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ORIGINAL RESEARCH article

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

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Abstract: The diversity of reactogenicity and its variation in terms of risk and prevalence among populations has 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 the 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 a subset of reactions that occur shortly after vaccination and are the physical expressions of the inflammatory response to vaccines 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

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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 8th, 2020 and December 8th, 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 3,616,272 individuals, whereas 2,275,934 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 has 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 the COVID-19 vaccine and to compare it with the three vaccines (AstraZeneca-Oxford, Sinovac and Sputnik V).

Materials and methods

Study design: This analytical cross-sectional study was conducted using a 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 interviews 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 the Aljamail Department of the National Center for Disease Control, Libya in a period from August 3rd, 2021 until September 2nd, 2021. The participants (n=430) were selected by simple randomization with the sampling framework involving 1,245 vaccinated. The inclusion criteria included adult Libyan individuals ≥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 the 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 percentages 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.

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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 the 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 9.0% (CI 6.6-11.5), respectively. This percentage difference was statistically significant (χ^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 (χ^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 (χ^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 (χ^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 (χ^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 11.7-18.0) 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 (χ^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, a 4.6% 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 (χ^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%

The Chi-square test was used with a significant level of 0.05

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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 (χ^2=3.010; P=0.222) between vaccines. However, only 1.7% of the participants visited physicians 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)
Systemic R.	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%)
Other systemic symptoms were less than 01.0%				
Local R.	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
Total	235	57.3%	0.232
<1 day	99	42.1%	
1- <3 days	107	45.6%	
3- <7 days	25	10.6%	
≥1 week	04	01.7%	

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

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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 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 the 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 such 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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Ethical issues: Including plagiarism, informed consent, data fabrication or falsification and double publication or submission were completely observed by the 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.

References

1. Li Y Der, Chi WY, Su JH, Ferrall L, Hung CF, Wu TC (2020) Coronavirus vaccine development: from SARS and MERS to COVID-19. Journal of Biomedical Sciences. 27 (1): 1-23. doi: 10.1186/s12929-020-00695-2
2. Bok K, Sitar S, Graham BS, Mascola JR (2021) Accelerated COVID-19 vaccine development: milestones, lessons, and prospects. Immunity. 54 (8): 1636-1651. doi: 10.1016/j.immuni.2021.07.017
3. Heinz FX, Stiasny K (2021) Distinguishing features of current COVID-19 vaccines: knowns and unknowns of antigen presentation and modes of action. npj Vaccines. 6 (1): 1-13. doi: 10.1038/s41541-021-00369-6

ISSN: 2789-1895 online
ISSN: 2958-3101 print

4. Hervé C, Laupèze B, Del Giudice G, Didierlaurent AM, Da Silva FT (2019) The how's and what's of vaccine reactogenicity. npj Vaccines. 4: 39. doi: 10.1038/s41541-019-0132-6
5. Almufty HB, Mohammed SA, Abdullah AM, Merza MA (2021) Potential adverse effects of COVID19 vaccines among Iraqi population; a comparison between the three available vaccines in Iraq; a retrospective cross-sectional study. Diabetes and Metabolic Syndrome. 15 (5): 102-207. doi: 10.1016/j.dsx.2021.102207
6. Riad A, Sağıroğlu D, Üstün B, Pokorina A, Klugrova J, Attia S, Klugar M (2021) Prevalence and risk factors of coronavac side effects: An independent cross-sectional study among healthcare workers in Turkey. Journal of Clinical Medicine. 10 (12): 2629. 1-13. doi: 10.3390/jcm10122629
7. World Health Organization (2021) Background document on the inactivated vaccine Sinovac-CoronaVac against COVID-19. WHO reference number: WHO/2019-nCoV/vaccines/SAGE_recommendation/Sinovac-CoronaVac/background/2021.1.
8. Montgomery J, Ryan M, Engler R, Hoffman D, McClenathan B, Collins L, Loran D, Hrnicr D, Herring K, Platzer M, Adams N, Sanou A, Cooper LT(2021) Myocarditis following immunization with mrna covid-19 vaccines in members of the US military. JAMA Cardiology. 6 (10): 1202-1206. doi: 10.1001/jamacardio. 2021.2833
9. Fernandes A, Chaudhari S, Jamil N, Gopalakrishnan G (2021) COVID-19 Vaccine. Endocrine Practice. 27 (2): 170-172. doi: 10.1016/j.eprac.2021.01.013
10. Mallapaty BS, Callaway E, Kozlov M, Ledford H, Noorden R Van (2021) How Covid vaccines shaped 2021 - in eight the race to vaccinate. The Nature. 600: 580-583. doi: 10.1038/d41586-021-03686-x
11. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC (2022) Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infectious Diseases. 3099 (22): 1-10. doi: 10.1016/s1473-3099(22)00320-6
12. National Center For Disease Control, Libya (2022) The epidemiological situation of corona disease. National Center For Disease Control-Libya. Published. Accessed July 13, 2022. https://ncdc.org.ly/Ar.
13. DeJonckheere M, Vaughn LM (2019) Semistructured interviewing in primary care research: a balance of relationship and rigour. Family Medicine and Community Health. 7 (2): 1-8. doi: 10.1136/fmch-2018-000057
14. Cohen J (1988) Statistical power analysis for the behavioral sciences. Second edition. Lawrence Erlbaum Associates, Publishers, USA. ISBN: 0-8058-0283-5.
15. Al Bahrani S, Albarrak A, Alghamdi OA, et al. (2021) Safety and reactogenicity of the ChAdOx1 (AZD1222) COVID-19 Vaccine in Saudi Arabia. International Journal of Infectious Disease. 110:359-362. doi: 10.1016/ j.ijid.2021.07.052
16. Riad A, Pokorná A, Attia S, Klugarová J, Koščík M, Klugar M (2021) Prevalence of covid-19 vaccine side effects among healthcare workers in the Czech Republic. Journal of Clinical Medicine. 10 (7): 1-18. doi: 10.3390/jcm10071428
17. Menni C, Klaser K, May A, Polidori L, Capdevila J (2021) Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID Symptom Study app in the UK: a prospective observational study. Lancet Infectious Diseases. 21 (7): 939-949. doi: 10.1016/S1473-3099(21)00224-3