



RESEARCH ARTICLE



## Self-reported side effects of COVID-19 vaccines among the public

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### ABSTRACT

**Background:** The safety, side effects and efficacy profile of COVID-19 vaccines remain subjects of ongoing concern among the public in Malaysia. The aim of this study was to determine the types of adverse effects following immunisation with COVID-19 vaccines and the differences based on various types of COVID-19 vaccines to raise public awareness and reduce vaccine hesitancy among the public.

**Methods:** A total of 901 Malaysian adults ( $\geq 18$  years) who received various COVID-19 vaccines were selected to participate in our cross-sectional study through an online survey between December 2021 and January 2022.

**Results:** A total of 814 (90.3%) of the participants reported  $\geq 1$  side effect following COVID-19 immunisation. Of these, the predominant symptoms were swelling at the injection site ( $n = 752$ , 83.5%), headache ( $n = 638$ , 70.8%), pain or soreness at the injection site ( $n = 628$ , 69.7%), fatigue or tiredness ( $n = 544$ , 60.4%), muscle weakness ( $n = 529$ , 58.7%) and diarrhea ( $n = 451$ , 50.1%). Recipients of the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine reported the highest number of adverse effects ( $n = 355$ , 43.6%), followed by mixed

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COVID-19 vaccines ( $n = 254$ , 31.2%), the Oxford-AstraZeneca (ChAdOx1-® [recombinant]) vaccine ( $n = 113$ , 13.9%) and the Sinovac (CoronaVac®) vaccine ( $n = 90$ , 11.1%). The study showed that individuals who reported significantly more side effects were of elderly age, female gender and high educational level [ $P$  value  $< 0.05$ ]. Mixed COVID-19 vaccine recipients also reported significantly more local and systemic symptoms after the first dose and third dose when compared with other single vaccine recipients.

**Conclusion:** This study demonstrated the types of self-reported adverse effects following immunisation with single and mixed COVID-19 vaccines. These findings may provide the side effects of different COVID-19 vaccines with the hope of educating the public on the safety profiles of these vaccines and reducing vaccine hesitancy among the public.

**KEYWORDS** Side (adverse) effect; COVID-19; vaccine hesitancy; mixed vaccine; single vaccine; communicable diseases; infectious disease

## 1. Introduction

Coronavirus Disease 2019 (COVID-19) has continued to be a significant threat to global public health since its first large-scale outbreak in December 2019. The combined discovery of its genetic sequence, adjuvants and vectors not only unravelled mysteries of this deadly virus but also triggered intense worldwide research and development of COVID-19 vaccines and therapeutic strategies at an unprecedented rate. Various new drugs and medical products without full Food and Drug Administration (FDA) approval were introduced to the public during the COVID-19 public health emergency. Currently, medications such as antiviral drugs, neutral antibody therapies, immunomodulators and cell and gene therapies emerged as the mainstay treatment of COVID-19 (Drozdal et al., 2021; Niknam et al., 2022). Although the development of potential drug candidates has shed some light for clinicians in treating patients with severe COVID-19 clinical symptoms, the effects of certain treatments including antiviral agents and neutralising antibody remain controversial. Some studies showed that combinational therapies generally show more promising results compared to single treatment (Zhai et al., 2023). Therefore, mass COVID-19 vaccination remains crucial in ending the pandemic status of this life-threatening virus. In Malaysia, there are a total of 7 COVID-19 vaccines that have received conditional approval by the Drug Control Authority (DCA), with more vaccines that are expected to arrive subject to the approval of DCA and the National Pharmaceutical Regulatory Agency (NPRA) (Malaysia MoH, 2021). Presently, there are three COVID-19 vaccines that are actively being administered in Malaysia: Pfizer-BioNTech (Comirnaty®), Sinovac (CoronaVac®) and Oxford-AstraZeneca (ChAdOx1-S®[recombinant]).

Since the approval and implementation of these vaccines globally, it has resulted in a reduction of at least 94% of COVID-19 infections in the vaccinated

group (Al-Kassmy et al., 2020). With the continuing upsurge in COVID-19 cases, there is rapid progress in the COVID-19 vaccination drive in Malaysia. As such, the daunting challenge faced by the Ministry of Health, Malaysia, gradually shifted from vaccination procurement and distribution to ensuring the broadest possible acceptance among all populations in this country. The term 'vaccine hesitancy' is used when one delays accepting or refusing vaccines despite the availability of vaccine services (Riad et al., 2021a). Based on available statistics dated until 31 October 2021, an overall 74.8% of the Malaysian population has been fully vaccinated, and at least 78.1% of the population has received their 1st dose (Malaysia MoF, 2021; Tang, 2021). However, despite the increasing vaccination rate in Malaysia, pockets of people are either misled by online disinformation that fuels preferences towards a specific vaccine or are unsure about vaccination, especially among people with higher education (Zainul, 2021). Several studies have reported that concerns regarding the adverse effects profile of a COVID-19 vaccine is one of the reasons behind the public's vaccine hesitancy (Dror et al., 2020; Mohamed et al., 2023; Razai et al., 2021; Saied et al., 2021). A study in the United Kingdom also revealed that the most frequent cause of vaccine hesitancy is the fear of vaccine side effects (Luyten et al., 2019).

Information that originates from half-truths, unfounded speculations and targeted disinformation rooted in conspiracy theories can mislead the public's understanding towards COVID-19 vaccines, especially their safety and efficacy profile. It has been found that information can shape an individual's perceptions and decision-making even if it is misinformation, which could eventually lead to a self-perpetuating cycle of negative news when it is left unchallenged (Faasse et al., 2012). People who were exposed to misleading or negative remarks about medication in the media reported more adverse events, thereby raising and validating other people's concerns. Therefore, strategies are necessary in addressing common misconceptions about vaccine adverse effects without elevating them through public discourse. One of the methods of tackling and decreasing COVID-19 vaccination hesitancy is to raise public awareness regarding the effectiveness of these vaccines and their side effects (Jarrett et al., 2015). Thus far, existing data on the side effects of COVID-19 vaccines revealed by manufacturer-funded studies have been included in the Clinical Guidelines on COVID-19 Vaccination in Malaysia (Malaysia MoH, 2021). In addition, various efforts have also been made by the Ministry of Health, Malaysia in identifying and addressing the side effects of COVID-19 vaccines, including clinical trials by the Institute of Clinical Research (ICR) in Malaysia which investigates the safety profile and efficacy of COVID-19 vaccines (National Institute of Health Malaysia, n.d.). The MySejahtera mobile application is another example that allows the public to report adverse effects following immunisation (AEFI) through a self-reporting method. However, it is anticipated that only moderate to severe side effects

that have an impact on the quality of life of recipients are reported, such as the reported cases received for adverse drug reactions (Banovac et al., 2017).

A few reliable methods are available to collect information on adverse drug effects. Among them are collecting practice data, spontaneous reporting through national pharmacovigilance databases, soliciting events from healthcare professionals, as well as direct observation and surveying of patients for drug-related adverse events (Mayer et al., 2010; Morimoto et al., 2004). In addition, the patient's role in reporting adverse drug effects has also long been established in a few countries (Van Grootheest & de Jong-van den Berg, 2004). Nonetheless, studies about the epidemiology of adverse drug effects in public settings are limited, especially when hospitalisation or medical intervention is not needed, which is likely for COVID-19 vaccines as well (Bouvy et al., 2015). On top of that, there is a lack of independent studies that investigate the occurrence of side effects upon receiving these COVID-19 vaccines, especially the three vaccines that are actively being distributed in Malaysia. Henceforth, the present study aims to explore the side effects profile of COVID-19 vaccines upon receiving them with the hope of educating the public on the safety profiles of these vaccines and decreasing vaccine hesitancy among the public. This study strived to explore the type of COVID-19 vaccines and the types of self-reported adverse effects following COVID-19 immunisation among the public in Malaysia.

## 2. Methods

### 2.1. Research design

A cross-sectional observational study was conducted between December 2021 and January 2022 via an online survey among citizens of Malaysia. Ethical approval was obtained from Medical and Research Ethics Committee (MREC) of Universiti Teknologi MARA (UiTM) (Code: REC/12/2021 (MR/925)). The questionnaire was constructed in such a way that self-reported symptoms experienced following COVID-19 vaccination among the public could be identified without collecting any personal identification details. Participants were required to agree to consent online to answer the survey.

### 2.2. Study participants

Participants who were adult Malaysians ( $\geq$ age 18 years) and (i) had received the COVID-19 vaccine at any stage of vaccination, be it dose 1 and/or dose 2 and/or dose 3, or (ii) were at least 2 weeks post-COVID-19 vaccination at any stage of vaccination, be it dose 1 and/or dose 2 and/or dose 3, were selected to participate in the study. The survey questionnaire was circulated through an internet-based survey platform (Survey Monkey), and participants were approached through social media platforms. The convenience sampling

method was applied due to the finite study period and movement control order (MCO) situation in Malaysia. As a result, a total of 901 samples were conveniently selected and used for further analysis.

### **2.3. Survey tool**

The questionnaire was developed according to previously published articles and Clinical Guidelines on COVID-19 Vaccination in Malaysia (Kadali et al., 2021; Riad et al., 2021a). It consists of questions on demographic data, medical history, vaccination history, side effects experienced and perceptions of COVID-19 vaccines that were prepared in both English and Malay languages. In addition, a team of experts consisting of academicians and practitioners and the public conducted the face validity of the questionnaire by evaluating the presentation of the questionnaire in terms of readability, clarity of the language used, feasibility as well as the consistency of style and formatting (Taherdoost, 2016).

### **2.4. Sample size**

Our study was conducted only among Malaysians aged 18 years and above. According to statistics available in 2022, the estimated population of Malaysians aged 18 years and above in 2021 is approximately 22 million (Statista Research Department, 2022). Using Yamane's formula with a margin error of 5% and confidence interval of 95%, the minimum sample size required is 400 (Yamane, 1967). However, 10% is required to be added to the calculated sample size to compensate for missing data. Therefore, the final sample size needed for this study was 440.

### **2.5. Statistical analysis**

The application software 'Statistical Package for the Social Sciences (SPSS)' version 25.0 was used for all statistical analyses (Statistical Package for the Social Sciences (SPSS) version 25.0, 2020). Categorical data for demographic data and vaccine side effects were represented as frequencies, percentages, means and standard deviations. Inferential analyses, such as independent t tests, chi-square tests and Fischer's exact tests, were performed to test the study's hypothesis. A  $P$  value  $< 0.05$  was considered to indicate statistical significance of data.

## **3. Results**

### **3.1. Demographic profile of Malaysian recipients of the COVID-19 vaccine**

Table 1 describes the demographic data of all the participants of this study. Based on our findings, the mean age of the respondents is 37.0 (SD = 12.6).

**Table 1.** Demographic profile of respondents ( $n = 901$ ).

Demographic profile	M	(SD)	<i>n</i>	(%)
<b>Age</b>	37.0	(12.6)		
18–30			344	(38.2%)
31–40			252	(28.0%)
41–50			167	(18.5%)
51–60			77	(8.5%)
61–70			57	(6.3%)
71–80			4	(0.4%)
<b>Gender</b>				
Male			217	(24.1%)
Female			684	(75.9%)
<b>Ethnicity</b>				
Malay			740	(82.1%)
Chinese			60	(6.7%)
Indian			67	(7.4%)
Others			34	(3.8%)
<b>Education level</b>				
Graduate/ Post graduate degree			737	(81.8%)
High school/ Diploma			117	(13.0%)
Less than high school			47	(5.2%)
<b>Comorbidities</b>				
Yes			222	(24.6%)
No			679	(75.4%)
<b>Employment status</b>				
Employed			608	(67.5%)
Unemployed			293	(32.5%)
<b>Previous COVID-19 infection</b>				
Yes			92	(10.2%)
No			809	(89.8%)
<b>Type of vaccine received</b>				
Pfizer-BioNTech (Comirnaty <sup>®</sup> )			381	(42.3%)
Sinovac (CoronaVac <sup>®</sup> )			117	(13.0%)
Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])			127	(14.1%)
Others (e.g. CanSino/Johnson & Johnson/Sinopharm)			3	(0.3%)
Mixed vaccines			273	(30.2%)
<b>Adverse effects</b>				
Yes			814	(90.3%)
No			87	(9.7%)

There were a total of 217 (24.1%) males and 684 (75.9%) females included in this study. Of the 901 participants who completed the survey, 740 (82.1%) were of Malay ethnicity, 737 (81.8%) held a graduate or postgraduate degree and 608 (67.5%) were employed. The majority of the respondents did not have any associated comorbidities or previous COVID-19 infection history, with findings of 679 (75.4%) and 809 (89.8%), respectively. Of the responses, a total of 381 (42.3%) people received the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine, 117 (13.0%) received the Sinovac (CoronaVac<sup>®</sup>) vaccine, 127 (14.1%) received the Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine, and 3 (0.3%) received other types of vaccines, including the CanSino, Johnson & Johnson and Sinopharm vaccines. Meanwhile, 273 (30.2%) of the respondents received mixed vaccines, and the details are listed in [Table 2](#). Of the 901 responses collected, 895 (99.3%) respondents

**Table 2.** Types of vaccines taken among mixed vaccines recipients ( $n = 273$ ).

Types of mixed vaccines	<i>n</i>	(%)
Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant]) + Sinovac (CoronaVac <sup>®</sup> )	5	(1.8%)
Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant]) + Pfizer-BioNTech (Comirnaty <sup>®</sup> )	70	(25.6%)
Sinovac (CoronaVac <sup>®</sup> ) + Pfizer-BioNTech (Comirnaty <sup>®</sup> )	197	(72.2%)
CanSino + Pfizer-BioNTech (Comirnaty <sup>®</sup> )	1	(0.4%)

had received more than one dose of the COVID-19 vaccine, whereas only 6 (0.7%) respondents had received a single dose.

### 3.2. Adverse reactions reported post-COVID-19 vaccination

Based on the responses collected, a total of 814 (90.3%) participants reported at least one adverse effect following COVID-19 immunisation. The types of symptoms experienced following COVID-19 vaccination that were reported by participants are shown in Table 3. When probed on the types of adverse reactions reported by respondents, the major adverse effects reported were swelling at the injection site ( $n = 752$ , 83.5%), headache ( $n = 638$ , 70.8%), pain or soreness at the injection site ( $n = 628$ , 69.7%), fatigue or tiredness ( $n = 544$ , 60.4%), muscle weakness ( $n = 529$ , 58.7%) and diarrhea ( $n = 451$ , 50.1%). Figure 1 portrays the percentage of these reported side effects based on the types of COVID-19 vaccines. Of them, recipients of the Pfizer-

**Table 3.** Side effects reported post COVID-19 vaccination ( $n = 901$ ).

Side Effects	<i>n</i>	(%)
<b>Local side effects</b>		
Swelling at injection site	752	(83.5%)
Pain or soreness at injection site	628	(69.7%)
Redness at injection site	376	(41.7%)
Itchiness at injection site	271	(30.1%)
Swollen lymph nodes	117	(13.0%)
<b>Systemic side effects</b>		
Headache	638	(70.8%)
Fatigue/ Tiredness	544	(60.4%)
Muscle weakness	529	(58.7%)
Diarrhea	451	(50.1%)
Nausea	450	(49.9%)
Skin rash	440	(48.8%)
Fever	424	(47.1%)
Chills and shivering	402	(44.6%)
Muscle pain	371	(41.2%)
Malaise	348	(38.6%)
Joint pain	371	(41.2%)
Constipation	285	(31.6%)
Dizziness	203	(22.5%)
Vomiting	176	(19.5%)
Insomnia	98	(10.9%)
Runny nose	71	(7.9%)
Cough	62	(6.9%)
Sore throat	51	(5.7%)

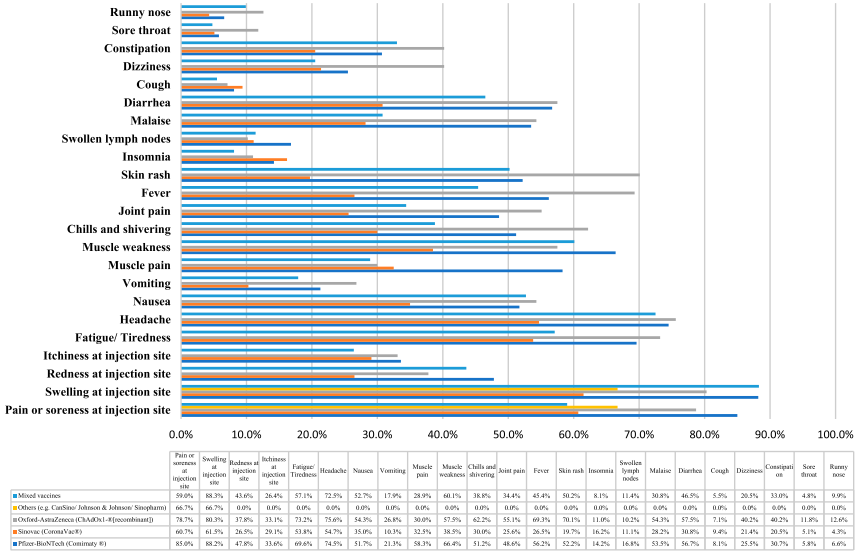


Figure 1. Side effects reported post COVID-19 vaccination based on types of COVID-19 vaccine (n = 901).

BioNTech (Comirnaty<sup>®</sup>) vaccine reported the highest number of adverse effects (n = 355, 43.6%), followed by mixed COVID-19 vaccine recipients (n = 254, 31.2%), Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine

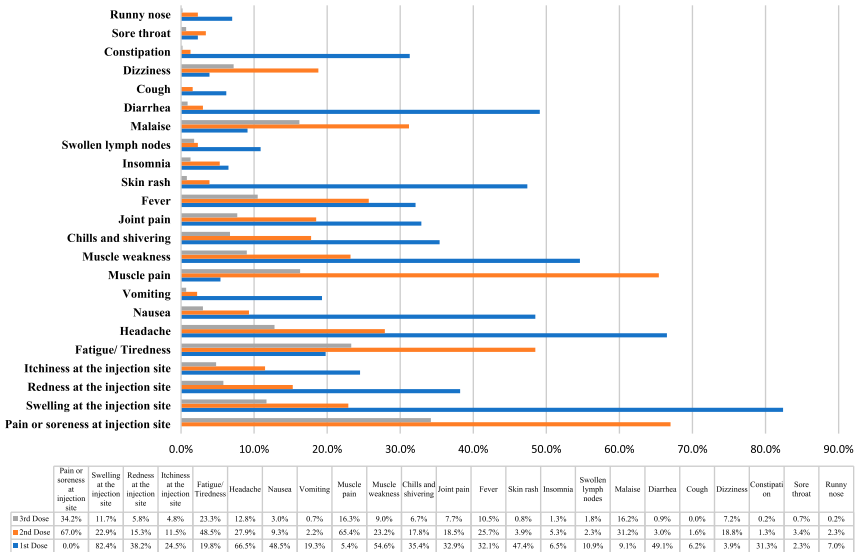


Figure 2. Side effects reported post COVID-19 vaccination based on vaccination dose (n = 901).



recipients ( $n = 113, 13.9\%$ ) and Sinovac (CoronaVac<sup>®</sup>) vaccine recipients ( $n = 90, 11.1\%$ ). Figure 2 depicts the self-reported adverse effects following COVID-19 immunisation based on the vaccination dose received.

### 3.3. Adverse effects following Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination and demographic profiles

Table 4 shows the association between the presence of side effects post-Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination and the demographic profile. A total of 355 (93.2%) recipients of the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine self-reported experiencing symptoms following vaccination. The analysis of various aspects of the demographic profile of respondents related to the reactogenicity of Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination found that people from the elder age group (>60 years), female gender, Indian ethnicity,

**Table 4.** The association between adverse effects post Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination and demographic profile ( $n = 381$ ).

Demographic profile	Adverse effects		$\chi^2$	(df)	P value
	Yes	No			
	n	(%)	n	(%)	
<b>Age</b>					0.380 <sup>a</sup> (379) 0.704
18–30	127	(93.4%)	9	(6.6%)	
31–40	123	(95.3%)	6	(4.7%)	
41–50	63	(88.7%)	8	(11.3%)	
51–60	20	(90.9%)	2	(9.1%)	
61–70	21	(95.5%)	1	(4.5%)	
71–80	1	(100.0%)	0	(0.0%)	
<b>Gender</b>					1.670 (1) 0.196
Male	83	(90.2%)	9	(9.8%)	
Female	272	(94.1%)	17	(5.9%)	
<b>Ethnicity</b>					1.381 <sup>a</sup> (3) 0.710
Malay	295	(93.4%)	21	(6.6%)	
Chinese	23	(88.5%)	3	(11.5%)	
Indian	26	(96.3%)	1	(3.7%)	
Others	11	(91.7%)	1	(8.3%)	
<b>Education level</b>					2.530 <sup>b</sup> (2) 0.282
Graduate/ Post graduate degree	296	(93.7%)	20	(6.3%)	
High school/ Diploma	43	(93.5%)	3	(6.5%)	
Less than high school	16	(84.2%)	3	(15.8%)	
<b>Comorbidities</b>					0.830 (1) 0.773
Yes	91	(93.8%)	6	(6.2%)	
No	264	(93.0%)	20	(7.0%)	
<b>Employment status</b>					0.589 (1) 0.443
Employed	257	(93.8%)	17	(6.2%)	
Unemployed	98	(91.6%)	9	(8.4%)	
<b>Previous COVID-19 infection</b>					0.721 <sup>c</sup>
Yes	32	(91.4%)	3	(8.6%)	
No	323	(93.3%)	23	(6.6%)	

<sup>a</sup>Independent T-test is performed.

<sup>b</sup>Pearson Chi Square test is performed.

<sup>c</sup>Fischer exact test is performed.

higher level of education and individuals with associated comorbidities reported a statistically greater number of postvaccination adverse effects than others. Independent t tests were performed for age [ $t(df) = 0.380$  (379),  $P$  value = 0.704]. There was no significant mean difference in age between respondents who reported with and without adverse effects following Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination. Pearson's chi-square test was performed for sex [ $P$  value = 0.196], comorbidities [ $P$  value = 0.773], and employment status [ $P$  value = 0.443]. In addition, the Pearson chi-square test was also used for ethnicity [ $P$  value = 0.710] and education level [ $P$  value = 0.282], whereas the Fischer exact test was performed for previous COVID-19 infection [ $P$  value = 0.721]. There was no significant association observed between the demographic profile and the presence of adverse effects following Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination, as shown in Table 4.

**Table 5.** The association between adverse effects post Sinovac (CoronaVac<sup>®</sup>) vaccination and demographic profile ( $n = 117$ ).

Demographic profile	Adverse effects		$\chi^2$	(df)	$P$ value
	Yes <i>n</i> (%)	No <i>n</i> (%)			
<b>Age</b>			-0.823 <sup>a</sup>	(115)	0.412
18–30	39 (70.9%)	16 (29.1%)			
31–40	24 (80.0%)	6 (20.0%)			
41–50	18 (5.3%)	18 (94.7%)			
51–60	5 (71.4%)	2 (28.6%)			
61–70	4 (66.7%)	2 (33.3%)			
71–80	0 (0.0%)	0 (0.0%)			
<b>Gender</b>			0.036	(1)	0.850
Male	25 (78.1%)	7 (21.9%)			
Female	65 (76.5%)	20 (23.5%)			
<b>Ethnicity</b>			2.576 <sup>b</sup>	(3)	0.462
Malay	66 (75.9%)	21 (24.1%)			
Chinese	12 (85.7%)	2 (14.3%)			
Indian	10 (83.3%)	2 (16.7%)			
Others	2 (50.0%)	2 (50.0%)			
<b>Education level</b>			3.698 <sup>b</sup>	(2)	0.157
Graduate/ Post graduate degree	73 (80.2%)	18 (19.8%)			
High school/Diploma	10 (58.8%)	7 (41.2%)			
Less than high school	7 (77.8%)	2 (22.2%)			
<b>Comorbidities</b>					1.000 <sup>c</sup>
Yes	12 (80.0%)	3 (20.0%)			
No	78 (76.5%)	24 (23.5%)			
<b>Employment status</b>			1.192	(1)	0.275
Employed	54 (80.6%)	13 (19.4%)			
Unemployed	36 (72.0%)	14 (28.0%)			
<b>Previous COVID-19 infection</b>					0.761 <sup>c</sup>
Yes	15 (83.3%)	3 (16.7%)			
No	75 (75.8%)	24 (24.2%)			

<sup>a</sup>Independent T-test is performed.

<sup>b</sup>Pearson Chi Square test is performed.

<sup>c</sup>Fischer exact test is performed.

### **3.4. Adverse effects following Sinovac (CoronaVac®) vaccination and demographic profile**

Table 5 shows the association between the presence of adverse effects post Sinovac (CoronaVac®) vaccination and the demographic profile. A total of 90 (76.9%) recipients of the Sinovac (CoronaVac®) vaccine reported side effects following vaccination with this vaccine. The analysis of various aspects of the demographic profile related to the reactogenicity of Sinovac (CoronaVac®) vaccination among the participants found that people from the 31 to 40 age group, female gender, Chinese ethnicity, higher educational level, individuals with associated health conditions and individuals with a history of COVID-19 infection showed a higher percentage of postvaccination side effects than others. Independent t tests were performed for age [ $t(df) = -0.823(115)$ ,  $P$  value = 0.412]. There was no significant mean difference in age between respondents who reported with and without adverse effects following Sinovac (CoronaVac®) vaccination. Pearson's chi-square test was performed for gender [ $P$  value = 0.850] and employment status [ $P$  value = 0.275]. In addition, the Pearson chi-square test was also used for ethnicity [ $P$  value = 0.462] and education level [ $P$  value = 0.157], whereas the Fisher exact test was used for comorbidities [ $P$  value = 1.000] and previous COVID-19 infection [ $P$  value = 0.761]. There was no significant association observed between the demographic profile and the presence of adverse effects following Sinovac (CoronaVac®) vaccination, as shown in Table 5.

### **3.5. Adverse effects following Oxford-AstraZeneca (ChAdOx1-®[recombinant]) vaccination and demographic profile**

Table 6 shows the association between the presence of adverse effects post Oxford-AstraZeneca (ChAdOx1-®[recombinant]) vaccination and the demographic profile. A total of 113 (89.0%) recipients of the Oxford-AstraZeneca (ChAdOx1-®[recombinant]) vaccine reported experiencing side effects after vaccination. The analysis of various aspects of the demographic profile related to the reactogenicity of Oxford-AstraZeneca (ChAdOx1-®[recombinant]) vaccination among these participants revealed that people from the younger age group (<50 years), male gender, Indian ethnicity, lower educational status, individuals without associated comorbidities and those with previous COVID-19 infection history reported a greater percentage of postvaccination symptoms than others. The median difference in age was tested using the Mann-Whitney U test with findings of [ $U = 800$ ,  $P$  value = 0.945]. Fisher's exact test was performed for sex [ $P$  value = 0.467], comorbidities [ $P$  value = 0.317] and previous COVID-19 infection [ $P$  value = 0.609]. In addition, the Pearson chi-square test was also used for ethnicity [ $P$  value = 0.666], education level [ $P$  value = 0.522] and employment status [ $P$  value =

**Table 6.** The association between adverse effects post Oxford-AstraZeneca (ChAdOx1-® [recombinant]) vaccination and demographic profile ( $n = 127$ ).

Demographic profile	Adverse effects		$\chi^2$	(df)	Mann-Whitney U	P value	
	Yes	No					
	<i>n</i>	(%)	<i>n</i>	(%)			
<b>Age</b>					800	0.945 <sup>a</sup>	
18–30	50	(86.2%)	8	(13.8%)			
31–40	25	(96.2%)	1	(3.8%)			
41–50	25	(100.0%)	0	(0.0%)			
51–60	5	(71.4%)	2	(28.6%)			
61–70	8	(72.7%)	3	(27.3%)			
71–80	0	(0.0%)	0	(0.0%)			
<b>Gender</b>						0.467 <sup>b</sup>	
Male	23	(95.8%)	1	(4.2%)			
Female	90	(87.4%)	13	(12.6%)			
<b>Ethnicity</b>					1.570 <sup>c</sup>	(3)	0.666
Malay	99	(89.2%)	12	(10.8%)			
Chinese	4	(80.0%)	1	(20.0%)			
Indian	6	(100.0%)	0	(0.0%)			
Others	4	(89.0%)	1	(11.0%)			
<b>Education level</b>					1.301 <sup>c</sup>	(2)	0.522
Graduate/ Post graduate degree	95	(89.6%)	11	(10.4%)			
High school/ Diploma	14	(82.4%)	3	(17.6%)			
Less than high school	4	(100.0%)	0	(0.0%)			
<b>Comorbidities</b>						0.317 <sup>b</sup>	
Yes	25	(83.3%)	5	(16.7%)			
No	88	(90.7%)	9	(9.3%)			
<b>Employment status</b>					2.982	(1)	0.084
Employed	75	(92.6%)	6	(7.4%)			
Unemployed	38	(82.6%)	8	(17.4%)			
<b>Previous COVID-19 infection</b>						0.609 <sup>b</sup>	
Yes	11	(100.0%)	0	(0.0%)			
No	102	(87.9%)	14	(12.1%)			

<sup>a</sup>Mann-Whitney U test is performed.<sup>b</sup>Fischer exact test is performed.<sup>c</sup>Pearson Chi Square test is performed.

0.084]. The aforementioned demographic factors had *P* values greater than 0.05, which was not significant. Thus, we fail to reject the null hypothesis, and there is no association between these variables and the presence of adverse effects following Oxford-AstraZeneca (ChAdOx1-® [recombinant]) vaccination, as shown in Table 6.

### 3.6. Adverse effects following mixed COVID-19 vaccination and demographic profile

Table 7 shows the association between the presence of side effects following mixed COVID-19 vaccination and the demographic profile. A total of 254 (93.0%) recipients of the mixed vaccination reported experiencing symptoms

**Table 7.** The association between adverse effects post mixed COVID-19 vaccination and demographic profile (*n* = 273).

Demographic profile	Adverse effects				$\chi^2$	(df)	P value
	Yes		No				
	<i>n</i>	(%)	<i>n</i>	(%)			
<b>Age</b>					0.848 <sup>a</sup>	(271)	0.397
18–30	88	(94.6%)	5	(5.4%)			
31–40	63	(95.5%)	3	(4.5%)			
41–50	47	(90.4%)	5	(9.6%)			
51–60	37	(90.2%)	4	(9.8%)			
61–70	16	(88.9%)	2	(11.1%)			
71–80	3	(100.0%)	0	(0.0%)			
<b>Gender</b>							0.269 <sup>b</sup>
Male	61	(89.7%)	7	(10.3%)			
Female	193	(94.1%)	12	(5.9%)			
<b>Ethnicity</b>					4.988 <sup>c</sup>	(3)	0.173
Malay	212	(94.6%)	12	(5.4%)			
Chinese	12	(85.7%)	2	(14.3%)			
Indian	19	(86.4%)	3	(13.6%)			
Others	11	(84.6%)	2	(15.4%)			
<b>Education level</b>					1.382 <sup>c</sup>	(2)	0.501
Graduate/ Post graduate degree	208	(93.7%)	14	(6.3%)			
High school/ Diploma	34	(91.9%)	3	(8.1%)			
Less than high school	12	(85.7%)	2	(14.3%)			
<b>Comorbidities</b>					0.069	(1)	0.792
Yes	73	(92.4%)	6	(7.6%)			
No	181	(93.3%)	13	(6.7%)			
<b>Employment status</b>					0.911	(1)	0.340
Employed	174	(94.1%)	11	(5.9%)			
Unemployed	80	(90.9%)	8	(9.1%)			
<b>Previous COVID-19 infection</b>							0.116 <sup>b</sup>
Yes	24	(85.7%)	4	(14.3%)			
No	230	(93.9%)	15	(6.1%)			
<b>Types of mixed vaccination</b>					17.898 <sup>c</sup>	(3)	<0.001
Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant]) + Sinovac (CoronaVac <sup>®</sup> )	5	(100.0%)	0	(0.0%)			
CanSino + Pfizer-BioNTech (Comirnaty <sup>®</sup> )	0	(0.0%)	1	(100.0%)			
Sinovac (CoronaVac <sup>®</sup> ) + Pfizer-BioNTech (Comirnaty <sup>®</sup> )	180	(91.4%)	17	(8.6%)			
Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant]) + Pfizer-BioNTech (Comirnaty <sup>®</sup> )	69	(98.6%)	1	(1.4%)			

<sup>a</sup>Independent T-test is performed.

<sup>b</sup>Fischer Exact test is performed.

<sup>c</sup>Pearson Chi Square test is performed.

after receiving vaccination. The analysis of various aspects of the demographic profile related to the reactogenicity of mixed COVID-19 vaccines among participants showed that people from the elder age group (>70 years), female gender, Malay ethnicity, higher level of education, individuals without associated health conditions and any previous COVID-19 infection history reported a higher number of postvaccination symptoms compared to others. Independent t tests were performed for age [ $t(df) = -0.848(271)$ ,

$P$  value = 0.397]. There was no significant mean difference in age between respondents who reported with and without adverse effects following mixed COVID-19 vaccination. Fisher's exact test was performed for sex [ $P$  value = 0.269] and previous COVID-19 infection [ $P$  value = 0.116]. In addition, the Pearson chi-square test was also used for ethnicity [ $P$  value = 0.173], education level [ $P$  value = 0.501], comorbidities [ $P$  value = 0.792], and employment status [ $P$  value = 0.340]. Among the types of mixed vaccination recipients who completed the survey, those who had received a mixture of Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) + Sinovac (CoronaVac<sup>®</sup>) and Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) + Pfizer-BioNTech (Comirnaty<sup>®</sup>) reported a significantly greater percentage of experiencing postvaccination symptoms when compared to others, as shown in Table 7.

### 3.7. Comparison of adverse effects between Pfizer-BioNTech (Comirnaty<sup>®</sup>), Sinovac (CoronaVac<sup>®</sup>), Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) and mixed COVID-19 vaccine recipients

Our findings showed that a significantly greater number of cases (93.2%) were reported among recipients of the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine than among recipients of other vaccines, including mixed COVID-19 vaccination. The comparison of reported postvaccination side effects between Pfizer-BioNTech (Comirnaty<sup>®</sup>), Sinovac (CoronaVac<sup>®</sup>), Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) and mixed COVID-19 vaccine recipients had  $P$  values less than 0.05, which is significant. Thus, the null hypothesis is rejected, and there is a significant association between types of COVID-19

**Table 8.** Association of adverse effects with types of COVID-19 vaccine based on vaccine status.

Adverse effects	COVID-19 vaccine status		$\chi^2$	(df)	$P$ value
	Single vaccine <sup>a</sup>	Mixed vaccines <sup>b</sup>			
	$n$	(%)	$n$	(%)	
Overall adverse effects	560	(89.2%)	254	(93.0%)	3.264 (1) 0.071
Local adverse effects	523	(83.3%)	245	(89.7%)	6.318 (1) 0.012
Systemic adverse effects	517	(82.3%)	236	(86.4%)	2.355 (1) 0.125
Adverse effects after 1st dose	560	(89.2%)	254	(93.0%)	3.264 (1) 0.071
Adverse effects after 2nd dose	529	(84.2%)	187	(68.5%)	28.882 (1) <0.001
Adverse effects after 3rd dose	192	(30.6%)	180	(65.9%)	98.151 (1) <0.001
Local adverse effects after 1st dose	517	(82.3%)	245	(89.7%)	8.027 (1) 0.005
Local adverse effects after 2nd dose	474	(75.5%)	154	(56.4%)	32.757 (1) <0.001
Local adverse effects after 3rd dose	178	(28.3%)	146	(53.5%)	52.205 (1) <0.001
Systemic adverse effects after 1st dose	517	(82.3%)	236	(86.4%)	2.355 (1) 0.125
Systemic adverse effects after 2nd dose	440	(70.1%)	151	(55.3%)	18.349 (1) <0.001
Systemic adverse effects after 3rd dose	159	(25.3%)	138	(50.5%)	54.818 (1) <0.001

<sup>a</sup> $n$  = 628.

<sup>b</sup> $n$  = 273.

**Table 9.** Association of types of adverse effects with types of COVID-19 vaccine based on vaccine status.

Side effects	COVID-19 vaccine status				$\chi^2$	(df)	P value
	Single vaccine <sup>a</sup>		Mixed vaccines <sup>b</sup>				
	n	(%)	n	(%)			
<b>Pain/ Soreness at injection site</b>					21.337	(1)	<0.001
Yes	467	(74.4%)	161	(59.0%)			
No	161	(25.6%)	112	(41.0%)			
<b>Swelling at injection site</b>					6.581	(1)	0.010
Yes	511	(81.4%)	241	(88.3%)			
No	117	(18.6%)	32	(11.7%)			
<b>Redness at injection site</b>					0.556	(1)	0.456
Yes	257	(40.9%)	119	(43.6%)			
No	371	(59.1%)	154	(56.4%)			
<b>Itchiness at injection site</b>					2.555	(1)	0.110
Yes	199	(31.7%)	72	(26.4%)			
No	429	(68.3%)	201	(73.6%)			
<b>Fatigue/Tiredness</b>					1.713	(1)	0.191
Yes	388	(61.8%)	156	(57.1%)			
No	240	(38.2%)	117	(42.9%)			
<b>Headache</b>					0.559	(1)	0.455
Yes	440	(70.1%)	198	(72.5%)			
No	188	(29.9%)	75	(27.5%)			
<b>Nausea</b>					1.231	(1)	0.267
Yes	306	(48.7%)	144	(52.7%)			
No	322	(51.3%)	129	(47.3%)			
<b>Vomiting</b>					0.626	(1)	0.429
Yes	127	(20.2%)	49	(17.9%)			
No	501	(79.8%)	224	(82.1%)			
<b>Muscle pain</b>					24.222	(1)	<0.001
Yes	292	(46.5%)	79	(28.9%)			
No	336	(53.5%)	194	(71.1%)			
<b>Muscle weakness</b>					0.299	(1)	0.584
Yes	365	(58.1%)	164	(60.1%)			
No	263	(41.9%)	109	(39.9%)			
<b>Chills and shivering</b>					5.312	(1)	0.021
Yes	296	(47.1%)	106	(38.8%)			
No	332	(52.9%)	167	(61.2%)			
<b>Joint pain</b>					7.355	(1)	0.007
Yes	277	(44.1%)	94	(34.4%)			
No	351	(55.9%)	179	(65.6%)			
<b>Fever</b>					0.422	(1)	0.516
Yes	300	(47.8%)	124	(45.4%)			
No	328	(52.2%)	149	(54.6%)			
<b>Skin rash</b>					0.285	(1)	0.593
Yes	303	(48.2%)	137	(50.2%)			
No	325	(51.8%)	136	(49.8%)			
<b>Insomnia</b>					3.209	(1)	0.073
Yes	76	(12.1%)	22	(8.1%)			
No	552	(87.9%)	251	(91.9%)			
<b>Swollen lymph nodes</b>					0.921	(1)	0.337
Yes	86	(13.7%)	31	(11.4%)			
No	542	(86.3%)	242	(88.6%)			
<b>Malaise</b>					10.193	(1)	0.001
Yes	264	(42.0%)	84	(30.8%)			
No	364	(58.0%)	189	(69.2%)			

(Continued)

**Table 9.** Continued.

Side effects	COVID-19 vaccine status				$\chi^2$	(df)	P value
	Single vaccine <sup>a</sup>		Mixed vaccines <sup>b</sup>				
	n	(%)	n	(%)			
<b>Diarrhea</b>					1.958	(1)	0.162
Yes	324	(51.6%)	127	(46.5%)			
No	304	(48.4%)	146	(53.5%)			
<b>Cough</b>					1.175	(1)	0.278
Yes	47	(7.5%)	15	(5.5%)			
No	581	(92.5%)	258	(94.5%)			
<b>Dizziness</b>					0.914	(1)	0.339
Yes	147	(23.4%)	56	(20.5%)			
No	481	(76.6%)	217	(79.5%)			
<b>Constipation</b>					1.073	(1)	0.300
Yes	192	(30.6%)	93	(34.1%)			
No	436	(69.4%)	180	(65.9%)			
<b>Sore throat</b>					0.592	(1)	0.442
Yes	38	(6.1%)	13	(4.8%)			
No	590	(93.9%)	260	(95.2%)			
<b>Runny nose</b>					2.180	(1)	0.140
Yes	44	(7.0%)	27	(9.9%)			
No	584	(93.0%)	246	(90.1%)			

<sup>a</sup>n = 628.<sup>b</sup>n = 273.

vaccination and the presence of adverse effects following these vaccinations, as shown in [Table 8](#).

### 3.8. COVID-19 vaccination status and adverse effects

[Tables 8](#) and [9](#) highlight the vaccination status disparities among COVID-19 vaccine recipients, with various side effects reported. A total of 814 (90.3%), 716 (79.5%) and 372 (41.3%) people experienced side effects following the first, second and third doses of vaccination, respectively. Pearson's chi-square test was performed to evaluate the relationship between adverse effects and types of COVID-19 vaccine based on vaccine status. According to the findings in [Table 8](#), when compared with recipients who received a single vaccine, mixed vaccine recipients reported a significantly higher number of adverse effects post vaccination. However, when compared based on vaccination dosage, single vaccine recipients reported a higher number of postvaccination side effects after receiving the 2nd dose of vaccine [*P* value < 0.001]. Furthermore, certain side effects reported had *P* values less than 0.05, as shown in [Table 9](#), further indicating that there is a significant association between these side effects and types of COVID-19 vaccine based on vaccine status. These side effects included pain or soreness at the injection site, swelling at the injection site, muscle pain, chills and shivering, joint pain and malaise.



### **3.9. Local and systemic side effects**

Among all COVID-19 vaccine type recipients who responded to our survey, mixed vaccine recipients reported a higher number of local and systemic symptoms, with 245 (89.7%) and 236 (86.4%) cases, respectively. A total of 523 (83.3%) and 517 (82.3%) people also reported local and systemic symptoms, respectively, after receiving a single type of COVID-19 vaccination. The results from [Table 8](#) also showed that a higher number of local and systemic symptoms were reported following the 2nd dose vaccination among single-type COVID-19 vaccine recipients [ $P$  value < 0.001]. Other details are explained in [Table 8](#).

### **3.10. Age and vaccine effects**

Recipients <60 years of age were found to more commonly experience side effects after receiving COVID-19 immunisation, with a significantly greater percentage of cases reported compared to those from the elderly age group (>60 years of age). The chi-square test showed that there was a significant association between the types of COVID-19 vaccination and the number of side effects among different age groups, specifically among recipients <60 years of age, with a  $P$  value less than 0.05, as tabulated in [Table 10](#).

### **3.11. Severity of side effects**

Of the COVID-19 vaccine recipients with reported adverse effects, 503 (61.8%) people required treatment to relieve postvaccination local and systemic symptoms. However, no severe symptoms that required hospitalisation were reported among the participants. The observed proportion of adverse events that required treatment was significantly higher among Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine recipients, excluding those from the 41 to 50 year age group, as shown in [Table 11](#). Recipients of the Pfizer-BioNTech (Comirnaty <sup>®</sup>) vaccine with reported adverse effects from the 41 to 50-year-old age group showed a significantly higher percentage of people requiring treatment for postvaccination side effects.

## **4. Discussion**

It is widely known that the risk of getting and spreading COVID-19 can be effectively curbed through vaccination drive (Bloom et al., 2021; Lipsitch & Dean, 2020). However, the safety, side effects and efficacy profile of COVID-19 vaccines remain a prevailing concern globally, as the reactogenicity of these vaccines has not been completely understood to date. Following vaccination, one may experience unpleasant symptoms in the process of building immunity

**Table 10.** Association of number of adverse effects reported with types of COVID-19 vaccine based on age group.

Age group	Types of COVID-19 vaccine	Number of side effects reported		Adverse effects		$\chi^2$	(df)	P value		
		$\leq 5$	$> 5$	$n$	(%)					
18–30 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	27	(7.1%)	100	(26.2%)	127	(33.3%)	44.742	(8)	<0.001
	Sinovac (CoronaVac <sup>®</sup> )	16	(13.7%)	23	(19.7%)	39	(33.3%)			
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	4	(3.1%)	46	(36.2%)	50	(39.4%)			
	Mixed COVID-19 vaccine	12	(4.4%)	76	(27.8%)	88	(32.2%)			
31–40 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	26	(6.8%)	97	(25.5%)	123	(32.3%)	20.285	(8)	0.009
	Sinovac (CoronaVac <sup>®</sup> )	10	(8.5%)	14	(12.0%)	24	(20.5%)			
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	3	(2.4%)	22	(17.3%)	25	(19.7%)			
	Mixed COVID-19 vaccine	15	(5.5%)	48	(17.6%)	63	(23.1%)			
41–50 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	3	(0.8%)	60	(15.7%)	63	(16.5%)	24.497	(6)	<0.001
	Sinovac (CoronaVac <sup>®</sup> )	5	(4.3%)	13	(11.1%)	18	(15.4%)			
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	3	(2.4%)	22	(17.3%)	25	(19.7%)			
	Mixed COVID-19 vaccine	18	(6.6%)	29	(10.6%)	47	(17.2%)			
51–60 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	2	(0.5%)	18	(4.7%)	20	(5.2%)	12.851	(6)	0.045
	Sinovac (CoronaVac <sup>®</sup> )	2	(1.7%)	3	(2.6%)	5	(4.3%)			
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	0	(0.0%)	5	(3.9%)	5	(3.9%)			
	Mixed COVID-19 vaccine	16	(5.9%)	21	(7.7%)	37	(13.6%)			
61–70 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	6	(1.6%)	15	(3.9%)	21	(5.5%)	9.454	(6)	0.150
	Sinovac (CoronaVac <sup>®</sup> )	0	(0.0%)	4	(3.4%)	4	(3.4%)			
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	4	(3.1%)	4	(3.1%)	8	(6.3%)			
	Mixed COVID-19 vaccine	8	(2.9%)	8	(2.9%)	16	(5.9%)			
71–80 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	0	(0.0%)	1	(0.3%)	1	(0.3%)	1.333	(1)	0.248
	Sinovac (CoronaVac <sup>®</sup> )	0	(0.0%)	0	(0.0%)	0	(0.0%)			
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	0	(0.0%)	0	(0.0%)	0	(0.0%)			
	Mixed COVID-19 vaccine	2	(0.7%)	1	(0.4%)	3	(1.1%)			

**Table 11.** Association of treatment for post COVID-19 vaccination adverse effects with types of COVID-19 vaccine based on age group.

Age group	Types of COVID-19 vaccine	Treatment for adverse effects		$\chi^2$	(df)	P value
		No	Yes			
		n	(%)	n	(%)	
18–30 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	44	(34.6%)	83	(65.4%)	41.200 (4) <0.001
	Sinovac (CoronaVac <sup>®</sup> )	28	(71.8%)	11	(28.2%)	
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	10	(20.0%)	40	(80.0%)	
31–40 years	Mixed COVID-19 vaccine	26	(29.5%)	62	(70.5%)	11.305 (4) 0.023
	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	46	(37.4%)	77	(62.6%)	
	Sinovac (CoronaVac <sup>®</sup> )	14	(58.3%)	10	(41.7%)	
41–50 years	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	6	(24.0%)	19	(76.0%)	8.876 (3) 0.031
	Mixed COVID-19 vaccine	26	(41.3%)	37	(58.7%)	
	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	14	(22.2%)	49	(77.8%)	
51–60 years	Sinovac (CoronaVac <sup>®</sup> )	10	(55.6%)	8	(44.4%)	1.338 (3) 0.720
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	9	(36.0%)	16	(64.0%)	
	Mixed COVID-19 vaccine	23	(48.9%)	24	(51.1%)	
61–70 years	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	9	(45.0%)	11	(55.0%)	1.690 (3) 0.639
	Sinovac (CoronaVac <sup>®</sup> )	3	(60.0%)	2	(40.0%)	
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	2	(40.0%)	3	(60.0%)	
71–80 years	Mixed COVID-19 vaccine	16	(43.2%)	21	(56.8%)	1.000 <sup>a</sup>
	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	8	(38.1%)	13	(61.9%)	
	Sinovac (CoronaVac <sup>®</sup> )	2	(50.0%)	2	(50.0%)	
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	2	(25.0%)	6	(75.0%)	
	Mixed COVID-19 vaccine	8	(50.0%)	8	(50.0%)	
	Pfizer-BioNTech (Comirnaty <sup>®</sup> )	1	(100.0%)	0	(0.0%)	
	Sinovac (CoronaVac <sup>®</sup> )	0	(0.0%)	0	(0.0%)	
	Oxford-AstraZeneca (ChAdOx1- <sup>®</sup> [recombinant])	0	(0.0%)	0	(0.0%)	
	Mixed COVID-19 vaccine	2	(66.7%)	1	(33.3%)	

<sup>a</sup>Fischer Exact test is performed.

depending on various factors, including the type of vaccine received, its composition, route of administration and host characteristics, which include age, gender and others (Hervé et al., 2019). According to studies, there is a vast difference in awareness, perception and acceptance of the COVID-19 vaccine among the public (Adedeji-Adenola et al., 2022; Batarseh et al., 2021; Enitan et al., 2020). Hesitancy towards receiving COVID-19 vaccines among the public is complicated by various factors, including concerns about the development of vaccines at an unprecedented rate and the assurance of the safety and effectiveness of these vaccines (Batteux et al., 2022; Jennings et al., 2021). As such, there is a need to monitor vaccine hesitancy, and authorities should consider various initiatives to encourage more participation in vaccination drive, in particular, these programmes should aim to address the factors underpinning vaccine hesitancy. Therefore, we conducted this study to explore the probable symptoms experienced following COVID-19 vaccination so that this information can be used to educate the public on the safety profile of COVID-19

vaccine to optimise COVID-19 vaccine uptake in Malaysia. The findings from this study revealed that the predictors of COVID-19 vaccination that are significant at the 5% level of significance are age, gender, type of COVID-19 vaccine and vaccination dose. These predictors are needed due to the diversity in vaccination response and its corresponding cellular changes of immune system post vaccination (Plotkin, 2010; Pulendran, 2014). For instance, a Saudi Arabia nationwide study identified the level of education, nationality of respondents, gender and general health status as significant predictors of severe adverse reactions following COVID-19 vaccination (Almalki et al., 2022). Another study in Turkey also identified gender and age as predictors of side effects following COVID-19 vaccination (Riad et al., 2021b).

Our findings revealed that 90.3% of the study participants reported at least one symptom following COVID-19 vaccination. However, none of them reported serious effects towards any of the COVID-19 vaccines received. Based on the results of our study, recipients of these COVID-19 vaccines can primarily expect the following symptoms following vaccination: swelling at the injection site, pain or soreness at the injection site, headache, fatigue or tiredness, muscle weakness and diarrhea. The most common adverse effects experienced among single vaccine recipients (e.g. Pfizer-BioNTech (Comirnaty<sup>®</sup>), Sinovac (CoronaVac<sup>®</sup>), Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) and others (e.g. CanSino/Johnson & Johnson/Sinopharm)) were pain or soreness at the injection site, swelling at the injection site, fatigue or tiredness, headache, nausea, muscle pain, muscle weakness, chills and shivering, fever, skin rash, malaise and diarrhea. Meanwhile, symptoms such as pain or soreness at the injection site, swelling at the injection site, fatigue or tiredness, headache, nausea, muscle weakness and skin rash were found to be the most common side effects reported by mixed COVID-19 vaccine recipients. The least reported adverse effects among single vaccine recipients (e.g. Pfizer-BioNTech (Comirnaty<sup>®</sup>), Sinovac (CoronaVac<sup>®</sup>) and Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant])) were cough, sore throat and runny nose, while among mixed vaccine recipients, symptoms such as insomnia, cough, sore throat and runny nose were the least reported symptoms. Interestingly, although swollen lymph nodes have been reported as the rarest adverse effect among vaccine recipients such as Pfizer-BioNTech (Comirnaty<sup>®</sup>) in a recent study, our findings showed otherwise (El-Shitany et al., 2021). Approximately 64, 13, 13 and 31 study participants reported experiencing swollen lymph nodes following vaccination with the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine, Sinovac (CoronaVac<sup>®</sup>) vaccine, Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine and mixed vaccine, respectively. Among these mixed vaccine recipients, 12 were recipients of Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) + Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccines, 1 was a recipient of Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) + Sinovac (CoronaVac<sup>®</sup>) vaccines and 18

were recipients of Sinovac (CoronaVac<sup>®</sup>) + Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccines. Furthermore, the reported adverse effects were similar to those described in the safety and efficacy studies of COVID-19 vaccines, including those that were concluded in the Clinical Guidelines on COVID-19 Vaccination in Malaysia but with a higher percentage of cases observed in this study (Malaysia MoH, 2021; Menni et al., 2021; Nassar et al., 2022; Saeed et al., 2021; Zhang et al., 2021).

Based on this study, side effects were significantly greater among the elderly age group among Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine and mixed vaccine recipients, which is similar to the findings from other studies (Nassar et al., 2022; Omeish et al., 2022). In contrast, recipients of the Sinovac (CoronaVac<sup>®</sup>) vaccine and Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine showed otherwise. A study by Saeed *et al.* reported similar results among Sinopharm vaccine recipients (Saeed et al., 2021). Several other studies have shown that individuals from younger age groups are more likely to experience postvaccination side effects than individuals from older age groups (Doroftei et al., 2021). In addition, our study also found that female recipients of Pfizer-BioNTech (Comirnaty<sup>®</sup>), Sinovac (CoronaVac<sup>®</sup>) and mixed vaccination reported significantly higher statistics of adverse effects, which is similar to the trend reported in other studies (Camacho Moll et al., 2022; Cuschieri et al., 2021; Mohammed et al., 2021). Various factors could contribute to the cause of the gender disparity in vaccine side effects. The differences in male and female hormones are highly associated with variations in immune responses in individuals. Several studies have reported that testosterone plays a role in the suppressive action of the immune response in adult males, whereas estradiol is related to a higher immune response against viral infections in adult females (Di Resta et al., 2021; Potluri et al., 2019). This theory could be a plausible explanation for why female participants reported more postvaccination adverse effects than male participants in this study. Nonetheless, this could also be attributed to the higher percentage (75.9%) of female participants in this study. Furthermore, participants of Indian ethnicity reported a significantly greater number of cases experiencing symptoms following vaccination with the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine and Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine. Meanwhile, recipients of Chinese ethnicity and Malay ethnicity were found to have higher side effects reported following vaccination with Sinovac (CoronaVac<sup>®</sup>) vaccine and mixed COVID-19 vaccines, respectively. A significantly greater percentage of people experiencing side effects was reported among COVID-19 vaccine recipients of higher educational status, excluding recipients of the Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine, which showed an opposing result. According to existing studies, the level of education and employment status are among the factors that positively impact vaccine acceptance (Gagneux-Brunon et al.,

2021; Maraqa et al., 2021). For instance, a linear relationship was observed between level of education and acceptance of vaccine in a study (Shekhar et al., 2021). Similarly, the results from our study also showed that the majority of the participants were at a higher educational level and had a job. In addition, individuals with associated comorbidities were found to have a significant association with adverse effects following vaccination with the Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine as well as the Sinovac (CoronaVac<sup>®</sup>) vaccine. This finding is in line with another study that demonstrated that the magnitude of COVID-19 side effects was comparatively higher among individuals associated with comorbidities (Alemayehu et al., 2022). In addition, this result is also aligned with the findings of studies that demonstrated a significant association of comorbidities with the development, frequency and severity of postvaccination side effects (Alghamdi et al., 2021; Ganesan et al., 2022; Hatmal et al., 2022). In contrast, another study conducted in Turkey reported no association between chronic illness and post-Sinovac (CoronaVac<sup>®</sup>) vaccination side effects (Riad et al. 2021b). Differences in the study population and type of COVID-19 vaccines could be the reason behind the inconsistency of results. Moreover, evidence from a recent study also portrayed a lower frequency of side effects following Sinovac (CoronaVac<sup>®</sup>) vaccination compared to other COVID-19 vaccines (Elnaem et al., 2021). These findings suggest the relationship between types of COVID-19 vaccine and the frequency of postvaccination side effects. We also discovered that individuals with a history of previous COVID-19 infection showed more side effects following vaccination with the Sinovac (CoronaVac<sup>®</sup>) vaccine and Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine, which is similar to the findings of other studies (Krammer et al., 2021; Saadat et al., 2021; Wise, 2021).

Before the introduction of mixed COVID-19 vaccination, it was a common practice to mix vaccines and use vaccines of different platforms as a subsequent second dose of vaccination or as a booster dose to improve the results of immunisation. A variety of techniques have been utilised, including different vaccine formulations between vaccine doses, in which encouraging results have been obtained. To date, studies have shown that higher immunity is achieved in both animal models and human trials when DNA and vector vaccines have been mixed together (Lin et al., 2010; Saeedi et al., 2014; Wang et al., 2008). In addition, scientific evidence has shown that mixtures of DNA vaccines with protein vaccines or viral and protein vaccines as well as virus-like particle vaccines with DNA vaccines have all been proven to produce greater immune responses among recipients (Alekseeva et al., 2009; Lu, 2009). Our study demonstrated similar results that support this finding in which, compared to single COVID-19 vaccine recipients, individuals who received mixed COVID-19 vaccination reported a statistically greater percentage of postvaccination symptoms. A few recent studies showed similar

results, which could possibly suggest that mixed vaccination may increase vaccine reactogenicity, especially systemic reactogenicity (Alshahrani & Alqahtani, 2022; Borobia et al., 2021; Hillus et al., 2021; Vogel, 2021). It is not clear why participants who received a single type of COVID-19 vaccination reported a statistically greater number of cases experiencing symptoms after receiving the 2nd dose of vaccination in contrast to mixed vaccination. Among the single vaccine recipients who had reported postvaccination side effects, Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccine recipients reported a significantly greater percentage of postvaccination symptoms compared to other single COVID-19 vaccines. In a study comparing Pfizer-BioNTech (Comirnaty<sup>®</sup>) and Sinopharm vaccines, more moderate to severe side effects were reported following Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination (Hatmal et al., 2021). Another study concluded that local side effects were more common following Pfizer-BioNTech (Comirnaty<sup>®</sup>) vaccination (Menni et al., 2021). Although no severe adverse events that required hospitalisation were reported, 503 (61.8%) participants still required treatment to relieve postvaccination local and systemic symptoms. The observed proportion of adverse effects that required treatment was significantly higher among Oxford-AstraZeneca (ChAdOx1-<sup>®</sup>[recombinant]) vaccine recipients, excluding those from the 41 to 50 year age group, as shown in Table 11. Our study provides evidence of mild symptoms, as participants in our study did not consult a physician for their adverse effects following immunisation. These side effects were managed conservatively, followed by self-mediations such as paracetamols, aspirin, antihistamines and medications of chronic illness such as antihypertensive medications. This is consistent with a recent study that reported that 64% of health care workers in Ethiopia used paracetamol as a remedy for the side effects they experienced.

## 5. Strengths and limitations

At the time of writing this article, this is the first study in Malaysia to assess the types of self-reported post-COVID-19 vaccination side effects associated with different COVID-19 vaccine regimens, to the best of our knowledge. However, this study has a few limitations. First, due to the pandemic and Movement Control Order (MCO) in Malaysia, this study was conducted via an online survey in which data collection was performed as a self-report survey and its dissemination depended on the authors' networks. This might result in a reporting bias and recall bias that cannot be disregarded in this study. Furthermore, our sampling method may limit the possibility of generalising our results to a larger population. Aside from that, the sample size of the two groups (single and mixed vaccination) was not comparable. A total of 628 participants were from the single vaccine group, whereas only 273 participants were in the mixed vaccine group. This is highly likely due to the implementation of the

COVID-19 vaccination regimen during the shortage of vaccines in Malaysia. This study also focused on the short-term postvaccination side effects, as the latent effects following COVID-19 vaccination were not studied or included in this study. Given these limitations, a clinical trial model evaluating the adverse effects between single and mixed COVID-19 vaccination is therefore recommended to (1) confirm and explore the types of postvaccination adverse effects based on types of COVID-19 vaccination, (2) provide information for educational purposes so that the public's concerns towards the COVID-19 vaccine can be better addressed and (3) increase the COVID-19 vaccine acceptance rate and reduce vaccine hesitancy among the public.

## 6. Conclusion

This study demonstrated the types of self-reported adverse effects following immunisation with single and mixed COVID-19 vaccines in Malaysia. Being older, female gender, mixed COVID-19 vaccination and number of vaccine dose were among the significant predictors of COVID-19 vaccine related side effects among COVID-19 vaccinated people in Malaysia. We also found that participants who received mixed COVID-19 vaccination reported significantly more local and systemic symptoms after the first and third doses compared with single-type COVID-19 vaccine recipients. By revealing the differences of the side effects for each single and mixed vaccines implemented in Malaysia, this study may thus provide better understanding for the public, and provide important baseline for regulatory agencies worldwide to carefully consider the risk-benefit profile of vaccine to make informed decisions during public health emergencies in future. Our findings on the side effects of these COVID-19 vaccines would also be highly beneficial for health authorities, pharmaceutical companies and government in shaping health policies and outreach programmes to facilitate immunisation programme in Malaysia against future health crisis. The findings from the present study could influence regulatory decision making and adjustments in pharmaceutical policies and regulations. Regulatory bodies may update guidelines, refine approval processes or implement new measures to enhance vaccine safety and efficacy. The results of the present study could also be further explored in the context of vaccine pre-medications to lessen the severity of side effects following vaccination. In summary, this present study has had far-reaching implications for the pharmacy community, health authorities and pharmaceutical policy and regulations globally. It underscores the importance of ongoing surveillance, collaboration and transparent communication to ensure the continued success of vaccination efforts and public health initiatives. Considering the possibility of different types of COVID-19 vaccination received among respondents, similar studies should be carried out in the future as a follow-up to explore the reactogenicity of these vaccines



and the factors associated with greater odds of postvaccination symptoms to overcome vaccine hesitancy among the public.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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