Original Article

Assessment of Adverse Events Following COVID-19 Vaccination: A Cross-sectional Study in Ibadan, Nigeria

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Abstract

Background: Vaccination has been described as the most critical tool to end the COVID-19 pandemic and to save lives and livelihoods. This study aimed to evaluate the spectrum of adverse events following immunization with the COVID-19 AstraZeneca/Oxford vaccine in Ibadan, south western Nigeria.

Methodology: A cross-sectional study. Adults aged ≥ 18 years who had received the Astra-Zeneca/Oxford COVID-19 vaccine at selected COVID-19 vaccination centres across three Local Government Areas in Ibadan, SW Nigeria were interviewed by means of a structured questionnaire to determine the spectrum of adverse events following immunisation (AEFI).

Results: We enrolled 369 adults; 179 males and 190 females, with a mean of age of 37.8 ±12.0 years. Three hundred and thirty two (90.0%) of the subjects experienced one or more AEFI. Of the total AEFIs reported, the most frequent were headache 225 (21.1%), fatigue/tiredness 186 (17.4%), pain at the injection site 99 (9.3%) and myalgia 97(9.1%). Nine in ten (96.4%) of these AEFIs occurred within 48 hours post-vaccination.Higher severity of adverse events score (p=0.049) and multiple AEFIs (p=0.01) were associated with the first dose of the vaccine. There were severe AEFI in 1.2 % (95% CI: 0.3-.9.0%) of the respondents. Presumed or confirmed COVID 19 infection before vaccination increased the odds of AEFI (OR 7.0, 95% CI: 1.8-27.8).

Conclusion: Our study showed a high frequency of AEFI among recipients of the Astra Zenecca/Oxford vaccine in Ibadan. Majority of the AEFIs are mild and self-limiting.Previous infection with COVID-19 appears to increase the risk of AEFI.

Keywords: COVID-19; Vaccine; Adverse event following immunization; Severe Acute Respiratory Syndrome Coronavirus 2; AstraZeneca/Oxford COIVD-19 Vaccine.

Introduction

As the world continues to grapple with the waves of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection, the short and long term effects of the pandemic continues to take its toll on all aspects of human life. A multi-pronged approach has been adopted for effective disease prevention and to curtail further spread of the pandemic. One of such key interventions is the global introduction of the vaccine against the SARS-CoV-2 in December 2020. The introduction of these vaccines appears to be the light at the end of the tunnel for a disease that seemed to have

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defied all odds. However, with the rapid discovery of the vaccine, the newer mechanism of immune induction has generated a lot of misconceptions and misinformation that have resulted in significant vaccine hesitancy. The confounders to the negative attitude toward receiving the vaccines is the mixed reported safety profiles, and possible adverse events, which may be fatal. Adverse events following immunization refer to any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine. They are further classified based on severity into minor and severe AEFIs. Minor AEFIs are non-life threatening events which require no hospitalization, e.g. skin rash, headaches, joint pains while severe AEFIs are those requiring hospitalization.

Nigeria, like the other nations of the world affected by SARS CoV-2 infection, has to grapple with the effect of the global information storm regarding the COVID-19 vaccine. Perhaps the limited reports on the symptomatology, bio-safety profile and tolerability may add to the hesitancy of the citizens to receive the COVID vaccine given that previous uptake of other vaccines among adults in Nigeria was poor. The current safety and efficacy profile of COVID 19 vaccine are limited to clinical trials conducted in a largely Caucasian population. The AEFIs reported include mild and short-lived post-vaccination symptoms like tiredness, pain, swelling, myalgia and fever, which were consistent with an immune response commonly associated with vaccines. Fewer individuals experienced intense symptoms after the second dose such as blood clots and blood disorder raising concerns about the biosafety profile of the vaccines. The ultimate bio-safety and tolerability profile of a vaccine however largely rests on real-world post-vaccination events rather than the limited observation from the clinical trials.

To enhance the vaccine uptake and allow for informed decision, local studies establishing the spectrum of symptoms, including the tolerability of COVID-19 vaccines are essential. Nigeria received donation of the AstraZeneca/Oxford COVID-19 vaccine under the WHO-led COVAX arrangement for the early phase of her COVID-19 vaccination programme in March 2, 2021.Due to limited resources, priority was given to frontline health workers, while the members of the general population were not exempted. There are mixed and concerning reports on the vaccination-related symptomatology, tolerability and safety profile of the AstraZeneca/Oxford COVID-19 vaccine from available literature and on the social media on the background of limited evidence-based report in the Nigerian population.

This study therefore set out to determine the prevalence, spectrum and risk factors for AEFIs among recipients of the first and second doses of the AstraZeneca/Oxford COVID-19 vaccine. We anticipate that the findings of this study will add to the information on the spectrum of AEFIs associated with the AstraZeneca/Oxford COVID-19 vaccine as well as provide useful information for prospective recipients of the vaccine in the African population. This will help to inform their vaccine choices and also dispel false narratives by vaccine hesitancy groups.

Methodology

Study design and location

This cross-sectional study was conducted between April and June 2021 in Ibadan, Oyo state, Southwestern Nigeria. Ibadan is the capital city of Oyo state, one of the six states in the southwestern geopolitical zone of Nigeria

Study population

The study population comprised of adults aged ≥18 years who received the AstraZeneca/Oxford COVID-19 vaccine. Ibadan is the third-largest city in Nigeria with an estimated population of 3,565,108 in 2021.The vaccination target for her population was 40%(142,605 adults) of the adult population by the end of December 2021 with focus on healthcare workers and high-risk group in Nigeria.

Sample size estimation and sampling technique

The minimum sample size required for this study was determined using the Raosoft software (Raosoft Inc., Seattle, Washington, USA). http://www.raosoft.com/samplessize.html). Adopting previously determined estimated 65.9% prevalence of symptomatology post COVID-19 vaccination for a population that is >20,000

(142,605 adults) at 80% power and an alpha level of probability of 0.05, a minimum sample size of 345 was obtained. The state COVID-19 vaccination programme began on March 24, 2021. Vaccinations were initially conducted in three LGAs in the state due to the limited supply of vaccines in the Country and State at the time. These were the LGAs of Ibadan North, Ibadan North West, and Ibadan North East, which have populations of 432,900, 216,400, and 465,700, respectively, as projected from the 2006 National Population Census. The list of the designated vaccination centers in the three LGAs was obtained from the State Coordinator of the immunization programmes. This list formed the sample frame for the study.

Simple random sampling was used to select four heath facilities from Ibadan North and Ibadan North East while 2 health facilities were chosen from Ibadan North West. The samples were proportionally distributed in ratio 2:2:1 for Ibadan North LGA, Ibadan North West LGA, and Ibadan North East LGA respectively. The list of the health facilities are as shown in Table. I below:

Table 1: List of selected Vaccination Centres in Ibadan

Ibadan North LGA	Ibadan North East LGA	Ibadan North West LGA
Bashorun PHC	Army Barack Hospital	Adeoyo Hospital
Agbowo PHC	Bashorun PHC Akeke	Oniyarin PHC
Kola Diasi Health centre	Iwo Road PHC	
Idi Ogungun	Aremo PHC	

PHC; Primary Health care facility NPI; National Programme on Immunization.

Half (5 out of 10) of the centers listed in Table 1 were selected via a computer-generated random number using GraphPad Prism 9 (GraphPad Software, 2365 Northside Dr. Suite 560 San Diego, CA 92108). We enrolled consecutive 84 participants that gave informed consent in each of the immunization site.

Inclusion criteria

We included adults aged ≥ 18 years who had received at least one dose of the AstraZeneca/Oxford COVID-19 vaccine.

Exclusion criteria

We excluded those that had not received the AstraZeneca/Oxford COVID-19 vaccine and those that did not consent to participate in the study.

Outcome indices measured

The primary outcome of this study was the occurrence of post-vaccination AEFI following administration of the AstraZeneca/Oxford COVID-19 vaccine. Participants' subjective numerical rating scale (NRS) ranging from 0 to 10 was used to determine the severity of adverse events. A numerical rating of zero indicated that there were no symptoms, 1–3 that there were mild symptoms, 4–6 that there were moderate symptoms, and 7–10 that there were severe symptoms. The secondary outcomes were to determine the factors that were associated with AEFI amongst the study participants, and also to assess the strength of recommending further doses of vaccine to the general population by the vaccine recipients (a10 point-scales previously validated was used with 0 representing not recommended while 10 stands for strongly recommended).Myalgia, joint pain and muscle swelling, were considered musculoskeletal system involvement, while manifestation of nausea, vomiting, diarrhoea, increased or decreased appetite was considered as digestive system involvement.

Participants' enrollment

A pre-tested structured questionnaire proforma was used by trained research assistants to obtain basic demographic information, and information related to the AEFI. We enrolled the subjects at the point of vaccination. The participants were asked about their observed symptoms when they returned to pick their vaccination card few days later and phone calls were made to those that did not return to pick up their vaccination card. Observed post-vaccination symptoms were recorded in the study proforma. Presumed or confirmed cases of COVID-19 infection were based on the World Health Organization (WHO) definitions. The questionnaire was designed with input from the general public. Thirty adults were chosen at random from the population to pretest the structured questionnaire. The participants were asked to provide feedback, and the research team held a debriefing session as a result. The feedback suggestions were incorporated into the questionnaire to improve its quality.

Data analysis

Data was analysed using the GraphPad Prism 9.

Percentage, multiple response frequencies and crosstabs, arithmetic mean, standard deviation and Chi-square or Fisher's exact test was used to report the statistics. Summary statistics were computed using MedCalc version 19.1.3 (MedCalc Software Ltd Acacialaan 228400 Ostend, Belgium). Level of statistical significance was set at $P<0.05$.

Ethical consideration

Ethical approval (OYSERB AD13/479/44121[B]) was obtained from the Oyo State Ethics Review Committee, Secretariat, Ibadan, Nigeria.

Results

General characteristic of the study population

A total of 420 adults were enrolled into the study, 51 of them had incomplete data and were therefore excluded from further analysis. Of the 369 respondents with complete data set, 179 (45.8%) were males and 190 (54.2%) were females with a mean age (SD) of 37.8 (12.0) years. The young adults' age group (18-39 years) accounted for the largest study respondents, 211 (57.2%). More married 243 (65.9%) individuals participated in the survey. A larger proportion of the study participants were healthcare workers 216 (58.5%) with medical doctors accounting for about half 110 (50.9%). About two-third 257 (69.6%) of the study respondents were in the upper social class. Table 2 shows the socio-demographic characteristics of the study population.

Table 2: Demographic Characteristics of study Population

Demographic Characteristics	Number(n)	Percentage
Age group (years)		
Young Adults 18 -39	211	57.2
Middle Age 40-59	133	36.0
Older Adults >60	25	6.8
Gender		
Male	179	48.5
Female	190	51.5
Marital Status		
Married	243	65.9
Separated	7	1.9
Single	112	30.4
Widow(er)	7	1.9
Occupation		
Senior public servants, professionals, managers, large-scale traders, contractors	127	34.4
Intermediate grade public servants, senior school teachers	154	41.7
Junior school teachers, drivers and artisans	27	7.3
Petty traders, messengers, labourers and similar grades	11	3.0
Unemployed, full -time housewives, students and Subsistence farmers	50	13.6
Social Class		
Upper	257	69.6
Middle	52	14.1
Lower	60	16.3
Study Group		
Health Workers	216	58.5
Clinical Students	52	14.1
General adult Population	101	27.4
Health Workers		
Doctors	110	29.8
Nurses	41	11.1
Lab Scientist	13	3.5
Pharmacist	18	4.9
Others health Workers	34	9.2
Clinical Students	52	14.1

The COVID-19 exposure status of the study participant pre-vaccination

One hundred and ninety-two (52.0%) respondents had presumed COVID-19 infection based on the WHO criteria.[20-22] Of the 192 with presumed infection, 58 (15.7%) were confirmed to have SARS-CoV-2 based on Polymerase Chain Reaction (PCR) testing. The interval between exposure and subsequent vaccination ranged from 3 months to 15 months (Table 3).

Table 3: SARS-Cov-2 infection status of study participants pre-vaccination

Variable	Number(n)	Percentage
Presumed COVID 19 infections		
Yes	192	52.0
No	177	48.0
Interval between presumed COVID-19 infection and vaccination		
1- 3month	102	53.1
3-6 months	37	19.3
>6-9months	19	9.9
>9 - 12months	20	10.4
12-15 months	14	7.3
Confirmed COVID-19 Infections		
Yes	58	15.7
No	311	84.3

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

The interval between vaccination and adverse events following immunization

One hundred and ninety three (58.1%) of 332 subjects with AEFI experienced symptoms within 24 hours of vaccination. This value rose to 320/332 (96.4%) within 48 hours of vaccination. Delayed manifestations (48 hour – 7 days) of AEFI was observed in only 12 (3.6%) subjects.

Spectrum of symptoms experienced post-COVID 19 vaccination

There were a total of 1,066 AEFIs from 332 (90.0%) study participants who reported at least one adverse event. The common adverse events following COVID-19 vaccination were: headache 225 (21.1%), fatigue or tiredness 186 (17.4%), pain at injection site 99 (9.3%), myalgia 97(9.1%) and

fever 91(8.5%). Other symptoms included: injection site swelling 67 (6.3%), chills/rigours 58 (5.4%) and joint pains 52 (4.9%) as shown in Figure 1.

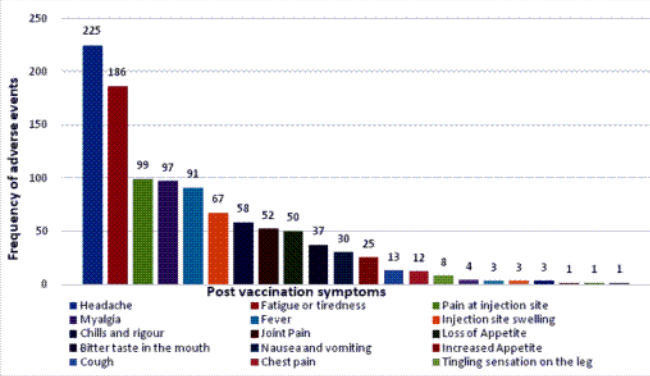

Figure 1: Spectrum of adverse events following COVID 19 immunization

Doses of Vaccines and Adverse events

a) Adverse events following the first COVID-19 vaccination

Two hundred and fifty-eight (69.9%) respondents received only one dose of the vaccine. A single dose of the vaccine was associated with higher frequencies of AEFI (805/1,066; 75.5%) compared with the receipt of two doses of the vaccine (261/1,066; 24.5%), (p< 0.0001). Gastrointestinal symptoms such as bitter taste [33(89.2) vis-à-vis 4 (10.8%)], nausea and vomiting [26(86.7%) vis-à-vis 4(13.3%)], chills and rigor [50(86.2%) vis-à-vis 8 (13.8)], pain at the injection site [83(83.8%) vis-à-vis 16 (16.2%)] were significantly (p <0.001) associated with the first dose rather than the second dose. Other details are shown in Table 4.

Table 4: Doses of Vaccines and Adverse events

Adverse event following immunization	Doses of COVID-19 vaccine		Total
	One	Two	
Injection site swelling	53(79.1)	14(20.9)	67
Pain at injection site	83(83.8)	16(16.2)	99
Fatigue or tiredness	133(71.5)	53(28.5	186
Headache	151(67.1)	74(32.9)	225
Myalgia	80(82.5)	17(17.5)	97
Chills and rigor	50(86.2)	8(13.8)	58
Joint Pain	43(82.7)	9(17.3)	52
Fever	65(71.4)	26(28.6)	91
Bitter taste in the mouth	33(89.2)	4(10.8)	37
Nausea and vomiting	26(86.7	4(13.3)	30
Cough	9(69.2)	4(30.8)	13
Loss of Appetite	37(74.0)	13(26.0)	50
increased Appetite	14(56.0)	11(44.0)	25
Other symptoms	28(77.8)	8(22.2)	36
Total	805	261	1066

Regarding severity of adverse events score on a scale of 10, the overall median score for the observed AEFI was 5/10 (95% CI 4-5) as shown in Table 5.

Significantly higher symptoms scores (median 3; IQR: 1, 5) compared to those who received two doses (median 2; IQR: 1, 3, p= 0.0025) was also observed with the first dose of the vaccine. Similarly, multiple AEFI were equally experienced at the first exposure to the vaccine compared with receipt of two doses as shown in Figure 2 (p=0.01)

Table 5: Severity of adverse events following immunization and vaccine recommendation

Variable Severity of adverse event scores	Responses	*P* value
Overall score	median 5, IQR 3,6	**0.0025***
Single dose severity score	median 3, IQR: 1,5	
Two doses severity score	median 2, IQR: 1,3	
Interference of AEFI with routine activities		
No	242 (86.7)	
Yes	32 (11.5)	
No response	5(1.8)	
Vaccine recommendation on a 10 point-scales		
First dose recommendation		0.4268
Two doses recommendation	6.6± 2.2	
Average recommendation	6.7± 2.4	
Participants wiliness to take booster doses of vaccine		
I will take it	117(42.4)	
I will take it and recommend others to do the same	86(31.2)	
I may take it	55(19.9)	
I will never take it	18(6.5)	

The recommendations of COVID-19 vaccine for future uptake on a scale of 10 by the recipients is shown in Figure 3. One hundred and seventeen (42.4%) subjects were willing to take additional doses of the vaccine(Table 5). First dose recipients (mean score: 6.8 ± 2.5) were enthusiastic about recommending the second dose of the vaccine. Only 18 (6.5%) perceived they would never take a repeat dose of the vaccine consequent on the AEFI. Other details are in shown Figure 2.

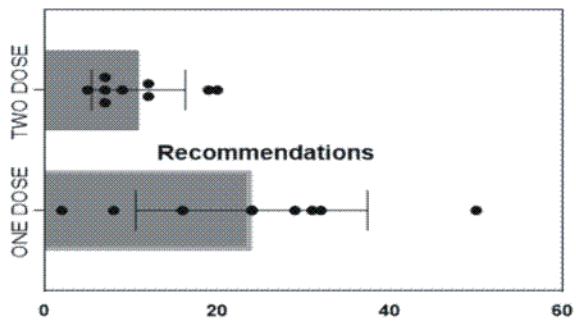

Figure 2: Distribution of vaccine recipients' recommendation of COVID-19 vaccine

b) Adverse events following the second dose of COVID-19 vaccine

One hundred and eleven (30.1%) of the study respondents received the two doses of the vaccine. The observed AEFI were attenuated with a second dose of the vaccine (Figure 2).

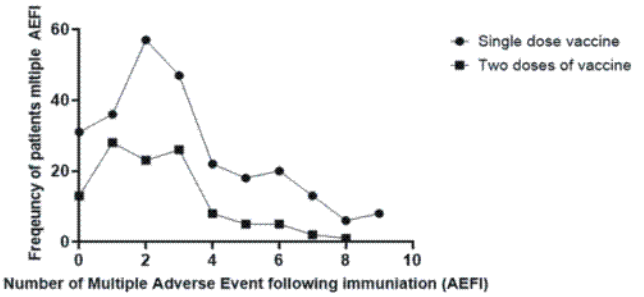

Figure 3: Frequency distribution of Multiple Adverse Event following COVID 19immunization

c) Vaccination-associated organ system adverse events

Of the organ systems in the body, musculoskeletal [112 (33.7 %; p< 0.001)] and gastrointestinal [106 (31.9 %; p< 0.001)] symptoms were the most common manifestations of AFEI. (Table 5)

d) Reporting of adverse events following immunization

Of the 332 who developed symptoms post-vaccination, only 6/332 (1.8%) acknowledged the provision of channels for AEFI reporting. Only 29/332 (8.7%) reported the symptoms to health workers.

e) Management of adverse events following immunization

Three hundred and twenty-eight of the respondents 328/332 (98.8%) self-managed their symptoms. About a quarter 86 (26.6%) did not use any medication. Two hundred and thirty-three (70.2%) used over the counter analgesia [Acetaminophen 197 (61.0%); NSAID 28 (8.7%) and other medications 8 (2.5%)]. About 2/3 (225- 66.8%) of the AEFI resolved within 48 hours. Of all the recipients, only four (1.2%; 95% CI: 0.3-3.0%) were admitted following severe AEFI.

Associations of socio-demographic characteristics, vaccine uptake and risk for adverse event

The relationship between age and frequencies of AEFI is non-linear, and two peak ages of 20-25 and 38 to 42 years were observed for AEFI. The presence of clinical symptoms was found to be lowest in people over the age of 58 years, as shown in Figure 4.

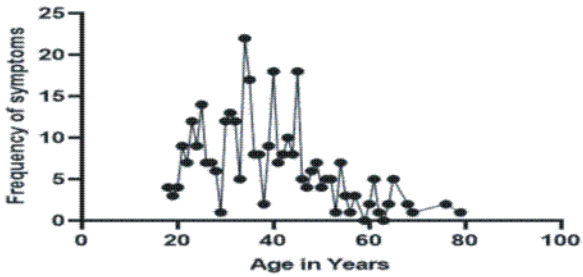

Figure 4: Ages of participants and adverse events following COVID 19 immunisation

There was no statistically significant association between gender, socioeconomic status and the risk of AEFI following COVID vaccination. Presumed or confirmed COVID 19 infections pre-vaccination and the duration of presumed infection were significantly associated with AEFI as shown in Table 6. In addition, only the participants with prior presumptive COVID 19 infection 9-12 months pre-vaccination were found to be at seven-fold increased odds for adverse event following immunization (OR 7.0, 95% CI: 1.8-27.8).

Table 6: Association between sociodemographic, clinical characteristics and post COVID-19 vaccine symptoms

Variables	Post COVID 19 vaccine symptoms			
	No	Yes	X	P-value
Age group (years)			1.32	0.347
18-39	20(9.5)	191(90.5)		
40-59	13(9.8)	120(90.2)		
>60	4 (16.0)	21(84.0)		
Gender			1.12	0.29
Male	21(11.7	158 (88.3)		
Female	16(8.4)	174(91.6)		
Social Class			1.985	0.371
Upper	23(8.9)	234(91.1)		
Middle	8(15.4)	44(84.6)		
Lower	6(10.0)	54(90.0)		
Study group			0.721	0.697
Health workers	23(10.6)	193(89.4)		
Clinical Students	6(11.6)	46(88.5)		
General population	8(7.9)	93(92.1		
Presumed COVID 19 infection			4.704	**0.03***
	24(13.6)	153(86.4)		
	13(6.8)	179(93.2)		
Duration of presumed COVID 19 infection			8.236	**0.046***
1- 3month	5(4.9)	97(95.1)		
3-6 months	2(5.4)	35(94..6)		
>6-9months	1(5.3)	18(94.7)		
>9-12months	5(25.0)	15(75.0)		
Confirmed COVID 19 infection			4.223	**0.017***
	36(11.9)	275 (88.4)		
	1(1.7)	57 (98.3)		
Gastrointestinal symptoms			16.6	**<0.001**
Yes	226 (68.1)	106 (31.9)		
No	37 (100)	0		
Musculoskeletal symptoms			17.9	**<0.001**
Yes	220 (66.3)	112 (33.7)		
No	37 (100)	0 (0.0)		

Discussion

As the world wrestles with the SARS CoV2 pandemic with the third and fourth waves, the need to intensify global vaccine coverage to achieve herd immunity cannot be overemphasized. Global vaccination remains a priority as there is still no evidence-based effective treatment for COVID-19 infection. We assessed post-vaccination symptoms among those that received AstraZeneca/Oxford vaccine in the early phase of COVID-19 vaccination in Ibadan, southwestern Nigeria.

This study showed that 9 out of 10 individuals who received the AstraZeneca/Oxford vaccine had post-vaccination symptoms. Majority of the adverse events were mild to moderate in severity. Whereas this is comparable to the report from Nepal (92.0%) and Jordan (90.0%), the frequency of AEFI was higher than those observed in clinical trials conducted in the United States, United Kingdom, and a published report from India. The reason for the differing prevalence of AEFI in the present study may be due to the difference in immune responses across regions and race. Only about 1.2% of those who received the vaccine had severe adverse reactions necessitating admission. The severe adverse events following immunization requiring hospitalization is in tandem with the reported solicited and unsolicited adverse events reported with this vaccine at the trial phase and the reported effect sizes in other population besides the African continent. The frequency of severe adverse events observed in the present study is far lower than the 23% recorded in Jordan, and observations in the Indian population. The median symptom severity score of 3/10 and 2/10 for the first dose and second dose of the vaccine on a 10 point-rating-scales appears encouraging contrary to the assumption that the AstraZeneca/Oxford vaccine brand will be less tolerated. The tolerability index is also not different from those reported for other brands of the COVID 19 vaccine like the Pfizer and Moderna brands.

The AEFI observed in this study included headache, fatigue or tiredness, pain at the injection site, myalgia, fever, chills, and joint pain.The symptoms were comparable to the observations during the clinical trials and among those that had received the ChAdOx1 nCoV-19 vaccine in Nepal. These symptoms are not unexpected, and are due to the immunologic response to the vaccines. Our study also observed early presentation of symptoms and their substantial resolution within 48 hours, which is consistent with what has been reported in the literature. The import of these findings is to allay fears and provide details required for informed decision as vaccine roll-out reaches various target populations. The summary effect size of the spectrum of these post-vaccination symptoms and their quick resolution may also provide some evidence to deter hesitancy and possibly improve vaccine uptake in the anti-vaxxers and in the general population.

The present study found no statistically significantly associated between younger adult age group and increased odds for developing AEFI contrary to other reports in literature. Interestingly two spike incidences of increased AEFI were observed in the present study. Perhaps increasing the power of the study may modify the narratives as observed with studies that reported a significantly higher odds for AEFI in the younger population.

The peaks at 20-25 years and at ages 38-42 years noted in this study may be connected to the robustness of immunological response at different ages in life course. An in-depth study of this isolated finding in a multicenter multiethnic may provide useful information on control of viral epidemics and in interpretation COVID19 vaccine efficacy.

We also observed lower uptake of the second dose of the vaccine compared with the first dose. This finding is similar to the report by Hatmal and associates and Hayes et al. The lower return for the second dose of COVID-19 vaccine may be related to the unpleasant experiences of the first dose recipient as shown in the present study. Besides, the non-availability of the AstraZeneca/Oxford vaccine, manufactured by the Serum Institute of India (SII) consequent on the up-surge in cases of COVID19 infection in India may play a role in the smaller number of subjects who received the second dose of the vaccine. There is a need for capacity development among African nations to manufacture this vaccine to meet up with the global need. This finding also calls on governments, corporate bodies, well-meaning private individuals, and religious bodies to garner up efforts to increase awareness on

the benefit of the vaccine and emphasize the need to achieve herd immunity if the war against this deadly virus will be won.

Our study also showed that recipients of the first dose of the vaccine were more likely to have multiple symptoms of AEFI and symptoms related to gastrointestinal, and musculoskeletal system. This finding is similar to the reports in the literature that showed that there are more symptoms after the first dose for most vaccines against COVID-19. Thus, this should be incorporated in educational materials for public enlightenment for COVID-19 vaccination.

We also observed that presumed COVID 19 infection or confirmed cases were associated with more post-vaccination symptomatology, which is consistent with other studies. People with previous infections tend to elicit strong inflammatory responses to most COVID-19 vaccines, including the AstraZeneca vaccine. This group of people should be provided with adequate information prior to vaccination and should be under the radar post vaccination.

Despite the high frequency of AEFI observed in this study, only 1.8% (6/332) of the study participants knew about the provision of reporting channels for adverse events. This abysmally low enlightenment regards reporting channels for adverse event is unacceptable and concerning. It is an index of poor communication between the healthcare workers and the vaccine recipient. There is therefore an urgent need to close up this gap to instill confidence in the health system. The use of self-reporting apps may also be leveraged on by the Government to improve monitoring of adverse events post vaccination.

Our study has some limitations. The adverse events in this study were self-reported, and because the responses were obtained over a short period of time, they may be subjective and less inclusive. The immunologic response assay was also not performed; this would have been an add-on to correlate the severity of the study participants' adverse events.

Conclusion

This study shows that post-vaccination AEFI was high among the recipients of the AstraZeneca/Oxford vaccine, but they were largely mild and self-limiting. Recipients with presumed or confirmed COVID 19 infections before vaccination were more likely to experience AEFI.

Competing interests

The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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References

1. Wang W, Enilov M. The global impact of COVID-19 on financial markets. University of Bradford, Working Paper No. 3588021. Available at: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3588021.[Accessed: 28 February 2022].
2. Maital S, Barzani E. The global economic impact of COVID-19: A summary of research. Samuel Neaman Institute for National Policy Research 2020: 1-12.Available at: https://www.neaman.org.il/EN/Files/Global%20Economic%20Impact%20of%20COVID19.pdf.[Accessed: 28 February 2022].
3. Hogan AB, Jewell BL, Sherrard-Smith E, Vesga JF, Watson OJ, Whittaker C, et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. Lancet Glob. Health 2020; 8: e1132-e1141.
4. World Health Organization (WHO) Coronavirus (COVID-19) Dashboard (2022). URL: https://covid19 who int/. [Accessed: 28 February 2022].
5. Migliori GB, Thong PM, Alffenaar J-W, Denholm J, Tadolini M, Alyaquobi F, et al. Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study. Eur. *Respir. J.* 2021; **58**.
6. Shen J, Duan H, Zhang B, Wang J, Ji JS, Wang

J, et al. Prevention and control of COVID-19 in public transportation: Experience from China. Environ. *Pollut*. 2020; **266**: 115291.
7. Shahroz M, Ahmad F, Younis MS, Ahmad N, Boulos MNK, Vinuesa R and Qadir J. COVID-19 digital contact tracing applications and techniques: A review post initial deployments. *J TranspEng* 2021; **5**: 100072.
8. Le TT, Andreadakis Z, Kumar A, Román RG, Tollefsen S, Saville M and Mayhew S. The COVID-19 vaccine development landscape. *Nat Rev Drug Discov* 2020; **19**: 305-306.
9. World Health Organization (WHO). Infection prevention and control during health care when COVID-19 is suspected: interim guidance, 19 March 2020. World Health Organization; 2020.
10. WaterAid Nigeria: Tackling COVID-19 in Nigeria. 2020 [cited 2021 Mar 31]; Available from: https://www.wateraid.org/ng/covid-19.
11. Adedokun ST, Uthman OA, Adekanmbi VT and Wiysonge CS. Incomplete childhood immunization in Nigeria: a multilevel analysis of individual and contextual factors. *BMC public health* 2017; **17**: 1-10.
12. Thunström L, Ashworth M, Finnoff D, Newbold SC. Hesitancy toward a COVID-19 vaccine. *Ecohealth*. 2021 Mar;**18**:44-60.
13. Callaghan T, Moghtaderi A, Lueck JA, Hotez PJ, Strych U, Dor A, et al. Correlates and disparities of COVID-19 vaccine hesitancy. SSRN 2020 https://doi.org/10.2139/ssrn.
14. World Health Organization (WHO). Classification of AEFIS: World Health Organisation. Available from: https://vaccine-safety-training.org/classification-of-aefis.html. [Last assessed on 2021 Aug 26].
15. World Health Organization (WHO). Adverse Events Following Immunisation (AEFI): World Health. Available from: https://www.who.int/vaccine_safety/initiative/detection/AEFI/en/. [Last assessed on 2021 Apr 16].
16. World Health Organization (WHO) Africa. COVID-19 pandemic slows progress against tuberculosis _. World Health Organizarion. Available from: https://www.afro.who.int/news/covid-19-pandemic-slows-progress-against-tuberculosis. [Last assessed on 2022 Apr 16]
17. Omotowo I, Meka I, Ijoma U, Okoli V, Obienu O, Nwagha T, et al. Uptake of hepatitis B vaccination and its determinants among health care workers in a tertiary health facility in Enugu, South-East, Nigeria. *BMC Infect.* Dis 2018; **18**: 1-9.
18. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. *The Lancet* 2021; **397**: 99-111.
19. Menni C, Klaser K, May A, Polidori L, Capdevila J, Louca P, et al. 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 Infect Dis* 2021; **21**:939-49.
20. Riad A, Pokorná A, Attia S, Klugarová J, Koščík M and Klugar M. Prevalence of COVID-19 Vaccine Side Effects among Healthcare Workers in the Czech Republic. *J. Clin. Med* 2021; **10**:1428.
21. Hatmal MM, Al-Hatamleh MA, Olaimat AN, Hatmal M, Alhaj-Qasem DM, Olaimat TM, Mohamud R. Side Effects and Perceptions Following COVID-19 Vaccination in Jordan: A Randomized, Cross-Sectional Study Implementing Machine Learning for Predicting Severity of Side Effects. *Vaccines* 2021; **9**:556.
22. Africa CDC. Statement to African Union Member States on the deployment of the AstraZeneca COVID-19 Vaccine to the continent and concerns about adverse event reports coming from Europe. Afr CDC [Internet]. 2021 Mar 19 [cited 2021 Mar 31]; Available from: https://africacdc.org/news-item/statement-to-african-union-member-states-on-the-deployment-of-the-astrazeneca-covid-19-vaccine-to-the-continent-and-concerns-about-adverse-event-reports-coming-from-europe/.[cited 2021 May 31].
23. Centre for Disease Control. Local Reactions, Systemic Reactions, Adverse Events, and

Serious Adverse Events: Moderna COVID-19 Vaccine [Internet]; Available from: https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html.[cited 2021 Dec 4].

24. World Health Organization (WHO). COVID-19 vaccines shipped by COVAX arrive in Nigeria.2021: Available from: https://www.afro.who.int/news/covid-19-vaccines-shipped-covax-arrive-Nigeria. 2020 [cited 2021 Mar 31].
25. Tobaiqy M, Elkout H and MacLure K. Analysis of thrombotic adverse reactions of COVID-19 AstraZeneca vaccine reported to EudraVigilance database. *Vaccines* 2021; **9**: 393.
26. Wise J. Covid-19: European countries suspend use of Oxford-AstraZeneca vaccine after reports of blood clots. BMJ2021;372:n699. doi:10.1136/bmj.n699 pmid:33707182. 2021.
27. World population Review. Population of Cities in Nigeria (2022). URL: https://worldpopulationreview.com/countries/cities/nigeria. (Accessed: June 2021).
28. Udejinta MO. Confidence on Government and Hesitancy to COVID-19 Vaccination among Staff of Tertiary Institutions in Oyo Metropolis. *SAU J. Manag. Soc. Sci.* 2021; **6**: 249-258.
29. World Health Organization (WHO). Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO classification. 2018.Available from: https://www.who.int/publications/i/item/9789241516990,2020 [cited 2021 Mar 31].
30. Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, et al. Studies comparing numerical rating scales, verbal rating scales, and visual analogue scales for assessment of pain intensity in adults: a systematic literature review. *J. Pain Symptom Manag* 2011; **41**: 1073-1093.
31. Pantilat SZ, O'Riordan DL, Dibble SL and Landefeld CS. Longitudinal assessment of symptom severity among hospitalized elders diagnosed with cancer, heart failure, and chronic obstructive pulmonary disease. *J Hosp Med.* 2012; **7**: 567-572.
32. Khalil M, Mahbub-Uz-Zaman K, Hossain A-S, Ahmed F, Chowdhury M, Karim F, et al. Adverse events following COVISHIELD vaccination among adult population in Bangladesh. *SN ComprClin Med.* 2021; **3**: 2207-2213.
33. Gilkey MB, Magnus BE, Reiter PL, McRee A-L, Dempsey AF and Brewer NT. The Vaccination Confidence Scale: a brief measure of parents' vaccination beliefs. Vaccine 2014; **32**: 6259-6265.
34. Verger P, Scronias D, Dauby N, Adedzi KA, Gobert C, Bergeat M, et al. Attitudes of healthcare workers towards COVID-19 vaccination: a survey in France and French-speaking parts of Belgium and Canada, 2020. *Eurosurveillance* 2021; **26**: 2002047.
35. Bai Y, Yao L, Wei T, Tian F, Jin D-Y, Chen L, Wang M. Presumed asymptomatic carrier transmission of COVID-19. *JAMA* 2020; **323**: 1406-1407.
36. Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, et al. Characteristics of COVID-19 infection in Beijing. *J Infect* 2020; **80**:401-406.
37. Long C, Xu H, Shen Q, Zhang X, Fan B, Wang C, et al. Diagnosis of the Coronavirus disease (COVID-19): rRT-PCR or CT? *Eur. J. Radiol.* 2020; **126**: 108961.
38. Gautam A, Dangol N, Bhattarai U, Paudel S, Poudel B, Gautam S, et al. ChAdOx1 nCoV-19 vaccine and its self-reported adverse events: a cross-sectional study from Western Nepal. *J. Glob. Health* 2021; **5**: e2021069.
39. Wu Z, Hu Y, Xu M, Chen Z, Yang W, Jiang Z, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. *Lancet Infect. Dis.* 2021; **21**: 803-812.
40. Chapin-Bardales J, Gee J, Myers T. Reactogenicity following receipt of mRNA-based COVID-19 vaccines. *JAMA* 2021; **325**: 2201-2202.
41. Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S, Belij-Rammerstorfer S, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a

preliminary report of a phase 1/2, single-blind, randomised controlled trial. *The Lancet* 2020; **396**: 467-478.

42. Kaur U, Ojha B, Pathak BK, Singh A, Giri KR, Singh A, et al. A prospective observational safety study on ChAdOx1 nCoV-19 corona virus vaccine (recombinant) use in healthcare workers-first results from India. *EClinicalMedicine* 2021; **38**:101038.
43. Müller L, Andrée M, Moskorz W, Drexler I, Walotka L, Grothmann R, et al. Age-dependent immune response to the Biontech/Pfizer BNT162b2 COVID-19 vaccination. *Clin Infect Dis* 2021;**73**:2065-2072.
44. Hayes L and Pollock AM. Mandatory covid-19 vaccination for care home workers. *BMJ.* 2021; **374**:n1684.
45. Shrestha S, Devbhandari RP, Shrestha A, Aryal S, Rajbhandari P, Shakya B, et al. Adverse events following the first dose of ChAdOx1 nCoV-19 (COVISHIELD) vaccine in the first phase of vaccine roll out in Nepal. *JPAHS*. 2021; **8**:9-17.
46. Kaur RJ, Dutta S, Bhardwaj P, Charan J, Dhingra S, Mitra P, et al. Adverse events reported from COVID-19 vaccine trials: a systematic review. *Indian J ClinBiochem.* 2021; **36**:427-439.