



## Prevalence of reactogenicity of COVID-19 vaccine among Libyan adults: a cross-sectional study

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### HOW TO CITE THIS

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**Abstract:** The diversity of reactogenicity and its variation in terms of risk and prevalence among populations had raised the need to study and evaluate the reactogenicity of different COVID-19 vaccines in our region. Thus, this study aimed to estimate the prevalence of reactogenicity of COVID-19 vaccines and compare the three vaccines (AstraZeneca-Oxford, Sinovac and sputnik V). An analytical cross-sectional study was conducted using a semi-structured telephonic interview with a sample size of 430 individuals who received one of the included COVID-19 vaccines (AstraZeneca, Sinovac or sputnik V) and were recorded at one of the vaccination centers' records that were affiliated with Aljamail Department of the National Centre for Disease Control, Libya. 410 Libyan participants met the inclusion criteria and were enrolled in the final analysis. The study has shown that 57.3% (CI 52.7-62) of the participants had at least one reactogenic event. Pyrexia (40.7%), headache (27.3%) and fatigue (19.5%) were the most common reactogenic events. In conclusion: the study found that reactogenic events were mild to moderate and the COVID-19 vaccines were safe and encouraged our community to be vaccinated. However, prospective studies with larger sample sizes, longer follow-up and inclusion of important laboratory parameters such as IgG and IgM immunoglobulins are recommended to better understand the relationship between the reactogenicities of COVID-19 vaccines with immunity system development and the factors associated with it.

### Introduction

The COVID-19 vaccine provides acquired immunity against the COVID-19 disease-causing coronavirus (SARS-CoV-2) [1]. Multiple COVID-19 vaccines with different mechanisms of action have been authorized or licensed for use [2]. Generally, these vaccines can be classified into two major categories according to general approach of vaccines as follows: the genetic-based approach

such as adenovirus vector vaccines (Oxford-AstraZeneca, Sputnik V) vaccines and the protein-based approach that depends on using a part or whole of the virus (Sinovac vaccine) [3]. Reactogenicity is the term used to describe subset of reactions that occur shortly after vaccination and are physical expression of the inflammatory response to vaccine such as fatigue, headache,

inflammation at the injection site, myalgia and others that have been observed with COVID-19 vaccines [4 - 6]. They are resolved on their own in a matter of days without the need for medical treatment [4, 7]. However, allergy is one of the serious and life-threatening reactogenic events of the COVID-19 vaccines that are typically rare but of considerable public interest [8]. The effectiveness of the COVID-19 vaccines in limiting COVID-19's spread as well as its severity and fatality has received widespread praise [1, 9, 10]. In 185 nations and territories between December 8, 2020 and December 8, 2021, COVID-19 vaccines prevented an additional 14.4 to 19.8 million deaths, according to a June study that has been published in the Lancet [11]. Whereas, on July 7, 2022, the accumulative number of those who received vaccines in Libya was 3 616272 individuals, whereas 2 275934 of them received only the first dose [12]. Therefore, reactogenicity and safety may influence a person's willingness to receive the vaccine. If a vaccine is thought to be overly reactogenic, the person may refuse additional doses or the healthcare provider may decide not to recommend it [4]. Although reactogenicity is generated by inflammatory mediators of the innate immune system, which can be good indicator of vaccine effectiveness, overexpression of these mediators may impair adaptive immune response [3]. Thus, the diversity of reactogenicity and its variation in terms of risk and prevalence among populations had raised the need to study and evaluate the reactogenicity of different COVID-19 vaccines in our region. Therefore, the objectives of this study were to estimate the prevalence of reactogenicity after the first dose of COVID-19 vaccine and to compare with the three vaccines (AstraZeneca-Oxford, Sinovac and Sputnik V).

## **Materials and methods**

*Study design:* This analytical cross-sectional study was conducted using semi-structured telephonic interview that was performed to collect information about the population of the study according to the recommendations of DeJonckheere and Vaughn [13]. The list of the interview included three major sections: The first section was demographic

variables (age and gender), the second section included clinical profile (chronic diseases, regular medicine intake and history of COVID-19 incidence) and the last section involved vaccine received, reactogenicity with terms of severity and duration, disability to perform daily activities, health care site utilization and taking of medication for reactogenicity.

*Subject sampling:* Participants were from Aljamail city and recorded at one of the vaccination centers affiliated with Aljamail Department of the National Center for Disease Control, Libya in a period from August 3<sup>rd</sup>, 2021 until September 2<sup>nd</sup>, 2021. The participants (n = 430) were selected by simple randomization with the sampling framework involving 1245 vaccinated. The inclusion criteria included adult Libyan individuals  $\geq 18$  who received the first dose of the following COVID-19 vaccines: AstraZeneca, Sinovac or Sputnik. They were contacted in the period from the second to the third week following vaccination. While the exclusion criteria were individuals who received other vaccines and individuals who had organ transplantation or one of the immunosuppressive diseases.

*Ethical consideration:* The study was reviewed and approved by the scientific and ethical committee of Faculty of Pharmacy, University of Sabratha, Sabratha, Libya (2021/07) while participants provided verbal consent before participation.

*Statistical analysis:* Data were analyzed by using the Statistical Package for the Social Science (SPSS) software version 26. Descriptive statistics were carried out using percentage and frequency. Inferential statistics were conducted with the Chi-square test and Kruskal-Wallis test with a significant level of 0.05. The Phi and Cramer's V tests to estimate effect size were used [14]. An additional confidence interval level of 95% with the Bias-corrected and accelerated (BCa) type was calculated using bootstrapping based on 10 000 bootstrap samples.

## **Results**

*Demographic characteristics:* Out of the total participants (n = 430), the responses were classified

as follows: one participant was dead and 429 were alive; four of them had been excluded from the study as they had not met study inclusion criteria; 15 individuals preferred not to participate in the study; the remaining 410 who gave verbal consent and completed the semi-structured telephonic interview were enrolled for final analysis. In general, the percentage of the participants who received AstraZeneca-Oxford vaccine was 56.6% (CI 52.0 - 61.3) followed by the percentage of Sinovac and Sputnik V receivers which were 34.4% (CI 30.2 - 38.8) and 09.0% (CI 6.6 - 11.5), respectively. This percentage difference was statistically significant ( $\chi^2 = 139.32$ ;  $P < 0.001$ ). Although 53.4% (CI 48.8 - 58.0) of the participants were female. The difference in vaccination demand between male and female subjects was not statistically significant ( $\chi^2 = 1.91$ ;  $P = 0.167$ ). 70.7% (CI 66.6 - 74.9) of the participants were from the age of 18 to 55 years. Furthermore, 36.6% of the AstraZeneca-Oxford vaccine receivers were older than 55 years which was statistically different ( $\chi^2 = 15.24$ ;  $P < 0.001$ ) but with a small effect size (Cramer's  $V = 0.193$ ; CI 0.095 up to 0.299). However, there was no significant difference ( $\chi^2 = 2.11$ ;  $P = 0.348$ ) between male and female subjects in the selection of certain brands of vaccines.

*Medical Anamneses:* A total of 23.4% (CI 19.5 - 27.3) of participants reported having at least one chronic disease with a significant difference ( $\chi^2 = 5.77$ ;  $P = 0.016$ ) between males (13.4%) and females (10.0%) with a small effect size (Phi = -0.119; CI -0.216 up to -0.20). Whereas, 22.2% of the participants with chronic diseases had taken medicine regularly. The most common chronic disease was diabetes mellitus at 14.9% (CI 11.7 - 18) followed by cardiovascular diseases at 07.3%

(CI 5.1 - 9.8) and respiratory disorders at 01.7% (CI 0.7 - 2.7), whereas other disorders were less than 01.0%. Additionally, 49.0% of the participants with chronic diseases preferred to receive the Sinovac vaccine with a significant difference ( $\chi^2 = 12.683$ ;  $P = 0.002$ ) compared to the other vaccines. Despite that, the difference had a small effect size (Cramer's  $V = 0.176$ ; CI 0.070 up to 0.297). Furthermore, only 04.6% of those vaccinated had a history of COVID-19 disease.

*Prevalence of Reactogenicity:* 57.3% (CI 52.7 - 622) of total participants reported at least one reactogenic event, with a significant difference ( $\chi^2 = 61.194$ ;  $P < 0.001$ ) between vaccines in the prevalence of reactogenicity. Whereas Sinovac receivers were more likely to experience reactogenicity than the other vaccinated (**Table 1**). This difference in the prevalence of reactogenicity among the vaccinated had a medium effect size (Cramer's  $V = 0.386$ ; CI 0.229 up to 0.478) that should be taken into account. Furthermore, 28.3% (CI 24.1 - 32.4) of the participants reported being unable to perform their daily activities. Systemic reactogenicities (SRs) with a percentage of 55.9% were more common than local SRs. Pyrexia was the most common reactogenic event with a percentage of 40.7%, followed by headache (27.3%) and fatigue (19.5%), whereas some reactogenic events such as burning on urine (0.7%), gastrointestinal upset (0.7%), chest pain (0.7%), loss of smell and taste (0.7%) and chill (0.7%) were rare. Furthermore, one of the AstraZeneca vaccinated had an anaphylactic shock and another one reported experiencing loss of appetite. In addition, one of the Sinovac vaccine receivers had suffered from blurred vision (**Table 2**).

**Table 1:** Severity of reactogenicity among Libyan participants

Outcome	AstraZeneca (n = 232)	Sinovac (n = 141)	Sputnik V (n= 37)	Total
Symptomatic	43.1%	83.7%	45.9%	57.3%
Mild-moderate	94.0%	93.2%	82.4%	92.8%
Severe	06.0%	06.8%	17.6%	07.2%

Chi-square test was used with significant level of 0.05.

**Severity and duration of reactogenicity:** **Table 2** shows that the percentage of participants with mild to moderate reactogenic events is 53.2% (CI 48.5 - 57.6) whereas 04.1% (CI 2.7 - 5.9) of vaccinated suffered from severe reactogenic events without a significant difference ( $\chi^2 = 3.010$ ;  $P = 0.222$ ) between vaccines. However, only 01.7% of the participants visited physician in either public hospitals or private clinics because of the SRs of vaccines, whilst, 27.6% of vaccine receivers

preferred to take medicines over-the-counter for the management of symptoms resulted due to vaccination. Regarding the duration of the reactogenicity, the result of the study has demonstrated that means of duration of reactogenicity is equal to 2.24 (CI 2.02 - 2.48) days without a significant difference (KW = 2.92;  $P = 0.232$ ) between vaccines in the duration of reactogenicity among the participants (**Table 3**).

**Table 2:** The prevalence of reactogenicities among COVID-19 vaccine receivers

Reactogenicity	AstraZeneca (n = 100)	Sinovac (n = 118)	Sputnik V (n = 17)	Total (n = 410)
<b>Systemic R.</b>	95	118 (100%)	16 (94.1%)	229 (55.9%)
Pyrexia	66	91 (77.1%)	10 (58.8%)	167 (40.7%)
Headache	37	70 (59.3%)	05 (29.4%)	112 (27.3%)
Fatigue	34	40 (33.9%)	06 (35.3%)	80 (19.5%)
Throat and nasal congestion	07	21 (17.8%)	00	28 (06.8%)
Nausea and vomiting	08	14 (11.9%)	01 (05.9%)	23 (05.6%)
Joint pain	08	12 (10.2%)	01 (05.9%)	21 (05.1%)
Sore arm/ P.	02	11 (9.3%)	02 (11.8%)	15 (03.7%)
Dizziness	04	07 (05.0%)	00	11 (02.7%)
Sneeze	02	04 (03.4%)	01 (05.9%)	07 (01.7%)
Myalgia	03	02 (01.0%)	01 (05.9%)	06 (01.5%)
<b>Other systemic symptoms were less than 01.0%</b>				
<b>Local R.</b>	24	28 (23.7%)	04 (23.5%)	56 (13.7%)
Pain at inj. site	19	26 (22%)	04 (23.5%)	49 (12.0%)
Redness	03	02 (01.7%)	00	05 (01.2%)
Swelling	01	00	00	01 (00.2%)
Itchiness	02	00	00	02 (00.5%)

**Table 3:** Duration of reactogenicities among COVID-19 vaccine receivers

Duration	Frequency	Percentage	P-Value
<b>Total</b>	235	57.3%	0.232
<b>&lt; 1 day</b>	99	42.1%	
<b>1 – &lt; 3 day</b>	107	45.6%	
<b>3 – &lt; 7 day</b>	25	10.6%	
<b>≥ 1 week</b>	04	01.7%	

Kruskal-Wallis test was used with a significant level of 0.05

## Discussion

This study evaluated the local and systemic reactogenicity of the three COVID-19 vaccines; similar to other vaccines. They were associated with several reactogenic events, some of which were more likely to occur with one than the other. The findings showed that 57.3% of the participants had at least one reactogenic event. This is higher than the finding of a study performed at King Fahad Military Medical Complex, Dhahran during the vaccination campaign in the KSA which showed that 34.7% of total participants reported an adverse reaction while it was lower compared to other studies [5, 6, 15, 16]. The reactogenicity of the Sinovac vaccine was greater in prevalence than that of the other vaccines which had nearly the same percentage. This contrasts with the results of the study from Iraq that indicated AstraZeneca vaccine receivers had the highest percentage of reactogenicity (52.7%) which could be due to differences in some factors such as gender, age and other factors that require further investigations [3 - 5]. The most common systemic reactions among the participants were pyrexia (40.7%), headache (27.3%) and fatigue (19.5%) which are similar to the other findings of the study performed on Iraqi citizens and another study from the Czech Republic

which demonstrated that fatigue, fever, headache and myalgia are the most common systemic reactogenic events [5, 16]. Furthermore, pain at the injection site was the most common local reactogenicity that in line with studies from Turkey and Iraq [5]. While one participant (0.4%) of the AstraZeneca-Oxford vaccine receiver suffered from allergic reactions that were lower than the study performed in the UK which found that 02.38% of those vaccinated with the first dose of the AstraZeneca-Oxford vaccine had allergic reactions [17]. It was higher than the study that included 608 Iraqi citizens which revealed that one case (0.16%) of those who received the AstraZeneca-Oxford vaccine suffered allergic reactions [6].

*Conclusion:* Reactogenicity of COVID-19 vaccine occurred in more than half of the vaccine recipients. Most reactogenicities were mild to moderate in severity and can be tolerated. More studies including laboratory parameters as IgG and IgM immunoglobulins are needed to understand the association between the reactogenicities of COVID-19 vaccines and immunity system development.

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**Conflict of interest:** The authors declare absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

**Ethical issues:** Including plagiarism, informed consent, data fabrication or falsification and double publication or submission have completely been observed by authors.

**Data availability statement:** The raw data that support the findings of this article are available from the corresponding author upon reasonable request.

**Author declarations:** The authors confirm that all relevant ethical guidelines have been followed and any necessary IRB and/or ethics committee approvals have been obtained.

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