The Association between COVID-19 Vaccine Types and Side Effects Following Vaccination: Cross-Sectional Study

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ABSTRACT

Many experts agree and believe that the COVID-19 vaccine is the best way to control the COVID-19 pandemic in a sustainable manner. Each type of vaccine has different side effects and effectiveness. Meanwhile, information regarding the relationship between the type of COVID-19 vaccines and side effects in real populations, especially in Indonesia, is still limited. The aim of this study was to investigate the association between COVID-19 post-vaccination side effects and COVID-19 vaccine type. From April to June 2022, a cross-sectional quantitative study will be conducted in Bekasi City, West Java, Indonesia. The population consists of all 1,885,014 residents of Bekasi City who have received the first dose of COVID-19 vaccination. The samples obtained were 428 respondents from online surveys employing a purposive sampling technique. Among 428 participants, there were 50.50% received Inactivated Virus (Sinovac/Sinopharm), 23.80% Viral Vector (AstraZeneca), and 25.70% mRNA (Moderna/Pfizer-BioNTech). The adjusted analysis showed a significant correlation between the type of viral vector vaccine (OR: 26.60; 95% CI: 11.04-64.30) and the type of mRNA vaccine (OR: 1.80; 95% CI: 1.17-3.04) with side effects of COVID-19 vaccination. There was a correlation between the type of vaccines with side effects after controlled variables of sex and history of infection.

INTRODUCTION

The world's media covered the discovery of the first Coronavirus Disease 2019 (COVID-19) case in Wuhan, China, in December 2019.[1] WHO declared that COVID-19 had been classified as a pandemic on March 11, 2020.[2] According to reports, there were 430,257,564 confirmed cases of COVID-19 worldwide as of February 25, 2022, with 5,922,047 deaths. As of February 25, 2022, there has been 147,568 fatalities and 5,457,775 confirmed cases of COVID-19 reported in Indonesia.[3]

A COVID-19 vaccination, in the opinion of many specialists from several nations, is the greatest option to both permanently contain the pandemic and lower COVID-19-related morbidity and mortality.[4] It is hoped that the COVID-19 vaccination will reduce the incidence of COVID-19 in the future.[5] The Indonesian government had set a target for vaccination at the national level to be 208,265,720 people. As of April 7, 2022, the total dose 1 vaccination throughout Indonesia has reached 197,243,959 doses (94.71%) of the vaccination target.[6]

The types of COVID-19 vaccines available in Indonesia include Sinovac, Sinopharm, AstraZeneca, Moderna, Novavax, and Pfizer-BioNTech. The six types of vaccines have different side effects and effectiveness. Other moderate local side effects including pain, redness, and swelling at the injection site are possible side effects that people may have after receiving the COVID-19 vaccine. Fever, muscular pains, fatigue, feeling unwell, nausea, vomiting, headaches, dizziness, chills, sleepiness, and changes in appetite are just a few of the systemic side effects. The COVID-19 vaccine's side effects are common and safe, thus the general public shouldn't be concerned about them. This proves that the body has reacted to the vaccination, particularly the antigen (molecule that initiates an immune response), and is getting ready to defend itself against the virus. Due to worries regarding vaccination safety and potential adverse effects, many people in various industrialized and developing nations are still apprehensive and reluctant to get the COVID-19 vaccine.[7,8]

It is still unknown if there is a connection between the kind of vaccine and the side effects observed by residents of Bekasi City because descriptions of COVID-19 vaccine side effects by types of vaccine used in the general population are still limited, especially in Indonesia. For example, a study conducted by Supangat et al, which only compared the side effects of one type of vaccine based on the first and the third dose in medical clerkship students in Jember, Indonesia.[9] Then the research conducted by Djanas et al, also only explained the side effects of one type of vaccine on national referral hospital staff in Indonesia.[10] Based on the information provided above, a research was done to ascertain how the kind of COVID-19 vaccination and the side effects in the community of Bekasi City in 2022 relate to one another.

MATERIAL AND METHOD

From April to June 2022, a cross-sectional study conducted in Bekasi City. The results of measuring both local (pain at the injection site, redness, and swelling) and systemic (fever, dizziness, headache, feeling unwell, fatigue, nauseous vomit, muscle ache, chills, sleepy, and changes in appetite) side effects of the COVID-19 vaccination were used to determine the dependent variable. The independent variable is the type of COVID-19 vaccine with measurements of inactivated virus (Sinovac/Sinopharm), viral vector (AstraZeneca), and mRNA (Moderna/Pfizer-BioNTech). Then, there are covariate variables, namely age with cut-off point mean, sex, history of COVID-19 infection, and history of comorbidities such as hypertension, kidney, diabetes, cardiovascular, and respiratory disease. All residents of Bekasi City who received the first dose of COVID-19 vaccination are included in the population. The calculation of the minimum number of samples is carried out using a two-sided hypothesis test formula with a 95% confidence level where P1 = 0.22 and P2 = 0.39 so that the minimum total number of samples is 372 respondents.[11,12]

The number of samples that were successfully obtained in the research was 428 respondents with the criteria of individuals living in Bekasi City, aged 18 years and over, have received the first dose of vaccination evidenced by a vaccination card and filling out the questionnaire completely.

The sampling technique used snowball sampling because the researcher collecting data from the first participants and then asking them to recommend more possible participants who

match the research requirements through social media. Data were collected using an electronic questionnaire (Google Form). Data obtained from the online questionnaire will be checked again by the researcher, whether the answers are complete and appropriate or not. Through social media platforms including WhatsApp, Instagram, Line, and Email, questionnaires were circulated. The distribution of the questionnaire link was carried out for 9 days.

The quantitative phase's data analysis employed a logistic regression model to clarify the adverse effects of various COVID-19 vaccine types. To choose a candidate as the independent variable, a bivariate (chi-square) analysis was carried out initially. In the second stage, the adjusted analysis took into account all parameters (kind of COVID-19 vaccine, history of COVID-19 infection, and history of comorbidities) with a p-value of 0.25 in the first phase. However, the variables of age and sex were analyzed with multivariate analysis because the variables are considered important and considered to be related to the side effects of COVID-19 vaccination. In the multivariate analysis, the crude odds ratio and adjusted odds ratio were evaluated at = 0.05 with a 95% confidence interval (95% CI). SPSS software (27th version, International Business Machines Corp., New York) was used for all statistical analysis. This was given acceptance by the National Veteran Development University of Jakarta's Health Research Ethics Commission, with approval number 302/VI/2022/KEPK.

RESULTS

The number of respondents was 428 people who live in the city of Bekasi. Based on COVID-19 vaccine and demographic data, the majority of respondents received vaccination with the Sinovac (46.30%), the majority of respondents were older than 22 years (64.50%), female (57.70%), had no history of COVID-19 infection (87.90%), and had no comorbid history (90%) (Table 1). The definition of comorbid history is a disease experienced by respondents such as hypertension, diabetes, kidney disease,

cardiovascular disease, respiratory disease. The majority of respondents (50.50%), according to the viral type, had the inactivated virus type vaccination (Table 2). According to COVID-19 side effects, the majority of respondents reported local side effects, such as pain at the injection site (78.30%), and systemic side effects, such as muscle pain (67.50%) and not feeling well (52.30%) (Figures 1 and 2).

Table 1. Distribution of Respondents Based on COVID-19 Vaccines, Demographic Data, History of Infection & Comorbid in Bekasi, Indonesia
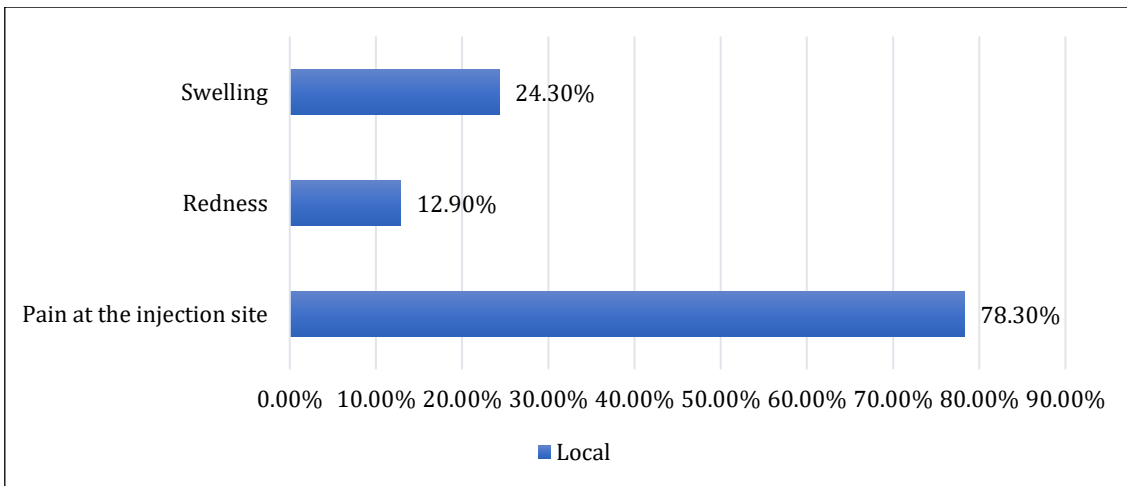
Variable	n = 428	%
Types of COVID-19 Vaccines		
Sinovac	198	46.30
Sinopharm	18	4.20
AstraZeneca	102	23.80
Moderna	12	2.80
Age (Years)		
< 22	152	35.50
≥ 22	276	64.50
Sex		
Male	181	42.30
Female	247	57.70
History of COVID-19 Infection		
No	376	87.90
Yes	52	12.10
Comorbid history		
No	385	90
Yes	43	10

Source: Primary Data, 2022

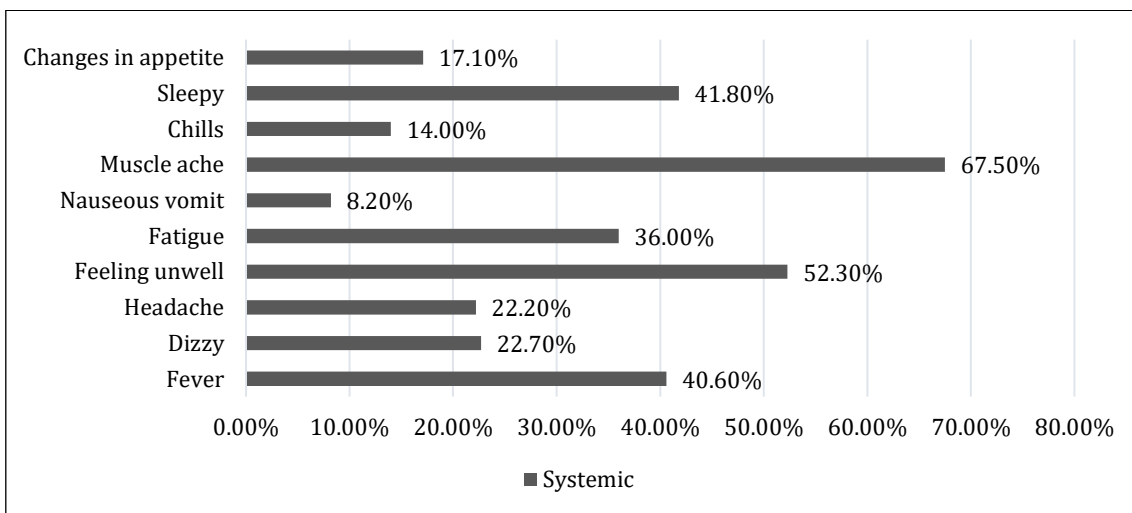**Table 2. Distribution of Respondents by COVID-19 Vaccine Virus in Bekasi Indonesia**

Variable	n = 428	%
Types of Virus Vaccine COVID-19		
Inactivated Virus (Sinovac/Sinopharm)	216	50.50
Viral Vector (AstraZeneca)	102	23.80
mRNA (Moderna/Pfizer-BioNTech)	110	25.70

Source: Primary Data, 2022

Source: Primary Data, 2022
Figure 1. Distribution of Respondents Based on Local COVID-19 Vaccination Side Effects

Source: Primary Data, 2022
Figure 2. Distribution of Respondents Based on Systemic COVID-19 Vaccination Side Effects

According to the results of multiple logistic regression, those who received the COVID-19 viral vector vaccine (AstraZeneca) had a 26.64 times (95% CI: 11.04-64.30) higher risk of developing systemic side effects than those who received the inactivated virus COVID-19 vaccine (Sinovac/Sinopharm). Additionally, respondents who received the COVID-19 vaccination with mRNA (Moderna/Pfizer BioNTech) had a 1.89 times (95% CI: 1.17-3.04) higher risk of developing systemic side effects than respondents who received the COVID-19 vaccination with inactivated virus (Sinovac/Sinopharm) (Table 3).

DISCUSSION

In this study, the main independent variable was the type of COVID-19 vaccine. This type of vaccine is divided into 3 categories according to the type of virus, namely inactivated virus, viral vector, and mRNA. The samples were 428 respondents. The findings indicated that the inactivated viral vaccine (Sinovac/Sinopharm) was a vaccination that the majority of responders had received. According to Hatmal et al.'s research from 2021, the majority of respondents had the Sinopharm vaccine, which uses an inactivated virus.[13]

Table 3. The Relationship Between Types of COVID-19 Vaccines and Side Effects of COVID-19 Vaccinations in Bekasi Indonesia

Variable	Side Effects of COVID-19 Vaccination		Unadjusted		Adjusted	
	Local	Systemic				
	n = 181	n = 247	OR (95% CI)	*p-value*	OR (95% CI)	*p-value*
Types of COVID-19 Vaccines						
Inactivated Virus	128	88	1		1	
Viral Vector	6	96	25.87 (10.67-62.74)	0.00	26.64 (11.04-64.30)	0.00
mRNA	47	63	1.86 (1.15-3.00)	0.01	1.89 (1.17-3.04)	0.00
Age (Years)						
< 22	65	87	1			
≥ 22	116	160	1.04 (0.65-1.65)	0.86		
Sex						
Male	82	99	1		1	
Female	99	148	1.60 (1.01-2.52)	0.04	1.60 (1.02-2.50)	0.03
History of COVID-19 Infection						
No	166	210	1		1	
Yes	15	37	2.21 (1.12-4.37)	0.02	2.20 (1.11-4.35)	0.02
Comorbid History						
No	156	229	1			
Yes	25	18	0.81 (0.41-1.62)	0.56		

Source: Primary Data, 2022

The findings revealed that most respondents had local side effects, namely pain and swelling (Figure 1). The majority of respondents also experienced systemic side effects, such as muscle pain and not feeling well. Similar to this, from the research study of Supangat et al the most common side effects following the first dose were pain at the injection site and malaise.[9] Experiencing some mild to moderate side effects is common when receiving vaccinations. It is proved that the immune system responds to the vaccine, in particular to antigens (substances that trigger an immune response), and prepares to fight the virus.[14]

The findings indicated that the majority of respondents were older than 22. The majority of responders, according to Riad et al.'s study, are older than 22.[15] The majority of respondents in this study are female. A study by Djanas et al which discusses the side effects of COVID-19 vaccination explained that the majority of respondents from this study were also female.[10]

Based only on data from respondents who filled out the Google form, the majority of respondents did not previously have COVID-19 infection. This result is consistent with a study by Tsai et al which found that the majority of respondents had no prior history of COVID-19 infection.[16] Most of the respondents had no history of comorbid conditions. The majority of respondents in Rosiello et al.'s study did not have a history of hypertension, diabetes, heart disease, or lung disease.[17]

After adjusting for the gender variable and a history of COVID-19 infection, the findings of the multivariate analysis revealed a strong correlation between vaccine type and side adverse effects. In comparison to respondents who received the COVID-19 vaccination with the inactivated virus (Sinovac/Sinopharm), respondents who received the COVID-19 viral vector (AstraZeneca) vaccine were 26.60 times (95% CI: 11.044-64.304) more likely to experience systemic side effects. Additionally, respondents

who received the COVID-19 vaccination with the mRNA type (Moderna/Pfizer BioNTech) were 1.80 times (95% CI: 1.17-3.04) more likely to experience systemic side effects than those who received the COVID-19 vaccination with the inactivated virus type (Sinovac/Sinopharm). According to a research conducted in Malaysia by Elnaem et al compared to the Pfizer-BioNTech and Oxford-AstraZeneca vaccines, the Sinovac vaccine showed much less side effects. Depending on the COVID-19 vaccine adminis-tered, different adverse effects may occur after COVID-19 vaccination.[18] According to the study by Alhazmi et al people who received the AstraZeneca vaccine were more likely to have systemic side effects such fatigue and fever than those who received the Pfizer-BioNTech or Sinovac vaccinations.[19]

The AstraZeneca vaccine is a type of viral vector with genetically modified adenovirus that has been attenuated. Adenovirus is a type of virus that can trigger fever (systemic side effect). Moderna and Pfizer-BioNTech vaccines are types of mRNA with components of genetic material that are chemically synthesized and engineered to resemble certain germs or viruses.[20]

The findings of the multivariate analysis revealed a strong correlation between the history of COVID-19 infection and the side effects of COVID-19 vaccination. In comparison to responders without a history of COVID-19 infection, those with a history of infection are 2.20 times more likely to experience systemic side effects after the COVID-19 vaccinations. This result is consistent with a research by Tissot et al which discovered that people with a history of COVID-19 infection usually reported signs of local and systemic adverse effects. This could be attributed to the increased immunogenicity resulting from the COVID-19 vaccination.[21]

Furthermore, compared to male respondents, female respondents were 1.60 times more likely to be at risk of systemic COVID-19 vaccine side effects. Similar with the research of Riad et al that female is a risk factor for the side effects of the COVID-19 vaccine.[22] Young women usually develop a stronger immune response than adult men, so women are more at risk of experiencing the side effects of the COVID-19 vaccination.[23]

Weaknesses of this study is the possibility of information bias because of the online data collection. However, this was done because of data collection during the COVID-19 pandemic.

CONCLUSION AND RECOMMENDATION

The majority of respondents were female, older than 22 years old, without a history of COVID-19 infection and comorbid, and had received an inactivated virus (Sinovac) vaccination. They also reported having local side effects of pain, systemic side effects of muscle pain, and generalized side effects of feeling unwell. After adjusting for gender-specific factors and COVID-19 infection history, there is an association between vaccine type and side effects of COVID-19 vaccination. The COVID-19 viral vector (AstraZeneca) and mRNA (Moderna/Pfizer BioNTech) vaccine types have more systemic side effects than inactivated viruses (Sinovac/ Sinopharm).

The advice that can be given to the community is not to worry if they experience side effects after vaccination. As long as it is available, they can select an inactivated viral vaccination if they desire a vaccine with little side effects. Other researchers are expected to add a second dose of the COVID-19 vaccine and a booster and add other less common side effects for further investigation.

AUTHOR CONTRIBUTIONS

AMS and CS contributed to the conceptualization of the research; AMS collects and processes data; AMS wrote the script; The manuscript and data analysis were evaluated by CS, LH, and UQK. The manuscript's published version has been approved by all authors, who have also reviewed and approved it. AMS = Alifia Maharani Setyoputri; CS = Chandrayani Simanjorang; LH = Laily Hanifah; UQK = Ulya Qoulan Karima.

CONFLICTS OF INTEREST

The authors state that no competing interest exists.

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