ORIGINAL ARTICLE

COVID-19 vaccines-related adverse events and associated factors reported among adult Egyptians

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ABSTRACT

COVID-19 vaccine recipients are more likely to experience post-vaccination adverse events, which are considered the source of concerns about vaccine safety. This study aims to describe the utilization of COVID-19 vaccines and the associated adverse events and their possible predictors among adult Egyptians. An online cross-sectional study was designed to collect data through a Google Form questionnaire in November 2021. Adults who received at least one dose of the COVID-19 vaccine were asked to report their experience with vaccination and associated adverse events. A total of 853 participants were included in the study after receiving Sinopharm/Sinovac (63%), AstraZeneca (27%), Pfizer-BioNTech (4.8%), and other vaccines (5.2%). Around 50% of participants thought that COVID-19 vaccines were safe, 30.8% advised others with vaccination, and 68.3% reported post-vaccination adverse events. The most commonly encountered adverse symptoms were injection site pain (82.5%), fatigue (67.4%), flu-like symptoms (59.6%), and bone and muscle pains (59.6%). Most adverse events were less likely reported by Sinopharm/Sinovac recipients than recipients of other vaccines. The significant predictors for reporting adverse events were female gender, the first dose of vaccination, and vaccine type (AstraZeneca versus Sinopharm/Sinovac) with multivariable-adjusted OR (95% CI) = 1.85 (1.34-2.54); 2.01 (1.24–3.25), and 3.86 (2.54–5.86). Findings revealed that adverse events of COVID-19 vaccines are common. Sinopharm/Sinovac recipients were reported to have lesser adverse events than other recipients. However, serious reactions were rare which ensures the safety of all vaccine types among the adult Egyptian population.

Key words:
COVID-19 vaccine; adverse events; Egyptian adults; Sinopharm/Sinovac; AstraZeneca

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INTRODUCTION

After more than two years of the World Health Organization (WHO) declaration that the COVID-19 outbreak is a global pandemic in March 2020, the disease continues as a major public health problem. Until June 2022, there have been over 529 million confirmed cases of COVID-19 worldwide, including more than six million deaths, reported to WHO.[1] Egypt reported about 514,000 confirmed cases and over 24,000 deaths of COVID-19, and about 90 million administered vaccine doses.[2]

The best strategy to gradually combat this pandemic was to develop and ensure effective vaccination.[3] In August 2021, Egypt received 1.76 million doses of COVID-19 vaccines in the third batch of vaccines delivered via the COVAX Facility. Egypt's Ministry of Health announced that five different vaccines are available in nearly 539 vaccine centers around the country against coronavirus infection. The available COVID-19 vaccines, which have obtained emergency approvals from the Egyptian Drug Authority are Sputnik V, Sinopharm, AstraZeneca, Johnson & Johnson, and Sinovac vaccines.[4]

Nearly by mid-2020, scientists began a race to produce safe and effective vaccines in record time with several technology platforms and extraordinary achievements due to the urgency of the pandemic. Every vaccine project has unique characteristics in terms of effectiveness, duration of induced protection, and/or vaccine safety.[5] The most commonly reported post-vaccination adverse events included pain, redness or swelling at the site of injection, tiredness, headaches, muscle pain, chills, fever, and nausea. Most of the reactions reported in published clinical trials of COVID-19 vaccines were mild to moderate and resolved within 3–4 days, whereas a few had severe intensity.[6]

Overall, COVID-19 vaccines are safe and effective tools to prevent severe forms of the disease, hospitalization, and death against all variants of concern.[7] However, some individuals still have concerns about receiving COVID-19 vaccination related to vaccine safety and efficacy. Several studies have shown that beliefs that vaccines may be not safe/effective were among the determinants associated with increased vaccine hesitancy, which may have an immediate influence on the success of the vaccination strategies.[8-10] Hence, further post-marketing studies are essential to declare the available vaccines' adverse events, mitigate anxiety elicited by post-vaccination reactogenicity, ensure vaccine efficacy and safety, and raise the acceptance of the vaccination.[6, 8, 11]

Regardless of what the producing companies reported about the safety and effectiveness of their COVID-19 vaccines and with no conflict of interest, we chose to directly approach and survey the experience of those who received the COVID-19 vaccines in Egypt. Thus, the present study aims to describe the utilization of COVID-19 vaccines and the reported immediate and short-term side effects of the COVID-19 vaccines on their recipients. In addition, the study sought to identify possible factors associated with the appearance of post-vaccination adverse events.

METHOD

Study design and population

A cross-sectional survey targeted Egyptian adults aged ≥ 18 years old who received at least one dose of the COVID-19 vaccine. This survey was conducted during the period between November 2nd and 16th, 2021. A google online self-administered survey was created and sent via different social media channels and by e-mails

through a link shared to some official and private internet websites.

Data Collection

The survey was designed as an Arabic Google form starting with an explanation of the aims and eligibility criteria of the study. The questionnaire collected data about the socio-demographic characteristics, type and utilization of COVID-19 vaccines, perceptions about the vaccines, and any adverse events experienced after vaccination. The questionnaire inquired about the onset and duration of adverse events and their relation to both first and second doses of vaccination.

The study started in three regions of Egypt (El-Minia, Beni-Suef, and Cairo) and was extended with a snow sample technique to include participants from other areas in Egypt. A pilot study was conducted on 20 participants, who were finally included in the study, to assess the clarity of questions and feasibility of the study. The reliability of this questionnaire was approved using Cronbach's alpha test (α = 0.92).

Statistical Analysis

Data were analyzed using the Statistical Package for Social Science (SPSS), Version 25.0.

Descriptive statistics were presented as mean± SD for normally distributed numerical variables, while numbers and percentages were used for categorical variables. Chi-squared tests and binary logistic regression were used to determine the factors that were significantly associated with adverse events after vaccination. Multivariable binary logistic regression was used to predict the possible risk factors for the appearance of COVID-19 post-vaccination adverse events. The significance level was $p < 0.05$.

Ethical Approval

This study was approved by the Research Ethics Committee of Minia University. The purpose, conditions, and eligibility criteria of the study were described in the 'Background' section of the questionnaire and participants had to agree before proceeding to fill out and submit the rest of the questions of the survey which was considered as approval and informed consent of participation.

RESULTS

The study included 853 adults who reported receiving at least one dose of the COVID-19 vaccine, with a mean (SD) age of 24.7 (9.1) years and 57.4% were females. More than half of the participants were college students (56.7% medical and 12.3% non-medical) and 173 (20.3%) reported a history of chronic disease (Table 1).

Table 1. Sociodemographic characteristics of the study participants

	Numbers (%) (n=853)
Age, (Mean ±SD)	24.73±9.10
18-20 years	449 (52.6)
21-30 years	232 (27.2)
30-60 years	172 (20.2)
Sex	
Male	363 (42.6)
Female	490 (57.4)

	Numbers (%) (n=853)
Marital status	682 (80)
Unmarried	171 (20)
Married	
Education	
Secondary or less	18 (2.1)
University	696 (81.6)
Postgraduate	139 (16.3)
Occupation	
Medical field	135 (15.8)
Medical student	484 (56.7)
Non-medical student	105 (12.3)
Other	129 (15.2)
History of chronic disease	
No	680 (79.7)
Yes	173 (20.3)
BMI, (Mean ±SD)	25.67±5.64
Normal	454 (53.2)
Overweight/Obese	399 (46.8)
Smoking	
Non-smoker	812 (95.2)
Smoker	41 (4.8)

The most utilized COVID-19 vaccines as reported by the Egyptian participants were; Sinopharm/ Sinovac (63%), AstraZeneca (27%), and Pfizer-BioNTech (4.8%) followed by other vaccines. The majority of participants (84.1%) received two doses and 36.8% felt protected after the second dose. Moreover, 8.9% of the participants reported COVID-19 infection after being vaccinated, 7.2% suffered the same symptoms or less severe infection after receiving the vaccines, and 30.8% advised others to receive COVID-19 vaccination as shown in Table 2.

Table 2. Utilization of COVID-19 vaccines among the study participants

	Numbers (%) (n=853)
Types of vaccine	
Sinopharm/Sinovac	537 (63)
AstraZeneca	230 (27)
Pfizer-BioNTech.	42 (4.8)
Johnson & Johnson's Janssen	12 (1.4)
Others/Don’t know	32 (3.8)
Number of doses	
One	136 (15.9)
Two	717 (84.1)

	Numbers (%) (n=853)
COVID-19 infection	
Not infected/not sure	527 (61.8)
Yes, before vaccination	250 (29.3)
Yes, after vaccination	76 (8.9)
Method of diagnosis	
Not infected	501 (58.7)
Clinical only	194 (22.7)
Radiological± blood tests	106 (12.4)
PCR	52 (6.1)
Severity of infection after vaccination	
Not infected	777 (91)
Less severe	41 (4.8)
Same severity	20 (2.4)
More severe	15 (1.8)
Stress during vaccination period	
Never	340 (39.9)
Sometimes	357 (41.8)
Often	156 (18.3)
Decision of vaccination	
Personal/family/community protection	350 (41)
Forcing employer/university/governmental	438 (51.4)
Both	65 (7.6)
Opinion about vaccine safety	
No	127 (14.9)
Yes	424 (49.7)
Neutral	302 (35.4)
Willing to take a third dose	
No	228 (26.7)
Yes	352 (41.3)
Maybe	273 (32)
Advice others with vaccination	
No	120 (14.1)
Yes	263 (30.8)
Neutral	470 (55.1)
Feel protected after vaccination	
No/maybe	464 (54.4)
Yes, after 1st dose	75 (8.8)
Yes, after 2nd dose	314 (36.8)
Need protective measures after vaccination	63 (7.4)
No	121 (14.2)
Yes	669 (78.4)
I don't know	

It was found that 68.3% of the study participants reported post-vaccination adverse events. Sinopharm or Sinovac recipients were more likely to report no or mild local symptoms and less likely to suffer from adverse events after the 1st dose (48.4% and 25.9%, respectively) compared to AstraZeneca recipients (23% and 61.3%, respectively). The most common adverse events regardless of the type of vaccine were injection site pain/swelling (82.5%), fatigue (67.4%), flu-like symptoms (59.6%), and bone and muscle pain (59.4%). About 65% of suffering persons took painkillers with rest at home, while 2.7% visited a doctor and 0.5% needed hospital admission (Table 3).

Table 3. COVID-19 vaccine related adverse events and relationship with the type of vaccine as reported by the Egyptian participants

Adverse events of COVID-19 vaccines	**Total numbers** (%) (n=853)	**COVID-19 vaccine** N (%)			**P-value**
		Sinopharm/ Sinovac (n= 537)	**AstraZeneca** (n= 230)	**Others** (n= 86)	
Timing					
No/mild local symptoms	344 (40.3)	260 (48.4)	53 (23)	31 (36)	
After 1st dose	312 (36.6)	139 (25.9)	141 (61.3)	32 (37.2)	
After 2nd dose	90 (10.6)	70 (13.0)	11 (4.8)	9 (10.5)	0.0001
After 1st and after 2nd dose	107 (12.5)	68 (12.7)	25 (10.9)	14 (16.3)	
Onset					
No	270 (31.7)	216 (40.2)	34 (14.8)	20 (23.3)	
< 1 day	442 (51.9)	227 (42.3)	163 (70.9)	51 (61.6)	
1-2 days	79 (9.2)	50 (9.3)	19 (8.3)	10 (11.6)	0.0001
≥ 3 days	61 (7.2)	44 (8.2)	14 (6.1)	3 (3.5)	
Duration					
No	270 (31.7)	216 (40.2)	34 (14.8)	20 (23.3)	
< 1 day	146 (17)	86 (16)	42 (18.3)	18 (20.9)	
1-3 days	286 (33.6)	141 (26.3)	114 (49.6)	31 (36.0)	0.0001
4-7 days	95 (11.1)	60 (11.2)	22 (9.6)	13 (15.1)	
>1 weeks	56 (6.6)	34 (6.3)	18 (7.8)	4 (4.7)	
Types *					
Injection site pain/swelling	704 (82.5)	421 (78.4)	210 (91.3)	73 (84.9)	0.0001
Hypersensitivity	195 (22.9)	117 (21.8)	62 (27)	16 (18.6)	0.181
Bone and muscle	507 (59.4)	272 (50.7)	176 (76.5)	59 (68.6)	0.0001
Flu-like symptoms	508 (59.6)	272 (50.7)	178 (77.4)	58 (67.4)	0.0001
Fatigue	575 (67.4)	317 (59.0)	193 (83.9)	65 (75.6)	0.0001
Gastrointestinal	245 (28.7)	131 (24.4)	85 (37)	29 (33.7)	0.001
Menstrual changes**	98 (23.1)	67 (23.8)	18 (18.2)	13 (30.2)	0.266
Miscellaneous	207 (24.3)	122 (22.7)	68 (29.6)	17 (19.8)	0.076
Serious	9 (1.1)	5 (0.9)	4 (1.7)	0 (0)	0.363
Management					
No	270 (31.7)	216 (40.2)	34 (14.8)	20 (23.3)	
Rest at home/painkillers	556 (65.1)	306 (57)	188 (81.8)	62 (72)	
Doctor visit	23 (2.7)	12 (2.2)	7 (3.0)	4 (4.7)	0.0001
Admission to hospital	4 (0.5)	3 (0.6)	1 (0.4)	0 (0)	

**The sum may not add up to 100% because the symptoms are not mutually exclusive as the questionnaire items allow multiple choices **Total= 424 females who experienced at least one menstrual period after being vaccinated*

The most frequently reported symptoms were arm pain with or without numbness (58.6%), fever and headache (42.7%), muscle pain (42.6%), and fatigue (26.5%). Moreover, about a quarter of the females have experienced menstrual pain (26.9%) and menstrual flow changes (24.1%). Other miscellaneous adverse events were reported such as blurred vision, numbness, burning micturition, hypertension, and purpura. Furthermore, only 1.1% of the participants experienced other serious adverse events in the form of trigeminal neuralgia, DVT, and myocardial infarction (Figure 1).

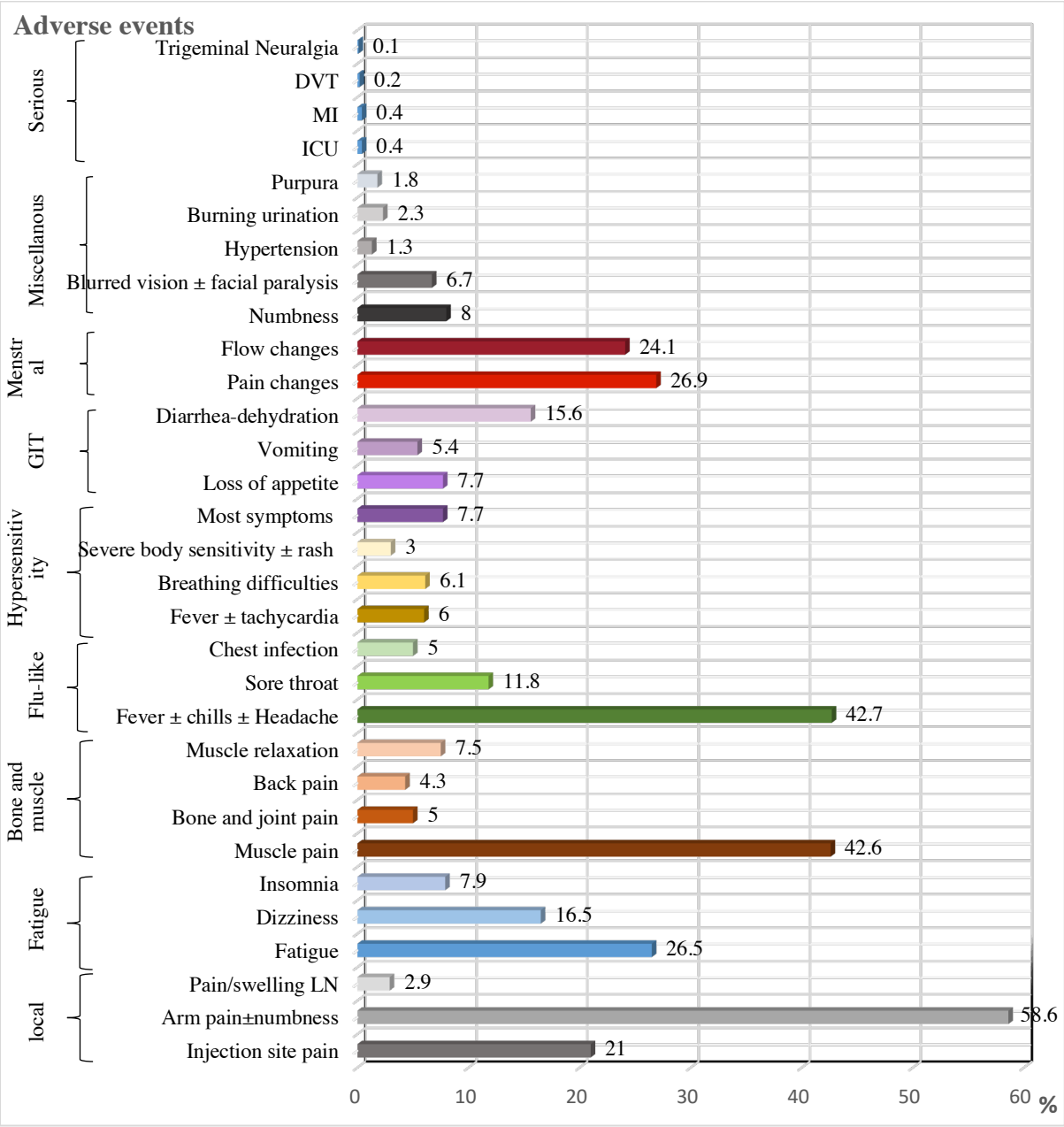

Figure 1. Frequency of adverse events after COVID-19 vaccination

The possible associations of participants' characteristics and vaccine type with post-vaccination adverse events were presented in Table 4. In the multivariable logistic regression analysis, female gender (OR: 2.11, 95% CI: 1.51–2.97, p-value: <0.0001), AstraZeneca vaccine (OR of AstraZeneca versus Sinopharm/Sinovac: 3.69, 95% CI: 2.38–5.72) and the first dose of vaccination (OR of first dose versus second doses: 2.01, 95% CI: 1.24–3.25, p-value: <0.0001) were significant predictors for post-vaccination adverse events.

Table 4. Predictors for development of adverse events after COVID-19 vaccination

	No adverse events (n= 270) N (%)	**Adverse events** (n= 583) N (%)	**Crude OR** (95% CI) p-value	**Adjusted OR** (95% CI) p-value
Age				
18-20 years	157 (58.1)	292 (50.1)	1	
21-30 years	70 (25.9)	162 (27.8)	1.24 (0.86-1.75)	
> 30 years	43 (15.9)	129 (22.1)	1.61 (1.09-2.40)	
			0.050	
Sex				
Male	147 (54.4)	216 (37)	1	1
Female	123 (45.6)	367 (63)	2.03 (1.52-2.72)	2.11 (1.51-2.97)
			<0.0001	<0.0001
Marital status				
Unmarried	232 (85.9)	450 (77.2)	1	
Married	38 (14.1)	133 (22.8)	1.80 (1.22-2.67)	
			0.003	
Residence				
El-Minia	144 (53.3)	250 (42.9)	1	
Benisuef	87 (32.2)	220 (37.7)	1.46 (1.06-2.01)	
Others	39 (14.4)	113 (19.4)	1.67 (1.10-2.53)	
			0.015	
Education				
University or less	238 (88.1)	476 (81.6)	1	
Postgraduate	32 (11.9)	107 (18.4)	1.67 (1.10-2.56)	
			0.018	
Occupation				
Medical field	36 (13.3)	99 (17.0)	1	
Medical student	174 (64.4)	310 (53.2)	0.65 (0.42-0.99)	
Non-medical student/other	60 (22.3)	174 (29.8)	1.06 (0.65-1.71)	
			0.009	
Chronic disease				
No	227 (84.1)	452 (77.7)	1	
Yes	43 (15.9)	130 (22.3)	1.52 (1.04-2.22)	
			0.031	
BMI				
Normal	143 (53)	311 (53.3)	1	
Overweight/Obese	127 (47)	272 (46.7)	0.92 (0.74-1.31)	
			0.917	

	No adverse events (n= 270) N (%)	Adverse events (n= 583) N (%)	Crude OR (95% CI) p-value	Adjusted OR (95% CI) p-value
Smoking				
Non-smoker	260 (96.3)	552 (94.7)	1	
Smoker	10 (3.7)	31 (5.3)	1.46 (0.71-3.02) 0.308	
Types of vaccine				
Sinopharm/Sinovac	214 (79.3)	323 (55.4)	1	1
AstraZeneca	34 (12.6)	196 (33.6)	3.82 (2.55-5.71)	3.69 (2.38-5.72)
Others	22 (8.1)	64 (11.0)	1.93 (1.15-3.22) 0.0001	2.10 (1.19-3.73) <0.0001
Number of doses				
One	33 (12.2)	103 (17.7)	1	
Two	237 (87.8)	480 (82.3)	0.65 (0.43-0.98) 0.044	
Order of dose				
Second dose	40 (14.8)	53 (9.1)	1	1
First dose	156 (57.8)	490 (84)	2.37 (1.51-3.71) 0.41	2.01 (1.24-3.25)
Both doses	74 (27.4)	40 (6.9)	(0.23-0.72) <0.0001	0.30 (0.16-0.56) <0.0001

DISCUSSION

The challenges of vaccine development do not end once an effective vaccine has been developed. There have always been rumors that vaccines are linked to various post-vaccination negative effects. Understanding the range of symptoms that vaccination might cause is a critical issue to decrease hesitation, increase public confidence in vaccine safety, and accelerate the vaccination process against COVID-19.[12-14] The current study investigated the utilization of COVID-19 vaccines in Egypt (Sinopharm, Sinovac, AstraZeneca, Pfizer, Johnson & Johnson, etc) and possible post-vaccination adverse events. Sinopharm/Sinovac was the most utilized vaccine type (63%), followed by AstraZeneca (27%), Pfizer-BioNTech (4.8%) and 68.3% of the study participants reported post-vaccination adverse events. However, a recent study in Netherlands reported that Pfizer-BioNTech was the most utilized vaccine type followed by AstraZeneca.[15]

Despite that 84% of the Egyptian participants who received two doses of vaccine, 32% and 26.7 % of them, respectively, were hesitant and unwilling to receive a COVID-19 booster vaccine. The proportions were much higher than reported by Paul and Fancourt (2021) who found that among fully vaccinated adults in the UK only 4% were uncertain about receiving and 4% were unwilling to receive a COVID-19 booster vaccine.[16] This can be explained by the fact that the increase in the number of recipients of the vaccine was due to the mandatory COVID-19 certification imposed by the Egyptian government and the large proportion of Egyptians are still having negative attitudes, hesitancy, or even refusal of the vaccines.

About 9% of the current study participants reported COVID-19 infection after being vaccinated, however, it was found that COVID-19 infection was less severe in the majority of the infected

participants after their first or second vaccine doses. In line with the current study, Antonelli and his colleagues (2022) in a large-scale community-based study in the UK stated that post-vaccination COVID-19 infection was less severe (both in terms of the number of symptoms in the first week of infection and the need for hospitalization).[17]

Our study showed that several adverse events have been reported after receiving COVID-19 vaccination, mainly including local symptoms at the injection site, fatigue, bone and muscle pain, flu-like symptoms, and gastrointestinal symptoms that occurred at a very early stage post-vaccination and particularly after receiving the first dose of vaccination. The reported adverse events were significantly higher among those who received the AstraZeneca vaccination than the other COVID-19 vaccines with a multivariable-adjusted OR (95% CI) was 4.31(2.85-6.51).

In line with our findings, a systematic review of 11 studies showed that reported adverse reactions were mild to moderate with few severe reactions, which were unrelated to the test vaccine. Common adverse events were pain at the site of injection, fever, myalgia, fatigue, and headache.[6] Evidence from previous studies documented that the most common post-vaccination adverse events were fatigue, injection site pain/swelling, headache, sleepiness and laziness, chills, myalgia, joint pain, and fever. However, most of these studies have assessed mainly the post-vaccination adverse events of the Pfizer–BioNTech, Moderna, and AstraZeneca vaccines.[11, 18, 19] Meanwhile, two different studies that were conducted in Jordan and the United Arab Emirates focused on the adverse events that were encountered by those who received the Sinopharm COVID-19 vaccine.[12, 20]

In the current study, local injection site symptom was the most common side effect reported by 82.5% of the participants followed by fatigue (67.4%). Similar to our study, local injection site symptoms were the most common adverse events observed in a randomized, cross-sectional study in which 88.04% of participants reported local pain compared to other local site adverse events.[18] These findings were also consistent with the FDA's report on Pfizer vaccine adverse events and that reported in Ramasamy *et al*. (2020) study with the administration of AstraZeneca vaccine.[21, 22]

Although with lower proportions than those observed with AstraZeneca or other vaccines, local symptoms were also the most commonly reported symptom on the administration of the Sinopharm/Sinovac vaccine, being reported by 78.4% of study participants. This prevalence was higher compared with a study that highlighted the adverse events of the Sinopharm vaccine among the Emirati population (32.6%),[20] and more than that were reported among the Jordanian and Bahranian populations (57.8% and 19% respectively).[23, 24] Vaccine shots can be a source of distress and trigger fear for individuals of any age, resulting in exaggerated pain expression. In addition, injection into a relaxed muscle leads to less pain compared with a tensed one; therefore, researchers recommend lowering the patient's arm for injection to reduce pain.[12, 19]

Consistent with our findings, fatigue was reported in several studies with the administration of Pfizer or AstraZeneca vaccines.[19, 22, 25, 26] However, higher proportions of those who received the Sinopharm/Sinovac vaccine in our study complained of fatigue compared to that observed in Xia et al. (2021) randomized controlled trial.[27] A study conducted by Riad and his colleagues (2021) among healthcare workers in Turkey found that injection site pain (41.5%), fatigue (23.6%), and headache (18.7%) were reported by more than 10% of the participants after receiving Sinopharm COVID-19 vaccine.[19]

In the current study, bone ache and flu-like symptoms (e.g. fever, sore throat, and headache) were reported in more than three-quarters of those who received the AstraZeneca vaccine, with lower proportions observed with the administration of the Sinopharm/Sinovac vaccine. This is consistent with a prospective observational study conducted in the UK with the administration of the AstraZeneca vaccine, where fever and chills were reported as systemic reactions.[28] Furthermore, in a study about the adverse events of COVID-19 vaccines among Jordanian people, the headache was observed among half of those who received either AstraZeneca or Pfizer vaccines.[23] Contradictory to these findings, randomized, phase 1 and phase 2 trials in China considered that administration of Sinopharm vaccine was accompanied by the occurrence of very rare adverse events among its recipients, with reported fever (6%), fatigue (3%), headache (1%), and myalgia and joint pain (1%) in lower proportions of vaccine-recipients.[27]

Gastrointestinal symptoms were reported among 28.7% of our study participants with higher proportions observed with AstraZeneca (37%) in comparison to Sinopharm (24.4%) and other vaccines (33.7%). Comparable findings were reported by Omeish et al., (2021) among the Jordanian population.[23] However, in a separate randomized trial with the administration of Sinopharm vaccine, gastrointestinal symptoms were reported only among 1% of participants.[27]

Generally, from our findings and other consistent studies, we can conclude that the rates of local and systemic adverse reactions were significantly lower with inactivated vaccines including Sinopharm/ Sinovac compared to AstraZeneca, Pfizer, and other vaccines. However, Wu et al. (2021) reviewed 87 publications on COVID-19 vaccines' safety data from clinical trials and speculated that the discrepancies in results may be attributed to population differences or methodologies used for reporting observed symptoms.[29] Our study revealed that most of the post-COVID-19 vaccination adverse events were low to moderate in severity and were not severe enough to require hospitalization and usually resolved within a few days after vaccination and the same trend was reported in several studies.[15, 22, 25, 29]

The present study also showed that the reported adverse events were significantly higher among female participants and those who received AstraZeneca vaccination with multivariable-adjusted OR (95% CI) of 2.26 (1.67-3.08) and 4.31 (2.85-6.51), respectively. Gender differences were observed in different studies on different populations with females being more prone to report the occurrence of post-COVID-19 vaccination adverse events than males e.g., Menni and colleagues (2021) on Pfizer and AstraZeneca vaccines in the United Kingdom[28], Omeish et al. (2021) in Jordan,[23] Saeed et al. (2021) on Sinopharm vaccine in the United Arab Emirates.[20] Moreover, a two-phased randomized clinical trial that was conducted in China on Sinopharm vaccine, exhibited more common adverse events in females (55%) compared to males (45%).[29] The difference in adverse events between genders was reported earlier for several inactivated virus vaccines such as influenza and measles-mumps-rubella combination vaccines. These differences are usually not in favor of females.[30, 31] Various hypotheses were proposed to explain these differences, including adaptive immunity-related theories, sex steroid-related theories, and innate immunity-related theories.[30] This finding calls for more research on the gender disparities in COVID-19 vaccine adverse events. Furthermore, findings revealed that 23.1% of the female

participants have experienced menstrual changes. This adverse event among females should be investigated further and confirmed through large longitudinal studies.

The current study found that adverse events tend to be more noticeable after the first dose (OR (95% CI): 4.17-10.58). Consistent with our findings, Omeish et al. (2021) reported that post-COVID-19 vaccination adverse events were more frequent after receiving the first dose than the second one.[23] On the contrary, several studies on Pfizer and AstraZeneca vaccines showed that the prevalence of local and systemic adverse events was higher after receiving the second dose compared to the first dose.[19, 25] In addition, a study on Sinopharm COVID-19 vaccination found that adverse events of the second shot of vaccine were slightly higher than the first dose except for nausea, allergy, cough, and abdominal and back pain.[20]

The major strengths of this study included being one of the few studies that investigated the COVID-19 post-vaccination adverse events in Egypt, the inclusion of different occupations and both sexes, and examination of the different adverse events of various brands of the utilized COVID-19 vaccines to be able to detect all possible types of adverse events and their determinants among the vaccine users. However, detection of the severe post-vaccination adverse events, which were uncommon or rare, needs studies with high numbers of participants, which constitutes a limitation in this study. Moreover, the study participants were mostly of young age, so the findings may fail to present the true association between age and adverse events after immunization. Another limitation of the current study is the utilization of an online-based questionnaire which could result in selection bias, recall bias, and non-response bias. Despite this, online web-based questionnaires were found to be a cost-effective and fast approach for reaching a large group of respondents and a way to reduce the sampling bias in this study was to distribute the survey in different online channels to improve its visibility among the target population and reaching persons who are difficult to reach by traditional methods. Moreover, increasing the response rate was done by sending pre-notification emails, personalized invitations, and survey reminders. Finally, the cross-sectional nature of the study does not allow an inference of causality, and the survey was done very soon after starting vaccination in Egypt, therefore, we evaluated only the immediate and short-term adverse events. Thus, longitudinal surveillance among the general population will be required to investigate the possible late or long-term adverse events of COVID-19 vaccines.

CONCLUSION

The reported side-effects for the Sinopharm/Sinovac, AstraZeneca, Pfizer, and other types of the administered COVID-19 vaccines in Egypt were mild to moderate in severity, of short duration, often lasting for only 1–3 days from the day of injection, and mostly self-limiting. Local symptoms at the injection site, fatigue, bone and muscle pain, and flu-like symptoms were the most common adverse events that occurred at a very early stage of post-vaccination and particularly after receiving the first dose of vaccination.

RECOMMENDATION

Further longitudinal studies including large numbers of participants from all age groups should be carried out to confirm the low incidence of serious COVID-19 post-vaccination adverse reactions, as well as study the long-term adverse events, and ensure vaccine safety. Moreover, more attention should be paid to studying potential post-vaccination adverse

events such as menstrual disorders. Such research studies should have a role in implementing health education programs, disseminating reliable information about vaccine safety, and increasing the acceptance and utilization of COVID-19 vaccines in Egypt.

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