Adverse event following immunisation of adsorbed-inactivated Coronavac (Sinovac) and ChAdOx1 nCOV-19 (Astra Zeneca) of COVID-19 vaccines

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ABSTRACT

Introduction: Countries around the world organised mass vaccinations using various types of vaccines against COVID-19, like inactivated viruses and mRNA. The study aimed to look at adverse events following immunisation (AEFI) of Coronavac® (SIN) and ChAdOx1 nCOV-19 ® (AZ) COVID-19 vaccines in Indonesia.

Materials and Methods: Subjects who received SIN or AZ vaccines were sent questionnaires twice: after they received the first and the second doses of vaccine, respectively. AEFI data on the first- and second-day post-vaccination were collected and analyzed descriptively.

Results: A total of 1547 people vaccinated with SIN vaccine, 529 (33.3%) responded to the first-dose and 239 (47%) to the second-dose questionnaires, whereas 936 people vaccinated with AZ vaccine, 483 (51.6%) answered the first-dose and 123 (25%) to the second-dose questionnaires. Some important AEFIs on the first- and second-day post receiving SIN vs. AZ vaccination were as follows: fever 4% vs 59%; pain at the injection site 27% vs 87%; redness and swelling at the injection site 4% vs 18%; nausea 5% vs 30%; diarrhea 1.8% vs 5.7%, respectively.

Conclusion: SIN seemed to have fewer AEFIs than AZ. Apart from different vaccine materials and excipients, the gap in AEFIs between SIN and AZ could be caused by the distinct population where AZ recipients were more exposed to COVID-19.

KEYWORDS:
AEFI, COVID-19, real-world evidence

INTRODUCTION

Numerous instances of pneumonia with an unknown eatiology were reported to the World Health Organisation (WHO) on December 31, 2019, in Wuhan City, Hubei Province, China. The SARS-CoV-2 new coronavirus was identified as the culprit. The distinctive illness-causing virus has been given the name COVID-19, which was declared pandemic in March 2020. Since then, the disease has expanded, having a significant negative influence on the health and welfare of people and populations around the world. The pandemic has caused major disruptions to the society and the economy across the globe. SARS-CoV-2 vaccines have been produced by numerous nations, organizations, and pharmaceutical firms.[1] The Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and WHO were compelled to grant Emergency Use Authorization (EUA) of the vaccinations because to the urgent necessity for vaccination.[2] It is beneficial to get immunised against the COVID-19 pandemic to stop the disease's spread and transmission. The present emphasis across all nations, including Indonesia, is on planning large immunization campaigns for their populations. Indonesia originally selected Sinovac, a vaccination based on inactivated viruses rather than the mRNA vaccine, from among the several vaccines that were already in use and those that were being developed. The Sinovac vaccine is developed with inactivated virus.

Its phase III clinical trials have been conducted in Indonesia, Brazil and China, with good efficacy results.[3,4] Aside from the vaccine's effectiveness, adverse event following immunisation (AEFI) is also crucial as it often happens within 24 to 72 hours of receiving the shot. Sometimes, reactions persisted for as long as 14 days.[5]

The Sinovac vaccine contains 3 ug/0.5 mL (equivalent to 600 SU per dose) of inactive viruses with aluminium hydroxide adjuvant (Al2OH3), which can also give a crossroads effect.[6,7] Astra Zeneca vaccine, like Sputnik and Johnson & Johnson is based on genetically engineered viral vector (adenovirus).[8] An extremely concerning side effect that can occur during vaccine development is thrombo-embolism, which can occur with or without bleeding and have a variety of symptoms, including cerebral venous sinus thrombosis and pulmonary embolism.[9] Some European countries like Germany, Finland and Denmark have suspended the use of this vaccine. After listening to the WHO Strategic Advisory Group of Experts on

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Table I: Demographics and list of adverse events following immunization

Vaccinated subjects	Coronavac (SIN) NSIN = 1547		ChAdOx1 nCOV-19 (AZ) NAZ = 936		Total	
	First dose n = 530 f (%)	Second dose n = 239 f (%)	First dose n = 483 f (%)	Second dose n = 123 f (%)	First dose n = 1013 f (%)	Second dose n = 372 f (%)
Female*	322 (61)	131 (55)	224 (46)	64 (52)	546 (53.9)	195 (52.4)
Male*	208 (39)	108 (45)	259 (54)	59 (48)	467 (46.1)	167 (44.9)
Fever 1st day	22 (4.2)	6 (2.4)	285 (59.0)	20 (16.3)	307 (30.3)	26 (7.0)
Fever 2nd day	5 (0.9)	3 (1.2)	155 (32.1)	8 (6.5)	160 (15.8)	11 (3.0)
Took pain killer	6 (1.1)	0 (0)	293 (60.7)	20 (16.3)	299 (29.5)	20 (5.4)
Pain at injection site	147 (27.7)	79 (33)	420 (87.0)	70 (56.9)	567 (56.0)	149 (40.1)
Bump at injection site	22 (4.2)	8 (3.3)	86 (17.8)	14 (11.4)	108 (10.7)	22 (5.9)
Drowsiness	112 (21,1)	28 (11,7)	30 (6.2)	12 (9.8)	142 (14.0)	40 (10.8)
Headache	3 (0.6)	6 (2.5)	311 (64.4)	35 (28.5)	314 (31.0)	41 (11.0)
Nausea	30 (5.7)	18 (7.5)	143 (29.6)	8 (6.5)	173 (17.1)	26 (7.0)
Vomit	6 (1.1)	2 (0.8)	19 (3.9)	1 (0.8)	25 (2.5)	3 (0.8)
Bloating	35 (6.6)	16 (6.4)	100 (20.7)	10 (8.1)	135 (13.3)	26 (7.0)
Diarrhea	10 (1.9)	5 (2.0)	27 (5.6)	9 (7.3)	37 (3.7)	14 (3.8)

Immunisation (SAGE) opinion, WHO finally approved the use of Astra Zeneca vaccine.[10]

In accordance with the national vaccination program; Sinovac, Astra Zeneca and Moderna vaccines have been used and given to the people through many public and private-sectors. The aim of the study was to assess and compare AEFIs between Sinovac and Astra Zeneca vaccines, as real-world evidence.[11,12]

MATERIALS AND METHODS

Universitas Kristen Indonesia organised a mass vaccination program. The vaccine was supplied by the Community Health Center of Kramat Jati, Jakarta. Vaccination was carried out in March to April 2021.

Two sets of questionnaires were developed to assess the AEFIs, each of which was developed for the first and second dose of vaccination.

AEFI data included symptoms on the first- and second-day post vaccination (fever, pain and swelling at the injection site, headache, vomiting, bloating, and/or diarrhea); as well as actions taken by the respondents if they experienced adverse events (i.e., pain-killers, consultation to health care workers, etc.).

Indonesian FDA approved the vaccination with SIN and AZ, which was carried out in accordance with the protocols outlined in the product description. Two separate 0.5 ml doses of Sinovac were administered; the second dose were given four weeks after the first dose.[13] The AZ vaccination consists of two separate doses of 0.5 mL each; where the second dose were administered between 4 and 12 weeks (28 to 84 days) after the first dose.[14]

The survey was ethically approved by the Ethical Committee: No. 15/Etik Penelitian/FKUKI/2021. An online questionnaire using Microsoft Form was distributed to all vaccine recipients recorded by the committee via WhatsApp (WA). The questionnaire consists of 14 questions for Sinovac respondents and 17 questions for Astra Zeneca respondents consisting of (1) demographics information (gender, age), (2) adverse effects, which were divided into nervous system and brain, skin, digestive system, and other adverse effects and (3) Actions taken by respondents if they experienced adverse effects. In the questionnaire for AZ respondents, we added questions on whether they were diagnosed or have had thrombose and had or were receiving blood thinning therapy.

The first questionnaire was sent to all first dose vaccine recipients and those who responded were sent the second questionnaire following the second dose. To increase response rate, each questionnaire was sent three times with one-week interval. Data were extracted from the MS forms. Distributions of the demographics, AEFIs and actions taken by the respondents were analysed descriptively. Analysis was done using SPSS version 25 (IBM, Armonk, NY, USA).

RESULTS

There was a total of 1574 subjects who were vaccinated with SIN and 936 subjects with AZ vaccines. In the SIN group 529 subjects responded (response rate 33%), whereas in the AZ group there were 483 respondents (response rate 51.6%). The response rate for the second questionnaire was lower in the AZ group. The low response rate could have occurred due to the delivery of the questionnaire through the WhatsApp application, in which people could receive hundreds of notifications per day. This could have made respondents did not pay attention to notifications of the questionnaire sent to them, despite our effort to send each questionnaire three times with one-week interval. This study was not a clinical trial with strict protocols that should be followed by subjects to increase adherence to the treatment. In this study, subjects were voluntarily asked to fill-out the questionnaire sent to them. Although web-based survey has many advantages such as: wider spread of distribution, lower cost, and efficient, comparison studies between web-based versus paper-based survey showed that response rate of wed-based or internet-based survey were lower up to 10-20% than paper-based.[15]

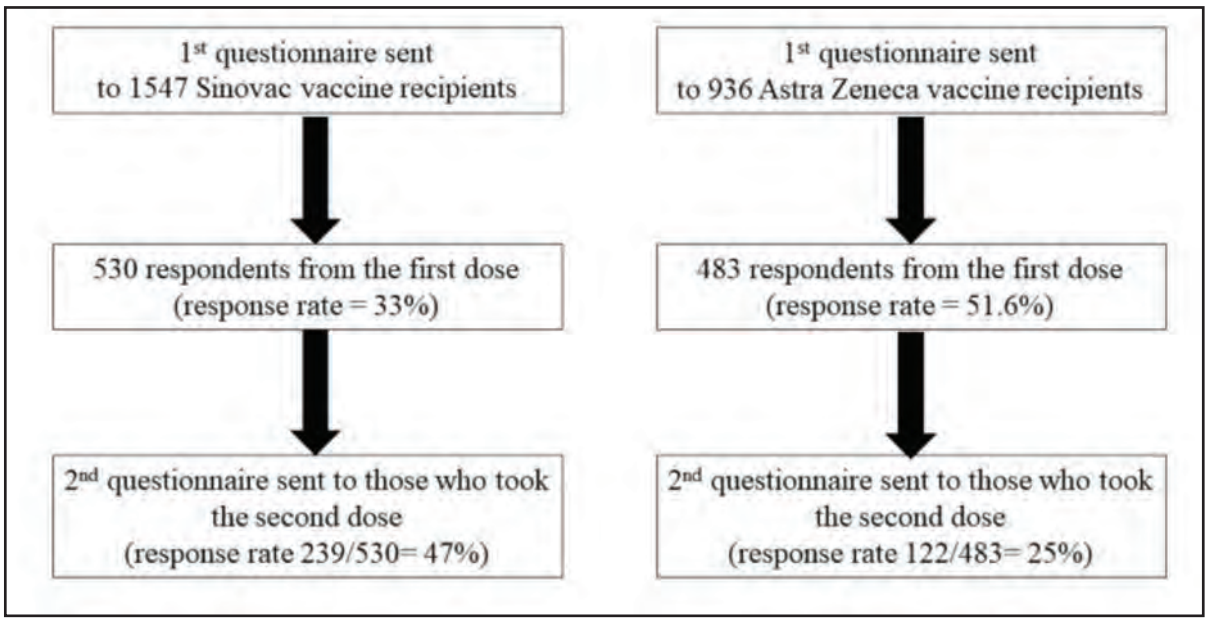

Fig. 1: Respondents' recruitment and number of subjects who responded to questionnaire.

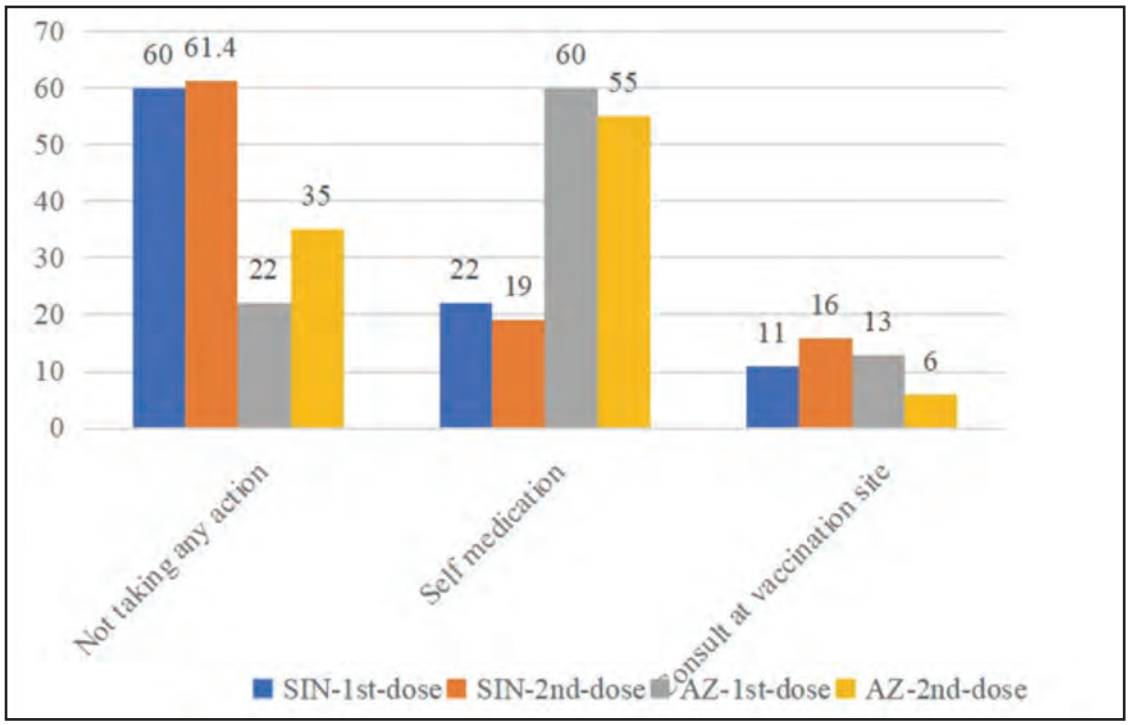

Fig. 1: Percentages of actions taken to the adverse effects experienced by the COVID-19 vaccine recipients (numbers represent percentages of respondents within each group of vaccine). SIN: Sinovac; AZ: Astra Zeneca.

The AEFI is shown in Table I, the most prominent adverse event in both vaccine groups was pain at the injection site, whereas the percentage was higher in the AZ than the SIN group (58.6% vs 20.5%, respectively). Fever both on the first day and the next day is also more prominent in the Astra Zeneca group. Overall, the percentages of AEFIs appeared to decrease after the second-dose compared to the first-dose of the vaccine. In contrast, drowsiness was more prominent in the SIN group than AZ. While the headaches were more in the AZ group. According to the Centers for Disease Control and Prevention (CDC), pain at the injection site was the most commonly reported local reaction among Pfizer-BioNTech COVID-19 vaccine users aged 18 to 55 years, and the percentage decreased after the second injection.[16,17]

Out of 483 AZ first dose vaccine recipients, 28 acknowledged that prior to vaccination they were diagnosed with symptoms of thrombo-embolism and 12 of them taking blood thinning

drugs such as Aspilet® or Ascardia®, which contains acetylsalicylic acid (n = 3); clopidogrel (n = 4), Plavix® (a brand name of clopidogrel, n = 1), or other blood-thinning medications (n = 4). No vaccine-induced immune thrombotic thrombocytopenia (VITT), or anaphylaxis reaction reported by recipients in both vaccine groups. Although it is possible that thromboembolism may occur. However, with the national integrated AEFI reporting system, if a vaccine recipient subject reports a severe AEFI, the local vaccine injection centre will be informed.

Figure 2 demonstrated actions taken by the vaccine recipients in the presence of adverse effect. Only a few respondents (≤3%, not shown in the figure) who consulted their concern to the nearest public health center, doctor, or hospital. None reported a severe adverse effect that required further treatment in the hospital. In the implementation of this mass immunization, the government established a tiered reporting system. If there are complaints that are directly felt by the subject after vaccination, can be directly handled by the doctors who serve at the vaccination sites. Interestingly, 60% respondents in AZ group (first dose) and 55% (second dose), whereas, in SIN group only 22% (first dose) and 19% (second dose) who took self-medication. It is certainly shown that more respondents in the SIN group did not take action for the side effects. This suggests that most of the adverse events in the SIN group were milder than AZ group (Table I). This also in accordance with a meta-analysis study by Chen at al., the AEFI report due to inactivated vaccines was lower than other types of vaccines.[18]

DISCUSSION

In general, the results of our analysis of the data from the AZ group were generally consistent with those of Jeon et al, who observed that the two AEFIs that were most frequently reported were tenderness at the injection site (94.5%) and fatigue (92.9%). Both the severity and number of AEFI were lower in the older age group. Sultana no significant incidents necessitated further medical treatment, and the majority of AEFIs subsided within a few days.[19] Recent report on safety of AZ (EudraVigilance) has added information that 28 people consisting of 19 women and nine men were diagnosed with AEFI associated with thrombosis problem, such as deep vein thrombosis (DVT), pelvic vein thrombosis, pulmonary embolism, etc. Three people died and six did not recover.[20] In our study, none reported VITT nor anaphylaxis reaction. As is stated elsewhere, the aetiology of AEFI due to inactivated virus could be from its vaccine material or its excipients. While the problem of thrombosis that appeared in the group of subjects who were vaccinated with Astra Zeneca triggered the expression of antiplatelet antibodies.[21] In contrast to our study, Hyun et al discovered that patients who got the ChAdOx1 nCOV-19 (AstraZeneca) vaccination experienced substantial adverse effects after just one dosage, including polyarthralgia and myalgia syndrome that lasted up to 47 days.22 Other non comparison study by Jain et al (2022) showed AEFI with ChAdOx1 nCOV-19 vaccine was generally mild and moderate, although one case of severe allergic reaction was obtained (mild – 31 [83.7%]; moderate – 5 [13.5%] and severe – 1 [2.7%]), respectively.[23] Although our study showed higher AEFI in AZ group than SIN, which may be due to differences in vaccine ingredients and excipients, no severe AEFI was found as other studies reported. In our center, AZ vaccine was administered to anyone, not limited to healthcare workers (HCWs). Profession with higher exposure to COVID-19 such as HCWs might pose higher risk of AEFIs.[24] However, unfortunately data on occupation (health care workers vs non health care worker) was not available.

CONCLUSION

This study focuses on the adverse events following immunisation (AEFI) of the Sinovac and Astra Zeneca COVID-19 vaccines and presents real-world evidence. Sinovac appeared to have fewer AEFI than ChAdOx1 nCOV-19 (Astra Zeneca), according to this investigation. No major adverse event, such vaccine-induced immune thrombotic thrombocytopenia or anaphylactic reaction, occurredA total of 60% respondents from the SIN group did not take any action concerning the adverse effect they experienced. On the contrary, 60% AZ vaccine recipients at least took pain-killer to reduce the pain at the injection site and their fever. To overcome AEFI, especially fever, respondents preferred self-medication. The limitation of this study is that the response given by respondents was not confirmed by medical examination. The response rate is small, especially the response obtained from the second dose of vaccination.

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