also included.

Data were double-entered by different researchers into an Excel® database. Databases were compared to correct errors and inconsistencies, and a single database was created for statistical analysis. Data were presented as absolute and relative frequencies. The Jamovi software (version 2.3) and R Core Team were used to perform associations (Chi-square test), and a $p < 0.005$ was considered statistically significant. The study was approved by the research ethics committee of FPS (no. 50489621.5.0000.5569) and conducted according to the Declaration of Helsinki and resolution 510/16 of the National Health Council.

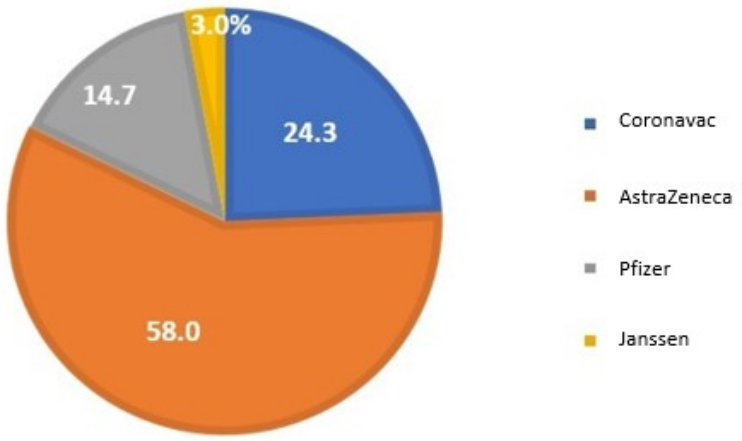

Figure 1: Distribution of COVID-19 vaccines administered in the vaccination schedule of medical students at the Faculdade Pernambucana de Saúde, Recife, 2022

Results

The sample included 300 medical students of the FPS from the first to the eighth semester. Sample characteristics are demonstrated in Table 1. The mean age was 21.8 ± 3.48 years, and most individuals were female (60.7%). Regarding race, 76.8% were white, 3.0% black, and 20% brown. Most students had a normal (70.3%) body mass index. A total of 281 medical students (93.6%) had no comorbidities. Those with comorbidities presented severe acute asthma (15.0%), followed by diabetes mellitus (2.0%), cardiovascular diseases (1.0%), and coagulopathies (1.0%).

Table 1: Sociodemographic, academic, and clinical characteristics of medical students at the Faculdade Pernambucana de Saúde vaccinated against COVID-19, Recife, 2022

Sociodemographic, academic, and clinical characteristics		
Age (years)		
· Median	21	
· Mean ± SD	21.8 ± 3.48	
Sex – n (%)		
· Male	118	39.3
· Female	182	60.7
Race		
· White	228	76.8
· Black	9	3
· Brown	60	20
Body mass index		
· < 18.5 kg/m^2	22	7.6
· Between 18.5 and 24.9 kg/m^2	204	70.3
· Between 25 and 29.9 kg/m^2	54	18.6
· Between 30 and 34.9 kg/m^2	9	3.1
· > 35 kg/m^2	1	0.3
Semester of the course – n (%)		
· First	50	16.7
· Second	1	0.3
· Third	59	19.7
· Fourth	0	0
· Fifth	53	17.7
· Sixth	28	9.3
· Seventh	107	35.7
· Eighth	2	0.7
COVID-19		
before vaccination – N (%)		
· Yes	94	31.3
· No	206	68.7
Comorbidities – n (%)		
· Yes	19	6.4

· No	281	93.6
Distribution of comorbidities – n (%)		
· Cardiovascular diseases	1	0.3
· Diabetes mellitus	2	0.7
· Severe acute asthma	15	5.1
· Coagulopathies	1	0.3

Ninety-four medical students (31.3%) had COVID-19. The most used vaccine was viral vector vaccine AstraZeneca (58.0%), followed by inactivated vaccine CoronaVac (24.3%), vaccine mRNA Pfizer (14.7%), and viral vector vaccine Janssen (3.0%) (Figure 1). Two hundred forty-six medical students (82.0%) had adverse effects (Table 2).

Table 2: Adverse effects of COVID-19 vaccines administered in the vaccination schedule among medical students at the Faculdade Pernambucana de Saúde, Recife, 2022

Vaccines	**CoronaVac**		**AstraZeneca**		**Pfizer**		**Janssen**		**p-value***
	73 (%)		**174 (%)**		**44 (%)**		**9 (%)**		
Local adverse effects									
Pain	7	9.60	20	11.50	6	13.60	0	0.00	0.656
Erythema	0	0.00	30	17.20	7	15.90	0	0.00	0.001
Systemic adverse effects									
Asthenia	3	4.1	14	8.0	6	13.6	23	7.7	0.231
Nausea	8	11.0	36	20.7	6	13.6	0	0.0	0.120
Headache	18	13.7	95	72.5	14	10.7	4	3.1	< 0.001
Vomiting	0	0.0	5	2.9	0	0.00	0	0.0	0.298
Coryza	3	4.1	12	6.9	2	4.5	0	0.0	0.690
Myalgia	10	13.7	77	44.3	6	13.6	4	44.4	< 0.001
Dizziness	0	0.0	10	5.7	0	0.0	0	0.0	0.058
Anorexia	3	4.1	18	10.3	2	4.5	0	0.0	0.219
Fever	18	24.7	120	69.0	10	22.7	4	44.4	< 0.001

Fever, headache, local erythema, and myalgia in the first dose were significantly associated with COVID-19 vaccines. The highest frequency of adverse effects was observed in those who received the viral vector vaccine (AstraZeneca) ($p < 0.01$).

Table 3 describes the vaccines used in the booster dose. One hundred thirty-four medical students received the vaccine mRNA (Pfizer) (56.5%), followed by eighty-five from viral vector vaccine (AstraZeneca) (35.9%), eleven from viral vector vaccine (Janssen) (4.6%), and five from inactivated vaccine (CoronaVac) (2.1%).

Table 3 Distribution of the booster dose related to the vaccination schedule against COVID-19 among medical students at the Faculdade Pernambucana de Saúde Recife, 2022

Vaccination schedule	Booster dose							
	CoronaVac		AstraZeneca		Pfizer		Janssen	
	N	(%)	N	(%)	N	(%)	N	(%)
CoronaVac	2	3.4	31	52.5	23	39.0	3	5.1
AstraZeneca	3	2.0	50	33.9	90	60.8	3	2.0
Pfizer	0	0.0	3	12.5	18	75.0	3	12.5
Janssen	0	0.0	1	16.7	3	50.0	2	33.3
Total	5		85		134		11	

Discussion

This study aimed to verify the frequency and severity of adverse effects of COVID-19 vaccines applied to Brazilian medical students. The adverse effects reported were mostly mild and appeared after the first and booster doses. The viral vector vaccine (AstraZeneca) was associated with a higher frequency of local (erythema) and systemic adverse effects (fever, headache, and myalgia) than other vaccines used in the vaccination schedule.

Fever was the most prevalent adverse effect (reported by 152 medical students), whereas headache was present in 131 students. In addition, myalgia occurred in 98 medical students. All adverse effects were considered mild.

Regarding the vaccination schedule, the most used vaccines were viral vector vaccine (AstraZeneca) and inactivated vaccine (CoronaVac). Considering the first and booster doses, the most used vaccine was viral vector vaccine (AstraZeneca), followed by vaccine mRNA (Pfizer), inactivated vaccine (CoronaVac), and viral vector vaccine (Janssen). The Vaccine mRNA (Pfizer) was the most utilized vaccine in booster doses, followed by viral vector vaccine (AstraZeneca). The vaccination schedule reflected the guidelines of the Brazilian MH that included students from health areas in the priority groups. At that time, inactivated vaccine (CoronaVac) and viral vector vaccine (AstraZeneca) were the only vaccines available [7].

The reported adverse effects were not different among the vaccines used in the booster dose. According to the Brazilian MH, a higher frequency of mild adverse effects was observed after the viral vector vaccine AstraZeneca vaccine, [6] corroborating our results. These findings were also observed in other studies that addressed the occurrence of adverse effects [10].

Adverse effects may vary according to the vaccine used in the vaccination schedule, and the expected adverse effects can be found in the leaflets of laboratories that produced the vaccine. For example, inactivated vaccine CoronaVac, an inactivated virus vaccine purified and adsorbed on aluminum hydroxide, may generate the following adverse effects: headache, fatigue, pain at the administration site, myalgia, fever, diarrhea, nausea, vomiting, lower abdominal pain, dizziness, loss of appetite, and allergic or immediate hypersensitivity [12,13].

The vaccine produced by the viral vector vaccine AstraZeneca laboratory is a recombinant adenovirus vaccine. The main adverse effects reported are sensitivity or pain at the administration site (or both), headache, fatigue, myalgia, malaise, pyrexia, chills, arthralgia, and nausea [13]. The vaccine mRNA Pfizer vaccine, composed of a single messenger RNA, caused the following adverse effects: pain or swelling (mild or moderate) at the administration site (or both), fatigue, headache, myalgia, chills, arthralgia, and fever [15].

Last, the viral vector vaccine Janssen vaccine, which contains adenovirus type 26 that encodes the spike SARS-CoV-2 glycoprotein,

may cause headache, pyrexia, arthralgia, cough, nausea, myalgia, fatigue, pain, erythema, or swelling at the administration site [21]. Therefore, our findings corroborate the expected adverse effects caused by COVID-19 vaccines.

The results presented in this study also agreed with the Epidemiological Bulletin no. 122 of the Brazilian MH, which observed a higher prevalence of mild adverse effects (headache, fever, and myalgia) in individuals between 18 and 49 years after receiving the AstraZeneca vaccine [6].

Severe adverse effects that were initially a worldwide concern (e.g., thrombotic events associated with thrombocytopenia [viral vector vaccine AstraZeneca vaccine], Guillain-Barré syndrome [rarely found in the viral vector vaccine Janssen], and myocarditis [vaccine mRNA Pfizer]) were not found in our study due to their rarity in young individuals and the relatively small sample size [14 - 20]

Since the beginning of the pandemic, the WHO and Pan American Health Organization reported that the main population affected by COVID-19 were older adults due to immunosenescence and increased vulnerability against infectious diseases [22, 23]. According to the National Network of Health Data from the Brazilian MH, 80.90% of the population was vaccinated until September 16, 2022, considering the primary schedule and the first and second booster doses. The first dose was applied in 84.26% of the population; 79.33% received the second or unique dose, and 48.16% received the booster dose [5].

Considering the entire vaccination schedule in Brazil, vaccine mRNA Pfizer was the most applied vaccine, followed by viral vector vaccine AstraZeneca, inactivated CoronaVac, and viral vector vaccine Janssen.

We assessed the associations between the vaccination schedule and the vaccine used in the booster dose. Some studies have shown the effectiveness of vaccines by comparing the vaccine used in the vaccination schedule and the booster dose in a homologous and heterologous regimen. According to literature, heterologous schedules are the best option for immunogenicity [15]. In our sample, 237 students received the booster dose until data collection and most used a different vaccine from the vaccination schedule.

This study is not free of limitations. We highlight the relatively small sample size obtained by convenience and the cross-sectional study design that did not allow a follow-up to verify COVID-19 infection after vaccination and possible later adverse effects.

The most used vaccines for COVID-19 among medical students in the vaccination schedule were inactivated vaccine (CoronaVac) and viral vector vaccine (AstraZeneca). The vaccine mRNA (Pfizer) was the most used vaccine in the booster dose in a heterologous schedule [24]. The vaccines applied were safe, and mild ad- verse effects (i.e., local erythema, fever, myalgia, and headache) and great reactogenicity of the viral vector vaccine (AstraZeneca) were observed compared with inactivated vaccine (CoronaVac), viral vector vaccine (AstraZeneca, and Janssen).

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Disclosure

The author reports no conflicts of interest in this work.

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