ORIGINAL ARTICLE

Comparison of adverse effects following immunisation degree after the administration COVID-19 vaccine of different platforms

Bastiana Bermawi, PhD[1], Adyan Donastin, Pulmonologist[2], Nathalya Dwi Kartika Sari, Clin.Path[3], Diyan Wahyu Kurniasari, Clin.Path[1], Agus Aan Adriansyah, MPH[4], Muhammad Auzan Ferdiansyah, MD[5], Ihsan Fahmi Rofananda, MD[5], Prima Ardiansah Surya, MD[5]

[1]Clinical Pathology Departement, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Indonesia, [2]Internal Medicine Departement, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Indonesia, [3]Health Analyst Study Program, Faculty of Health, Universitas Nahdlatul Ulama Surabaya, Indonesia, [4]Public Health Siences Study Program, Faculty of Health, Universitas Nahdlatul Ulama Surabaya, Indonesia, [5]Research and Community Development Unit, Faculty of Medicine, Universitas Nahdlatul Ulama Surabaya, Indonesia

ABSTRACT

Introduction: Vaccination is an effective way to overcome the spread of Coronavirus Disease 19 (COVID-19). However, it can give rise to adverse event following immunisation (AEFI). AEFI is an important aspect that is assessed in vaccine safety standards. It is assumed that different vaccine platforms can give rise to different degrees of AEFI severity, but so far there have been no studies that discuss the differences in the degree of AEFI on each type of COVID-19 vaccine platform. Aim: Evaluate the differences in the degree of AEFI on each type of COVID-19 vaccine platform.

Materials and Methods: The research used a quantitative analytical observational design with a cross sectional approach. Data collection from participants was carried out by filling out questionnaires. The collected data was tabulated and statistical analysis was carried out.

Results: A total of 217 respondents who received three doses of vaccine participated in the study. Of the 651 vaccine doses studied, the results showed that there were significant differences in the degree of AEFI between the three types of vaccine platforms. The degree of AEFI was significantly different ($p < 0.05$) between each type of vaccine platform, with the degree of AEFI starting from the lowest, namely inactivated vaccine, then viral vector vaccine and the highest was nucleic acid vaccine.

Conclusion: The degree of AEFI differs significantly between each COVID-19 vaccine platform. The degree of AEFI, from the mildest to the most severe, was inactivated vaccine, viral vector vaccine and nucleic acid vaccine. No serious AEFI was reported.

KEYWORDS:
Vaccine, COVID-19, adverse effect

INTRODUCTION

Since the end of December 2019, Coronavirus Disease 19 (COVID-19), an infectious disease caused by the SARS-COV2 virus, has rapidly spread from Wuhan, China, throughout the world and caused a pandemic.[1] WHO designated COVID-19 as a public health emergency of international concern (PHEIC) from 30 January 2020 to 5 May 2023.[2,3] To date (24 September 2023), the number of COVID-19 cases has reached 770 million cases and has resulted in almost seven million deaths.[4]

One way to overcome the impact of COVID-19 is by vaccination. Vaccination aims to form specific immunity against the SARS-COV2 virus, so it is hoped that it can reduce virus transmission, illness and death rates. Apart from that, vaccination is expected to form herd immunity in protecting groups that have contraindications to vaccination. According to a study, COVID–19 vaccination has prevented 14.4 to 19.8 million additional deaths in 185 countries from December 8, 2020 to December 8, 2021.[5]

However, like other vaccines, COVID-19 vaccination are associated with adverse effects following immunisation (AEFI).[1] World Health Organization defines AEFI as any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. AEFI can be caused by immune reactions to vaccine components, procedural errors, anxiety reactions or coincidences with things that are not related to vaccination.[6,7]

In the COVID-19 AEFI vaccination, various types of reactions can occur, starting from no reaction, local reactions such as pain, redness, swelling at the injection site, and severe reactions such as cellulitis, and systemic reactions, namely fever, muscle pain throughout the body (myalgia), joint pain (arthralgia), body weakness, headache. Other reactions can include allergic reactions such as urticaria, edema, anaphylactic reactions and syncope.[8] Severe AEFI can cause morbidity and death for vaccine recipients, and community resistance to vaccination.[9]

Until now, the COVID-19 vaccine circulating in Indonesia can be divided into three based on platform type, namely inactivated vaccine (Sinovac), viral vector vaccine (AstraZeneca) and nucleic acid vaccine (Moderna, Pfizer).[10] These three types of platforms have different types of vaccine

This article was accepted: 21 February 2024
Corresponding Author: Bastiana Bermawi
Email: dr.bastiana@unusa.ac.id

ingredients and additional components, so they have different reactogenicities, and of course this will influence the incidence of AEFI. Until now, the differences in the severity of AEFI on different vaccine platforms circulating in Indonesia are still not clear yet, even though this is an important issue because the presence of AEFI affects vaccine safety and the level of community participation in the COVID-19 vaccination program. Therefore, this study aims to evaluate the differences in the degree of AEFI on each type of COVID-19 vaccine platform.

MATERIALS AND METHODS

Study Design and Population

This research used a quantitative analytical observational design with a cross sectional approach. The population studied was all Indonesian people who had received the COVID-19 vaccine, with the sample being population that met the inclusion criteria, namely: (1) had been administered with two doses of COVID-19 vaccine and (2) filled out the questionnaire completely. The sampling technique in this research was snowball sampling, where participants were recruited online using social media.

A previous study reported AEFI prevalence of about 17% in Jakarta, Indonesia.[11] We used this prevalence data to calculate the sample size in OpenEpi web-based program, using theformula n = [DEFF*Np(1-p)]/ [(d2/Z21-α/2*(N-1) + p*(1-p)] and taking 95% confidence level. This resulted in a requirement of 217 participants.

Respondents submitted the data using an online Google Forms questionnaire (docs.google.com/forms). Before filling out the questionnaire, respondents received an informed consent form provided in Google Forms. By filling in the questionnaire the respondent is deemed to agree to participate in this research. Data collection was carried out in the period from 21 September 2022 to 26 October 2022.

Variables

The variables studied consisted of vaccine platform type and the degree of AEFI. The independent variable was vaccine platform type, which includes inactivated vaccine, nucleic acid vaccine and viral vector vaccine with a nominal measuring scale. The independent variables were the degree of AEFI, which includes no complaints, local AEFI (pain at the injection site) and systemic AEFI (headache or muscle pain, joint pain, chills, fever (body temperature > 37.5°C, fatigue and nausea or vomiting) with an ordinal measuring scale. An online questionnaire was used to measure the two variables.

Statistical Analysis

Data were extracted from Google Forms to Microsoft Excel 2019 for cleaning and coding. Statistical analysis for the data was carried out using SPSS 24.0. Kruskal-Wallis test (p = 0.05) was perfomed to test whether there was a significant difference of the degree of AEFI on different platforms. If there was a significant difference, analysis continued with a post hoc test to assess the differences between different groups.

RESULTS

Demographic Characteristic of Participants

A total of 217 participants were included in this study. A majority of the participants were female (67.3%), and most have education level of diploma/bachelor degree (60.3%). Age varied between participants, from 18 to 65 years old, with a median age of 35 years (IQR: 22-44). Most participants were in the 21 to 30 years age group (32.7%). The demographic characteristic of participants is presented in Table I.

All the respondents received three doses of vaccine, with three different types of vaccine platforms used, inactivated vaccine (Sinovac), nucleic acid vaccine (Moderna, Pfizer) and viral vector vaccine (AstraZeneca), with the number of recipients for each type of vaccine are shown in Table II.

A comparison of AEFI degrees between platforms, along with the results of the Kruskal Wallis test, are shown in Table III. No serious AEFI was reported in our study. The lowest AEFI degrees were found in the inactivated vaccine, while the highest were found in the nucleic acid vaccine. It can be seen that the p-value of the Kruskal Wallis test is less than 0.05, which indicates that there was a significant difference between the degrees of AEFI on the three types of platforms. Since there were significant differences in the degree of AEFI, a post hoc test was done and its results are shown in Table IV.

The post hoc test results showed significant differences ($p < 0.05$) in the degree of AEFI between the three types of vaccine platforms compared to other vaccine platforms.

DISCUSSION

Vaccination is one way to deal with COVID-19, but just like the vaccination of other diseases, it is associated with adverse effects (AEFI). In this study, AEFI from 651 vaccine doses was studied and the results showed that there were significantly different in the degree of AEFI in the three vaccine platforms. The difference in the incidence of AEFI between each type of vaccine platform can be explained by differences in the reactogenicity of the immune system to vaccines.[12]

The lowest degree of AEFI was found after the administration of inactivated vaccine and the majority of inactivated vaccines administration were not followed by AEFI. Majority of viral vector vaccine recipients also did not report AEFI, however the degree of AEFI on this type of vaccine platform was higher than the inactivated vaccines. Administration of nucleic acid had the highest incidence of AEFI among the three vaccine platforms studied, with the majority of vaccine recipients experiencing systemic AEFI. In this study, there were no respondents who reported serious, life-threatening AEFI.

AEFI in COVID-19 vaccination is very common in all types of currently available vaccines,[13] and AEFI can appear in a matter of minutes – days.[14] The results of this study are in accordance with several previous studies, where the incidence of AEFI in the inactivated vaccine and viral vector vaccine was lower than that on the nucleic acid vaccine, and there were more moderate-severe AEFIs after administration of the

Table I: Demographic characteristic of participants (n = 217)

Variable	n	(%)
Sex		
Male	71	32.7
Female	146	67.3
Age (years)		
< 21	25	11.5
21-30	71	32.7
31-40	32	14.7
41-50	62	28.6
51-60	22	10.1
> 60	5	2.3
Level of education		
Primary school	1	0.05
Secondary school	46	21.2
Diploma/bachelor degree	131	60.4
Master degree	39	18.0

Table II: Number of administered vaccine doses

Vaccine platform	1st dose n (%)	2nd dose n (%)	3rd dose n (%)	Total n(%)
Inactivated vaccine	188 (86.6)	181 (83.4)	15 (6.9)	384 (60.0)
Nucleic acid vaccine	8 (3.7)	10 (4.6)	155 (71.4)	173 (26.6)
Viral vector vaccine	21 (9.7)	26 (12.0)	47 (21.7)	94 (14.4)
Total	217	217	217	651

Table III: Comparison of AEFI degrees between different vaccine platforms

Vaccine platform	AEFI degree	n	(%)	*p*-value
Inactivated vaccine	No AEFI	228	59.4	0.000
	Local AEFI	100	26.0	
	Systemic AEFI	56	14.6	
Nucleic acid vaccine	No AEFI	44	25.4	
	Local AEFI	49	28.3	
	Systemic AEFI	80	46.2	
Viral vector vaccine	No AEFI	39	41.5	
	Local AEFI	21	22.3	
	Systemic AEFI	34	36.2	

Table IV: Post hoc test results

Variable comparation	*p*-value
Inactivated vaccine – nucleic acid vaccine	0.000
Inactivated vaccine – viral vector vaccine	0.000
Nucleic acid vaccine – viral vector vaccine	0.012

nucleic acid vaccine.[12,15] A meta-analysis study revealed that administration of nucleic acid vaccine produces more and more severe side effects compared to other platforms.[1,16] However, another study stated that systemic AEFI occurred more often when administering the viral vector vaccine compared to the nucleic acid vaccine.[17] This is because these differences can be caused by the factors of the vaccine itself (such as differences in vaccine components and route of vaccine administration) and other factors (age, race, gender, comorbidities, etc.).[8,17,18] Of these factors, the number of doses administered has the greatest influence on the incidence of AEFI following COVID-19 vaccination.[18]

Even though it causes more severe AEFI, administration of a nucleic acid vaccine is considered safer than the the inactivated vaccine because it is not infectious, so there is no risk of infection and is safe for people with immunocompromised diseases.[12] After the administration of viral vector vaccines, most AEFIs are mild and systemic and very rarely can cause serious side effects in the form of thromboembolism and thrombocytopenia.[13,19] Nucleic acid vaccine may be associated with allergic reactions, which may be caused by the pegylated lipid component used to transport the vaccine's mRNA components into cells.[20] Severe AEFIs was not reported by respondents in this study.

To the extent of the author's knowledge, there has been no similar research discussing AEFI on different types of vaccine platforms in Indonesia. Another interesting thing about this research is that no serious or life-threatening side effects were reported. Severe side effects have been reported in some cases of COVID-19 vaccine administration, these events are very rare when compared with the total dose injected.[11] There are several limitations in this research. The sample used in this

study was small, and dominated by women, so there are limitations in generalisation to the general population. We have a small number of respondents who are over 60 years old. The participants were recruited using social media, which is infrequently used by older people, thus only a few respondents were over 60 years old. Another study conducted in Jakarta, Indonesia, showed that there was no correlation between the adults and elderly age group with the incidence of AEFI.[11] Until today, there were very few serious AEFI recorded in Indonesia and there was no mortality linked to COVID-19 vaccination in Indonesian adults and elderly.[21,22] Thus, we think the result will not be significantly different if more elderly respondents were participating in this study.

In addition, this study compared different types of vaccine platforms as a determinant of the degree of AEFI, but did not assess the existence of other factors that could influence the incidence of AEFI. In this study, the effect of the order and number of vaccine doses received by respondents on the incidence of AEFI was also not assessed. In addition, the use of a cross-sectional approach in this study limits drawing causal relationships between the two variables. Further research is needed to answer issues related to the limitations of this research, and open a wider horizon of knowledge regarding AEFI in vaccination.

CONCLUSION

There are differences in the degree of adverse event following immunisation (AEFI) for each COVID-19 vaccine platform in Indonesia, starting from the lowest inactivated vaccine, then viral vector vaccine and the highest nucleic acid vaccine, and this difference is related to difference in vaccine reactogenicity. Most inactivated vaccine administration caused no AEFI, but viral vector and nucleic acid vaccine receiver reported AEFI, with systemic AEFI more prevalent than local AEFI. Our study found that COVID-19 vaccines used in Indonesia are safe to use, with no serious AEFI reported. Further research is required to find other factors that influence the AEFI of the COVID-19 vaccine in Indonesia.

CONFLICT OF INTEREST

Protocol used in this study has been ethically approved by the Health Research Ethics Committee of Universitas Nahdlatul Ulama Surabaya (No 243/EC/KEPK/UNUSA/2022).

ACKNOWLEDGEMENTS

The authors would like to thank the Universitas Nahdlatul Ulama Surabaya for the support of this research.

REFERENCES

1. Fan YJ, Chan KH, Hung IF. Safety and efficacy of COVID-19 vaccines: a systematic review and meta-analysis of different vaccines at phase 3. Vaccines (Basel) 2021; 9(9): 989.
2. World Health Organization, Geneva. 2020. COVID-19 Public Health Emergency of International Concern (PHEIC) Global research and innovation forum.
3. World Health Organization, Geneva. 2020. Statement on the fifteenth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic.
4. Ritchie H, Mathieu E, Rodés-Guirao L, Appel C, Giattino C, Ortiz-Ospina E, et al. Coronavirus pandemic (COVID-19): our world in data [cited Sep 2023]. Available from: https://ourworldindata.org/coronavirus.
5. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis 2022; 22(9): 1293 1302.
6. Tran VN, Nguyen HA, Le TTA, Truong TT, Nguyen PT, Nguyen TTH. Factors influencing adverse events following immunization with AZD1222 in Vietnamese adults during first half of 2021. Vaccine 2021; 39(44): 6485-91.
7. World Health Organization. 2018. Serious AEFI. [cited January 2024]. Accessed from: https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/aefi/serious-aefi
8. Haas JW, Bender FL, Ballou S, Kelley JM, Wilhelm M, Miller FG, et al. Frequency of adverse events in the placebo arms of COVID-19 vaccine trials: a systematic review and meta-analysis. JAMA Netw Open 2022; 5(1): e2143955.
9. Altman JD, Miner DS, Lee AA, Asay AE, Nielson BU, Rose AM, Hinton K, Poole BD. Factors affecting vaccine attitudes influenced by the COVID-19 pandemic. Vaccines; 11(3): 516.
10. Government of the Republic of Indonesia. Vaksinasi COVID-19. [cited Sept 2023]. Available from: https://covid19.go.id/vaksin-covid19
11. Satari HI, Kaswandani N, Medise BE, Sundoro J, Hadinegoro SR, Leonard E, Putra A, Angkasa PF. Safety profile of inactivated COVID-19 vaccine in indonesian adults. Vaccine X 2023; 14: 100331.
12. Ganesan S, Al Ketbi LMB, Al Kaabi N, Al Mansoori M, Al Maskari NN, Al Shamsi MS, et al. Vaccine side effects following COVID-19 vaccination among the residents of the UAE-an observational study. Front Public Health 2022; 10: 876336.
13. Deng S, Liang H, Chen P, Li Y, Li Z, Fan S, Wu K, Li X, Chen W, Qin Y, Yi L, Chen J. Viral vector vaccine development and application during the COVID-19 pandemic. Microorganisms 2022; 10(7): 1450.
14. Liu Y. Ye, Q. Nucleic acid vaccines against SARS-CoV-2. Vaccines 2022; 10(11): 1849.
15. Baghban R, Ghasemian A, Mahmoodi S. Nucleic acid-based vaccine platforms against the coronavirus disease 19 (COVID-19). Arch Microbiol 2023; 205(4): 150.
16. Kouhpayeh H, Ansari H. Adverse events following COVID-19 vaccination: A systematic review and meta-analysis. Int Immunopharmacol. 2022; 109: 108906.
17. Klugar M, Riad A, Mekhemar M, Conrad J, Buchbender M, Howaldt HP, et al. Side effects of mRNA-based and viral vector-based COVID-19 vaccines among German healthcare workers. Biology (Basel) 2021; 10(8): 752.
18. Beatty AL, Peyser ND, Butcher XE, Cocohoba JM, Lin F, Olgin JE, et al. Analysis of COVID-19 vaccine type and adverse effects following vaccination. JAMA Netw Open 2021; 4(12): e2140364.
19. Vanaparthy R, Mohan G, Vasireddy D, Atluri P. Review of COVID-19 viral vector-based vaccines and COVID-19 variants. Infez Med 2021; 29(3): 328 38.
20. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines — a new era in vaccinology. Nat Rev Drug Discov 2018; 17(4): 261 79.
21. Ministry of Health of Republic of Indonesia. 2024. Vaksinasi COVID-19 Nasional. [cited January 2024] Accessed from: https://vaksin.kemkes.go.id/#/vaccines
22. Ministry of Health of Republic of Indonesia. 2022. Komnas KIPI: Belum ada Kasus Meninggal yang disebabkan Vaksinasi COVID-19 [cited January 2024] Accessed from: https://sehatnegeriku.kemkes.go.id/baca/rilis-media/20220101/1039078/komnas-kipi-belum-ada-kasus-meninggal-yang-disebabkan-vaksinasi-covid-19/