EVALUATION COMPARISON BETWEEN ASTRAZENECA AND MODERNA VACCINE'S SIDE EFFECTS AND EFFICACY AMONG INDONESIA SOCIETY BASED ON SOCIODEMOGRAPHY

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ABSTRACT

Objective: To evaluate the potential side effects and efficacy also to find the risk factors that contributed to the side effects of both vaccines in Indonesia.

Methods: This is a prospective cross-sectional study was conducted in October-December 2021; informations collection was carried out by using a standardized questionnaire and disseminated through social media. All full-dosed AstraZeneca and Moderna vaccine participants above 18 y old were included.

Results: Among 406 participants, 73.4% were female, 87.2% were in the group of 18-30 y, 80 % were Java race, and 52.6% of them had asthma. In this study, the number of participants between AstraZeneca and Moderna was almost the same (50.5% and 49.5%). The most common side effects experienced after first of AstraZeneca and Moderna vaccine were fever (65.8% and 45.3%) respectively, sore arm (77.5% and 63.6%) respectively, headache (52.7% and 40.8%) respectively, and drowsiness (64.4% and 53.7%) respectively. After the second dose were fever (26.8% and 55.2) respectively, nausea (4.8% and 18%) respectively, diarrhea (0.5% and 5%) respectively, headache (27.3 and 44.8%) respectively and allergic reaction or skin rash (1% and 6%) respectively. After the first and second dose, participants with the AstraZeneca vaccine were most likely to get infected by COVID-19 (6.3% and 4.3%), respectively.

Conclusion: Both AstraZeneca and Moderna vaccines' most common side effects were mild-moderate such as fever, sore arm, headache, drowsiness, and nausea. Several risk factors contributed to the side effects, such as younger age (median: 22), and female participants, and non-overweight BMI (median: 21.8).

Keywords: Vaccine, COVID-19, Side effects, Risk factors

INTRODUCTION

The first case of pneumonia outbreak was reported in Wuhan, Hubei China and it is found to be a novel coronavirus related to Sars-Cov-2 (severe acute respiratory syndrome coronavirus 2) [1]. The most common clinical characteristic of COVID-19 were including fever (98.6%), fatigue (69.6%), dry cough (59.4%), myalgia (34.8%), and dyspnea (31.2%) [2]. A study found that there is an association between increasing age and death, where 100% of 79-85 y old patients died during the treatment of COVID-19 [3]. Patients with pneumonia and multiple comorbidities also have a higher risk of undergoing longer treatment and have a higher mortality rate due to inadequate response to the treatment [4].

SARS-CoV-2 outbreak that was reported in the middle of December 2019 led to a worldwide crisis; numerous lockdowns have been implemented in hundreds of countries that are affected by the COVID-19 outbreak [5]. The number of daily deaths has been increasing since early 2020; according to the Indonesian COVID 19 handling force the recent data for December 22nd, 2021 showing new cases for 4.260.893 and 144.024 deaths [6]. In response to the COVID-19 outbreak, several companies and countries have been producing and distributing vaccines around the world to prevent the spread of COVID-19 and to protect people with high-risk complications [7], and develop herd immunity in society.

The vaccine is used to expose a recipient to a non-infectious substance of a pathogen that can cause disease, the vaccine can stimulate recipients' immune system to prevent or reduce the possibility of infection to the exposed pathogen in the future [8]. There are several types of vaccine around the world namely: life attenuated vaccine; this vaccine used a pathogen strain that has been weakened to be non-infectious in non-human tissue, this strain is then injected into a recipient and will be recognized by the immune system; this vaccine is mostly used for influenza, polio, typhus, measles, mumps, and rubella [8, 9]. Inactivated vaccine acts similarly to live attenuated vaccine however this vaccine can produce a weaker

immune system than live attenuated vaccine, where a recipient can lose their immune memory over time [10, 11]. Sub-unit/recombinant vaccine is currently used for Hepatitis B, HPV. A DNA vaccine is generally used for influenza, HIV, malaria, TB, and leishmaniasis [12].

Currently, Indonesia has been using 6 types of COVID-19 vaccines two of the vaccines used are AstraZeneca and Moderna. AstraZeneca is one of the vaccines for treating SARS-CoV-2 was developed at Oxford University consisting of a replication-deficient chimpanzee adenoviral vector containing SARS-CoV-2 structural glycoprotein antigen (spike protein; n-CoV-19) gene [13]. According to the research that was conducted in 3 different continents the number for the efficacy of AstraZeneca vaccine is 70,4% after two doses and 64,1 % after one standard dose is given; according to research conducted in the UK, South Africa, and Brazil the percentage of protection of AstraZeneca vaccine was varied between the UK with 60,3% efficacy and Brazil 64,2% [13]. A research was conducted in Ethiopia reporting the data about side effects after being injected with AstraZeneca vaccines showing among 672 participants, 63,53% experienced pain, and 57,89% experienced tenderness, among 70,89 % experienced mild symptoms with 52,08% and 50,15% reported tiredness and headache lastly only 6,1% experienced severe symptoms [14].

On the other hand, the Moderna vaccine also has been one of the preferred vaccines as it has a higher efficacy which is 94-95% vaccine efficacy that was tested in less than a year [15, 16]. Moderna vaccine is recommended for 18 y old people and has been proven to have benefits in preventing SARS-CoV-2 [16]. According to research in Saudi Arabia including 3732 participants with 2489 received Moderna vaccine and 1243 participants received placebo for first and second doses, reported participants in the Moderna vaccine group experience pain in injection site 93,1% and 92,4% respectively, participants who experienced headache 44,6% and 70,2% respectively, and fatigue in 47,9 and 67,8% respectively [17].

In the middle of December, Indonesia became the country with the highest Covid-19 cases in Southeast Asia [18] At the same time,

there are approximately 39% of Indonesian people have received the full dose of the vaccine [19] therefore the government still has to pursue the target of vaccinating 70% of the Indonesian population by the end of December 2021 [20]. There are still some concerns regarding potential side effects and efficacy of these Vaccines in Indonesia because of the lack of information and research and the lack of trust in government and manufacturers; therefore this study aims to provide and compare the data about side effects and to evaluate the risk factors that contribute in side effects post-vaccination also to compare the efficacy of AstraZeneca and Moderna vaccination in Indonesia.

MATERIALS AND METHODS

Study design

This is a prospective randomized cross-sectional study was conducted in October-December 2021. A standardized questionnaire was utilized to collect the data from Indonesian respondents. The questionnaire included personal data including (age, weight, height, gender, and residency), clinical data including (comorbid disease), and vaccine data, including (vaccine type, COVID-19 vaccination date, side effects) was given via google form.

Participants

Participants were 406 of Indonesian citizens spread across Sumatera, Kalimantan, Java, Sulawesi, Bali and Nusa Tenggara islands. Individuals aged>18 who have received AstraZeneca or Moderna vaccine full dosed.

Ethical approval

This study was reviewed and approved by the University of 17 August 1945 Jakarta ethical committee on November 23rd, 2021 (No.05/KEPK-UTA45JKT/EC/EXP/11/2021). Participants had been given and submitted a consent form before research.

Statistical analysis

The results collected were analyzed using Statistical Package for the Social Sciences (SPSS) software version 25. Descriptive statistics were carried out for demographic variables and medical data. Fisher's exact, Chi-square, Mann-Whitney U test, and Kruskal-Wallis test were used to find an association between risk factors and side effects. A P-value of ≤ 0.05 was considered significant.

RESULTS

Lately, COVID-19 vaccination has been implemented by the Indonesian government, with the number of second vaccination recipients being 37.9% of Indonesia's population as of December 2021 [21]. In this study, we conducted in 406 participants, where 205 participants had received AstraZeneca vaccine and 201 participants had received Moderna vaccine full dosed. Participants received the questionnaire through social media platforms i. e: Facebook, Instagram, WhatsApp, and Twitter.

Demographic characteristics

In total 410 participants, we excluded 4 participants as they did not meet the inclusion criteria in this study, 406 participants consisted of 108 men (26.6%), and 298 women (73.4%) with the most age range is 18-30 y old (87.2%), the participants also spread across several regions in Indonesia, about 1.5% participants are from Sumatera, 12.6% from Kalimantan, 80% from Java, 3.9% from Bali, 1.2% from Sulawesi lastly 0.7% from Nusa Tenggara [table 1].

Table 1: Demographic character of study population N= 406

Variables	Frequency	Percentage
Gender		
Male	108	26.6
Female	298	73.4
Age		
18-30	353	87.2
31-49	43	10.3
50-66	10	2.5
Domicile		
Sumatera	6	1.5
Kalimantan	51	12.6
Jawa	325	80
Bali	16	3.9
Sulawesi	5	1.2
Nusa Tenggara	3	0.7
Comorbidity		
Asthma	10	52.6
HTN	3	15.8
Diabetes	2	10.5
Diabetes+HTN	1	5.3
Autoimmune	1	5.3
Antiphospolipid syndrome	1	5.3
Hepatomegaly with fatty liver	1	5.3
Vaccine type		
AstraZeneca	205	50.5
Moderna	201	49.5
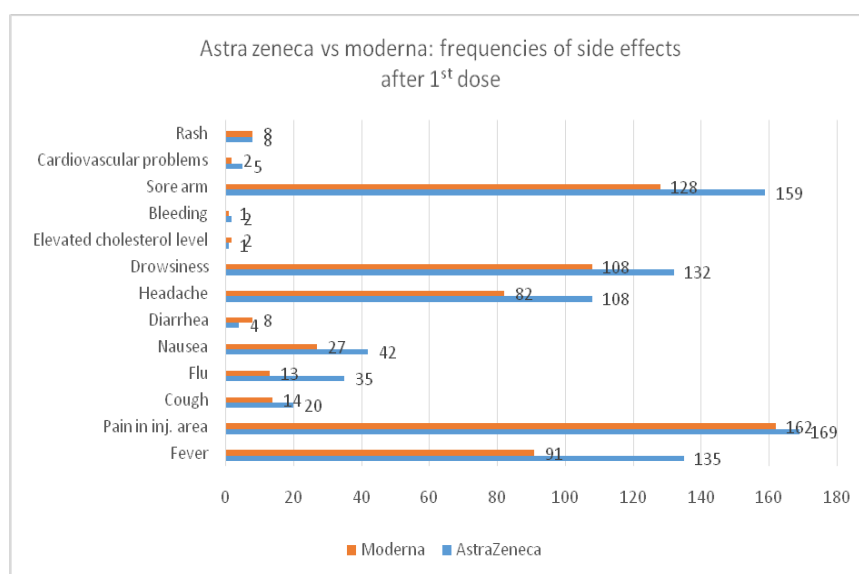
Fig. 1: Astra zeneca vs moderna: frequencies of side effects after 1st dose
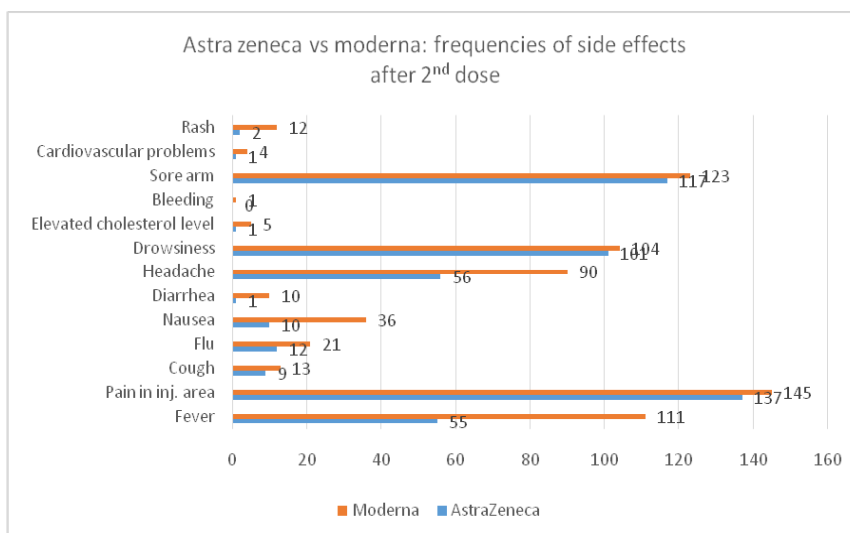
Fig. 2: Astra zeneca vs moderna: frequencies of side effects after 2nd dose

The most common side effects after the first dose of vaccination were fever after AstraZeneca and Moderna vaccination, respectively (65.8% and 45.3%), sore arm respectively (82.4% and 80.6%), headache respectively (52.7% and 40.8%), drowsiness respectively (64.4% and 53.7%), nausea respectively (20.5% and 6.5%) and cardiovascular problems, respectively (2.4% and 1%). Meanwhile, in the second vaccination, the most common side effects from AstraZeneca and Moderna vaccine were fever respectively (26.8% and 55.2%), sore arm respectively (66.8% and 72.1%), headaches respectively (27.3% and 44.7%), drowsiness respectively (49.2% and 51.7%) nausea respectively (4.9% and 18%) and cardiovascular problems respectively (0.5% and 2%). And allergic reaction like skin rash only occurred in 2 participants with AstraZeneca vaccine and 12 participants with Moderna vaccine (3.4%), as shown in fig. 1 and fig. 2.

Association of vaccine types with side effects

Table 2: Correlation between the type of vaccine and side effects

Variables	Frequency		p-value
	AstraZeneca (n=205)	Moderna (n=201)	
Mean age			
Gender			0.032*
Male	45(22.0)	63 (31.3)	
Female	160 (78.0)	138 (68.7)	
Side effects 1st vaccination			
Fever	135 (65.8)	91 (45.3)	0.000*
Sore arm	159 (77.5)	128 (63.6)	0.002*
Headache	108 (52.7)	82 (40.8)	0.01*
Drowsiness	132 (64.4)	108 (53.7)	0.034*
Covid-19 infection after 1st dose	13 (6.3)	2 (1)	0.006*
Anosmia	14	2	0.004*
Fever	102	74	0.009*
Headache	101	65	0.001*
Side effects 2nd vaccination			
Fever	55 (26.8)	111 (55.2)	0.000*
Nausea	10 (4.8)	36 (18)	0.000*
Diarrhea	1 (0.5)	10 (5)	0.005*
Headache	56 (27.3)	90 (44.8)	0.000*
Skin rash	2 (1)	12 (6)	0.006*
Covid-19 infection after 2nd dose	9 (4.3)	1 (0.5)	0.020*
Fever	41	87	0.000*
diarrhea	3	14	0.006*
Headache	50	74	0.007*
Monitoring after 1-3 mo			
Irregular menstruation	24 (8)	46 (15.4)	0.000**

*Fisher exact test, **chi-squared test

The side effects of post-vaccination have a significant correlation with both vaccines. Based on the data above with the highest reported side effect incidents of the first dose were found in AstraZeneca participants; otherwise, the highest reported side effect incidents of the second dose were found in Moderna participants. participants with the AstraZeneca vaccine had a higher chance to be infected with COVID-19. On monitoring one, to three months, we found reports in female participants, where there were menstrual problems. This result was found to be highest in Moderna vaccine recipients (15.4%) as shown in table 2.

Association of risk factors with side effects

Table 3: Correlation between age and side effects

Variables	Frequency	p-value
	Age (n: 406 median: 22)	
Side effects 1st vaccination		
Sore arm	331 (81.5%)	0.048#
Headache	190 (46.8%)	0.028#
Drowsiness	240 (59.1%)	0.002#
Fever	176 (43.3%)	0.049#
Cough	50 (12.3%)	0.005#
Side effects 2nd vaccination		
Drowsiness	205 (50.5%)	0.005#
Difficulty of breathing	12 (3%)	0.025#

#Mann-Whitney test, Age was found to be one of the risk factors of side effects post-vaccination with a median of 22 y old as shown in table 3.

Table 4: Correlation between gender and side effects

Variables	Frequency		p-value
	Male (n=108)	Female (n=298)	
Side effects 1st vaccination			
Sore arm	59 (54.6%)	228 (76.5%)	0.000*
Drowsiness	50 (46.3%)	190 (63.75%)	0.002*
Fever	38 (35.18%)	138 (46.3%)	0.046*
Side effects 2nd vaccination			
Sore arm	46 (42.6%)	194 (65.1%)	0.000*
Drowsiness	45 (41.67)	160 (53.7%)	0.032*
Fever	24 (22.2%)	104 (34.9%)	0.015*
Diarrhea	7 (6.4%)	4 (1.3%)	0.005*

*Fisher exact test, Most of the female participants experienced sore arm side effects after the first and second dose (76.5% and 65.1), respectively. Male participants reported the most diarrhea after the second vaccination than female participants (6.4%), as shown in table 4.

Table 5: Correlation between BMI and side effects

Variables	Frequency	p-value
	BMI (n: 406 Median: 21.8)	
Side effects 1st vaccination		
Cough	34 (8.4%)	0.018#
Sore arm	287 (70.7%)	0.048#
Side effects 2nd vaccination		
fever	166 (40.9%)	0.037#
flu	33 (8.1%)	0.044#
Headache	146 (36%)	0.033#
Cardiovascular problems	5 (1.2%)	0.021#
Headache	124 (30.5%))	0.031#
Fatigue	89 (22%)	0.021#
Irregular menstruation	70 (17.2%)	0.034##

#Mann-Whitney test##Kruskall-Wallis test, BMI also had a significant correlation with side effects post-vaccination with a median of 21.8 as shown in table 5.

DISCUSSION

To our knowledge, this is the first study to evaluate the potential side effects affected by risk factors post-AstraZeneca and Moderna vaccination in Indonesia. This study involved 406 fully vaccinated participants who were given a questionnaire regarding the side effects of the vaccine they experienced. According to WHO the common side effects after vaccination were pain at the injection site, fever, fatigue, headache, muscle pain, chills, and diarrhea with a less common side effect being a severe allergic reaction [22]. In this current study, we compare both side effects of vaccines (fig. 1 and fig. 2) with a study conducted in Iraq; there were slightly different results, with the AstraZeneca vaccine side effects were fever (68.4%), sore arm (54.2%), headache (48%), and nausea (10.3%) and cardiovascular problems (1%)[23], and a study that has been done in the US, the side effects of the Moderna vaccine were fever (35.65%), headache (59.26%), sore arm (94.21%), nausea (26.62%) and chest pain (1.85%) [24].

In the current study, there was a significant correlation between side effects and efficacy with vaccine type. AstraZeneca is a vaccine made by Oxford, which is a type of Adenoviral vector vaccine, while Moderna is a type of mRNA (messenger ribonucleic acid) vaccine [14]. mRNA was made of the blueprint of protein of a pathogen and is non-infectious and does not enter the nucleus or alter the DNA [25, 26].

Based on this current study that has been conducted on respondents who have received the AstraZeneca and Moderna vaccine, it has been found that on average the recipients of the second full dose of vaccine experienced mild to moderate side effects, the most side effects reported for the first vaccination were felt by AstraZeneca vaccine recipients, with the presentation of mild side effects being mild to moderate, common side effects are fever (65.8%) $p= 0.000$, sore arm (77.5%) $p= 0.002$, headache (52.7%) $p= 0.01$ and drowsiness (64.4%) $p= 0.034$. Meanwhile, there was a significant difference in the second vaccination where the side effects felt by

respondents from the AstraZeneca vaccine were quite low, while the recipients of the second dose of Moderna vaccine experienced a large increase in the frequency of side effects. The percentage of side effects experienced by recipients of the second dose of Moderna vaccine is as follows; fever (55.2%) $p=0.000$, nausea (18%) $p=0.000$, diarrhea (10%) $p=0.005$, headache (44.8%) $p=0.000$ and rash (6%) $p=0.006$ as shown in table 2. This finding is consistent with a study conducted in Korea where the adenoviral vector type vaccine caused more adverse events at the first dose, while the mRNA vaccine caused more adverse events at the second dose, namely pain in injection site (75.2%), fatigue (53.9%), headache (46.7%), myalgia (44%) and fever (21.5%)[27]. Furthermore, the efficacy of each type of vaccine is determined from the frequency of individuals who were infected by COVID-19 after receiving the vaccine, with the highest efficacy being owned by the Moderna vaccine; from the study recently, it has been found that after the first vaccination there were 13 (6.3%) cases of COVID-19 infection in recipients of AstraZeneca vaccine, while the respondents who received the Moderna vaccine were 2 cases (1%). Meanwhile, after the 2nd vaccination, there were 9 cases of COVID-19 infection in AstraZeneca vaccine recipients and 1 case of COVID-19 infection in Moderna vaccine recipients, see table 3. This finding is very relevant with previous studies that have been conducted in 15,209, where the mRNA 1273 vaccine had greater efficacy than AstraZeneca, which was 93.2% [28], whereas the adenoviral vector or AstraZeneca vaccine has an efficacy of 74% [29]. The presence of skin rash felt by Moderna vaccine recipients (6%) and AstraZeneca (1%) was also reported in this study, Moderna vaccine recipients are more likely to experience a side effect of skin rash, this is due to a hypersensitivity or minor reaction local allergic reaction in individual Moderna vaccine recipients [30]. Moderna vaccine had a greater effect on the menstrual cycle (15.4%) than the AstraZeneca vaccine ($p=<0.000$) and there was a significant statistical relationship between the menstrual cycle and the type of vaccine. In contrast, a study in the UK showed there is no relationship between the brand of vaccine and the menstrual cycle, while the factors that can cause changes in the menstrual cycle are: hormonal contraception those who are diagnosed with endometriosis or PCOS [31].

We found several risk factors that could affect the side effect incidents of the COVID-19 vaccine in this study, such as age, gender, type of vaccine received, comorbidities, and body mass index (BMI) status. From the studies that was brought, most of the side effects felt by young people (median: 22 y old), while the side effects felt were; sore arm (81.5%) p= 0.048%, headache (46.8%) $p=$ 0.028, drowsiness (59.1%) $p=$ 0.002, fever (43.3%) $p=$0.049,cough (12.3%) $p=$ 0.005, and difficulty of breathing (3%) $p=$0.025 see table 3, while respondents who are older have lower side effects.

We also found a study conducted in the Czech Republic on 877 health workers who had received the Pfizer vaccine, showing a general incidence of adverse events in the≤43 age group [32], These two findings are also consistent with reports from the Food Drug Administration which showed that individuals>55 y of age were less likely to experience significant side effects [33]. This result was found due to the Immunosenescence phenomenon where there is a decrease in functional capacity and a reduction in the efficiency of the immune system with increasing age, in other words, older individuals experience a reduction in antibody production [34], This is because in old age there is a reduction in interleukin-2 while there is an increase in the production of interferon-γ and interleukin-4 [35]. Moreover, we also found a higher frequency of side effect incidents in the female gender group, with 45.6% of women from the total population experiencing side effects from the first dose, while only 37.6% of women from the overall population experiencing side effects from the second dose. The most frequently felt by the female sex group after the second vaccination was sore arm($p=$0.000), drowsiness ($p=$0.032), and fever ($p=$0.015), see table 4. (45.3% women and 12% men), Our results can be compared with a study conducted by a vaccination center in Germany, they found that the female gender group was more likely to experience side effects from COVID-19 vaccination (79.1%)[34]. This is because women have higher antibody titers where women produce higher interleukin-6 than men; these antibodies are related to the concentration of estradiol or the female hormone [36].

The third risk factor found was BMI (Body Mass Index), our study showed that non-overweight individuals had a higher likelihood of experiencing side effects from the COVID-19 vaccine, than in our study, individuals who experienced a side effect of coughing (p =0.018), fever ($p=$0.037), flu ($p=$0.044), headache ($p=$0.033), cardiovascular problems ($p=$0.021), fatigue ($p=$0.021), and irregular menstruation ($p=$0.034) were those with BMI status underweight-normal weight, while the side effect of the sore arm ($p=$0.048) was statistically significant among each BMI range. our results are comparable to a study conducted in the Spain community in that non-overweight individuals are more likely to experience adverse effects from COVID-19 vaccination; fever (underweight: 25%, normal: 14.8%, overweight: 13.2%, obese: 10.9%), headache (underweight: 58.3%, normal weight: 23.2%, overweight: 20.3, obese: 25.5%) [37]. There has been no further investigation regarding the relationship between BMI and the side effects of COVID-19 vaccination, but the study found that central obesity has an association with lower antibody titers such as those who smoke, and also those who have comorbidities such as hypertension which causes lower side effects after COVID-19 vaccination [38], female sex groups, as well as young individuals, are most likely to experience side effects from the COVID-19 vaccination due to a robust immune system which causes high antibody titers after vaccination [39]. In addition, a statistically significant relationship was found between menstrual problems in women and low BMI status after the second vaccination (23.4%) $p=$ 0.034. in contrast, a study showed that BMI has no relationship with the menstruation cycle, but BMI had a relationship with menstrual blood loss [40]. Our study has several limitations where the male sample is only 26.6% of the total population; therefore this sample cannot represent the entire population in Indonesia, over other risk factors such as comorbidities cannot be analyzed because the population size is not large and individuals with comorbidities are fairly small. small; therefore, the calculation for this result is difficult, our research uses an online questionnaire, this instrument provides several advantages such as being accessible throughout the region but the obstacle is that it cannot be done face-to-face interviews; therefore we take data such as age, weight, height, type of vaccine and dose using the respondent's personal data such as ID and vaccine card.

CONCLUSION

In conclusion, the most common side effects of both AstraZeneca and Moderna vaccines were mild-moderate such as fever, sore arm, headache, drowsiness, nausea; only 7 cases of cardiovascular problems were reported in the first dose of vaccination however, 5 cases of cardiovascular problems were reported in the second dose of vaccination, in 6% of Moderna recipients we found a report of an allergic reaction, in addition only 2% of Moderna recipients reported for cardiovascular problems. We found there were several risk factors associated with the side effect of both vaccines such as type of vaccine, with the first dose of AstraZeneca had the highest chance to give side effects than Moderna; otherwise, second dose Moderna had the highest chance of side effects than the second dose of AstraZeneca, female participants are most likely to feel side effects due to high antibody titers, as well as young individuals and non-overweight BMI status. Overall, based on this study, both COVID-19 vaccines are safe for any age and gender; our study did not find any severe side effects or any fatal allergic reaction in the recipients.

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declare none

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