Article title: PUBLIC HEALTH SURVEILLANCE FOR ADVERSE EVENTS FOLLOWING COVID-19 VACCINATION IN AFRIC/
Events and Fatal Cases Following COVID-19 Vaccination in Africa
Authors: AbdulAzeez Anjorin[1], Ismail Odetokun [2], Jean Nyandwi [3], Hager Elnadi[4], Kwame Awiagah[5], Joseph Eyedo[6], Ajibola Abioye[7], George Gachara[8], Aala Maisara[9], Youssef Razouqi[10], Yusuf Mohamud Mohamed[11], Zuhal Mhgoob[12], Tunde Ajayi[13], Lazare Ntirenganya[14], Morounke Saibu[15], Babatunde Salako[16], Nusirat Elelu[17], Kikelomo Wright [18], Folorunsho Fasina [19], Rasha Mosbah[20]
Affiliations: Department of Microbiology (Virology Research), Lagos State University[1], Department of Veterinary Public Health & Preventive Medicine, University of Ilorin, Nigeria[2], Department of Pharmacy, University of Rwanda[3], Tours University, Egypt[4], Training and Research Unit, Korle Bu Teaching Hospital, Ghana[5], Department of Microbiology (Virology Research), Lagos State University, Nigeria[6], Harvard University, Boston MA, United States of America[7], Department of Medical Laboratory Science, Kenyatta University, Nairobi, Kenya[8], Department of Nephrology and Hemodialysis Center, Bahre Teaching Hospital and Faculty of Medicine, International University of Africa, Khartoum, Sudan[9], Biological Engineering Laboratory, Sultan Moulay Slimane University Beni Mellal, Morocco[10], Mogadishu Somali Turkish Education and Research Hospital[11], Department of Infection Control, Al Jawad Hospital, Sudan[12], Lagos State Ministry of Health[13], Pharmacovigilance and Safety Monitoring, Rwanda Food and Drugs Authority, Rwanda.[14], Walter Sisulu University, Mthatha campus Eastern Cape South Africa and Department of Biochemistry, Lagos State University.[15], Department of Medicine, University of Ibadan and Director General, Nigerian Institute of Medical Research, Nigeria.[16], Department of Veterinary Public Health & Preventive Medicine, University of Ilorin and Chairperson, Kwara State COVID-19 Technical Working Group, Nigeria.[17], Department of Public Health and Community Medicine, Lagos State University College of Medicine & Lagos State University Teaching Hospital, Nigeria.[18], Emergency Centre for Transboundary Animal Diseases (ECTAD), Food and Agricultural Organisation (FAO), Tanzania and University of Pretoria, South Africa[19], Faculty of Oral and Dental Medicine, Ahram Canadian University and Zagazig University Hospitals, Egypt.[20]
Orcid ids: 0000-0002-4152-8659[1]
Contact e-mail: abdul-azeez.anjorin@lasu.edu.ng

Funder: Non
DOI: 10.14293/111.000/000024.v1
Preprint first posted online: 27 January 2022
Keywords: Keywords: Vaccine adverse events, SARS-CoV-2, COVID-19 vaccine, Public health, Vaccination, Adverse events following immunization (AEFI)

PUBLIC HEALTH SURVEILLANCE FOR ADVERSE EVENTS FOLLOWING COVID-19 VACCINATION IN AFRICA

Sub-title: Rare Adverse Events and Fatal Cases Following COVID-19 Vaccination in Africa

*AbdulAzeez Adeyemi Anjorin, PhD
Department of Microbiology (Virology Research), Lagos State University, Nigeria
+2348020956357; abdul-azeez.anjorin@lasu.edu.ng

Ismail A. Odetokun, PhD
Department of Veterinary Public Health & Preventive Medicine, University of Ilorin, Nigeria

Jean Baptiste Nyandwi, PhD
Department of Pharmacy, University of Rwanda

Hager Elnadi, MBBCH, MSc
Tours University, Egypt

Kwame Sherrif Awiagah, MPhil
Training and Research Unit, Korle Bu Teaching Hospital, Ghana

Joseph Eyedo, BSc
Department of Microbiology (Virology Research), Lagos State University, Nigeria

Ajibola Ibraheem Abioye, MBBS, MPH
Harvard University, Boston MA, United States of America

George Gachara, PhD
Department of Medical Laboratory Science, Kenyatta University, Nairobi, Kenya.

Aala MohmedOsman Maisara, MBBS, MSc
Department of Nephrology and Hemodialysis Center, Bahre Teaching Hospital and Faculty of Medicine, International University of Africa, Khartoum, Sudan

Youssef Razouqi, MSc
Biological Engineering Laboratory, Sultan Moulay Slimane University Beni Mellal, Morocco

Mohamed Farah Yusuf Mohamud, MBBS
Institution of Medical Research, SIMAD University, Mogadishu, Somalia.

Zuhal Ebrahim Mhgoob, MSc
Department of Infection Control, Al Jawad Hospital, Sudan

Tunde Ajayi, MBBS, MPH.
Lagos State Ministry of Health.

Lazare Ntirenganya, MSc., BPharm.
Pharmacovigilance and Safety Monitoring Department, Rwanda Food and Drugs Authority, Rwanda.

Morounke Saibu (PhD)
Department of Biochemistry, Lagos State University, and Walter Sisulu University, Mthatha campus Eastern Cape South Africa.

Babatunde Lawal Salako, MBBS, FWACP, FRCP (Edin), FRCP (Lond).
Department of Medicine, University of Ibadan and Office of the Director General, Nigerian Institute of Medical Research, Nigeria.

Nusirat Elelu, PhD
Department of Veterinary Public Health & Preventive Medicine, University of Ilorin and Kwara State COVID-19 Technical Working Group, Nigeria.

Kikelomo Ololade Wright
Department of Community Medicine, Lagos State University College of Medicine & Lagos State University Teaching Hospital, Nigeria.

Folorunsho O. Fasina, PhD
Department of Veterinary
Tropical Diseases, Emergency Centre for Transboundary Animal Diseases (ECTAD), Food and Agricultural Organization of the United Nations (FAO), and University of Pretoria, Pretoria, South Africa.

Rasha Mosbah, PhD, MBA
Faculty of Oral and Dental Medicine, Ahram Canadian University, and Zagazig University Hospitals, Egypt.

***Corresponding author**: AbdulAzeez Adeyemi Anjorin, PhD
Department of Microbiology (Virology Research), Lagos State University, PMB 0001, LASU Post Office, Ojo, Lagos, Nigeria
+2348020956357; abdul-azeez.anjorin@lasu.edu.ng

ABSTRACT

Background: The death toll and economic disaster caused by SARS-CoV-2/ COVID-19 is still on the rise globally and in Africa with a case fatality ratio (CFR), 2.58 from 220,958 deaths out of 8,556,890 cases recorded across the continent as of 14th November 2021. Local, national and international health agencies have advocated multi-pronged public health strategies to limit infections and prevent deaths. The availability of a safe and effective vaccine is critical in the control of a pandemic. Several adverse events have been reported globally for different vaccines including COVID-19 with limited or no data from Africa.

Methods: This cross-sectional epidemiological study investigated the adverse events following COVID-19 vaccination in Africans between April- June, 2021 using a structured questionnaire distributed via the web for public health surveillance.

Results: Out of the 1200 participants recruited, a total of 80.8% (n = 969) respondents from 35 countries including 22 African countries and 13 countries where Africans live in the diaspora reported different adverse events following COVID-19 vaccination. More than half of the vaccinee were male (53.0%) and frontline healthcare workers (55.7%), respectively. A total of 15.6% (n = 151) reported previous exposure to SARS-CoV-2 while about one-fourth, 24.8% (n = 240) reported different underlying health conditions prior to vaccination. Fatal cases were 5.1% (n = 49) while other significant heterogenous events were reported in three categories: very common, common, and uncommon adverse events including enlarged lymph nodes 2.4% (n = 23), menstrual disorder 0.5% (n = 5), and increased libido 0.2% (n = 2).

Conclusions: The study provided useful data for concerned authorities and institutions to prepare plans that will address issues related to COVID-19 vaccines.

Keywords: Vaccine adverse events, SARS-CoV-2, COVID-19 vaccine, Public health, Vaccination, Adverse events following immunization (AEFI).

INTRODUCTION

As the COVID-19 pandemic progresses, multilateral agencies under the coordination of the World Health Organization (WHO) are working round the clock to stem the tide of continuing infection and transmission, by not only supplying medical kits and equipment to various health care systems, but also through coordinated distribution of safe and effective vaccines. Vaccination and immunization remain the best alternative for the prevention and control of diseases worldwide (1). To date, 15th November 2021, more than 7.5 billion doses of COVID-19 vaccines have been administered among 52.1% of the global population, with an approximate of 31.2 million new doses administered daily. However, only 4.5% of the population in low-income countries have been vaccinated with approximately 300 million doses administered for full or partial vaccination in Africa (https://ourworldindata.org/covid-vaccinations?country=OWID_WRL). It is instructive to understand that Africa has an estimated population of 1.4 billion (amounting to only 21.4% of Africans vaccinated).

The COVID-19 Vaccines Global Access (COVAX) facility was launched on the 24th of February, 2021 to improve COVID-19 vaccine deliveries to Africa (2). Ghana and Cote D'Ivoire were the first two countries to receive the WHO approved COVISHIELD vaccine on 24th and 26th of February, 2021 respectively. These deliveries were followed by that of Nigeria, Angola, Democratic Republic of Congo and Gambia on the 2nd of March 2021. Then Rwanda on the 3rd of March, the same day as Kenya, Sudan, and Malawi, with Rwanda being the first country to

157 receive both AstraZeneca/Oxford vaccine and Pfizer-BioNTech mRNA vaccine from the COVAX
158 facility (2). In addition, Benin received 144,000 COVISHIELD vaccines on the 11th March 2021.
159 The Oxford AstraZeneca vaccine was the most widely used because of its ease of storage at a
160 temperature of +2 to +8 °C and associated logistics, but not without its adverse events, as is
161 observed for other COVID-19 vaccines. Generally, vaccines may produce adverse reactions due
162 to idiosyncrasies or because the body immunological system is set to always recognise foreign and
163 infectious agents and there is the possibility to respond physiologically through the cellular and/or
164 humoral pathways. According to the CDC, 2021, any local or systemic health problem or side
165 effect that occurs after vaccination or immunisation is referred to as adverse events (ADE)
166 following vaccination or immunisation (AEFI) (3). Global adverse events following COVID-19
167 vaccination vary based on the type of vaccine but the most common symptoms reported include
168 fatigue, headache, muscle and joint pain, allergic skin reaction, and chills while the most prevalent
169 events include low-grade fever, pain or redness at the site of injection often felt a few days after
170 vaccination. Severe adverse events are possible but the chances are rare (4-8).
171
172 Nevertheless, despite the identification of serious and fatal adverse events following COVID-19
173 vaccination, a causal relationship has not been really established (9-11). Severe adverse events
174 following vaccination have been identified by the United States of America (USA) Vaccine
175 Adverse Event Reporting System (VAERS). According to the report of May 2021, 2 to 5 people
176 per million vaccinated in the USA developed a severe and rare anaphylactic reaction that occurred
177 30 minutes after vaccination. VAERS also filed 32 confirmed reports of people who developed
178 thrombosis with thrombocytopenia syndrome (TTS) after getting the Johnson & Johnson (J&J)
179 vaccine.

Moreover, other reports identified the occurrence of myocarditis and pericarditis mostly in adolescents and young adults who were vaccinated with the Pfizer-BioNTech and Moderna COVID-19 vaccines. In addition, VAERS reported 9,810 human deaths from 442 million doses of COVID-19 vaccines administered in the USA from December 14, 2020, through November 15, 2021 (12). Although a causal link of death to COVID-19 vaccines is still being examined, important reports attributed the death that occurred to a rare, serious adverse event involving blood clots with low platelets following the J&J vaccine (12). On the other hand, thrombotic and thromboembolic adverse events and related causes of death have been reported across European countries following AstraZeneca/COVISHIELD vaccine administration (13), including but not limited to the United Kingdom (14).

Until November 14, 2021, there are a total of 15,287 (0.07%) AEFI reported following 22,749,817 doses of COVID-19 vaccines administered in Ontario with an overall reporting rate of 67.2 per 100,000 doses, and a specific rate of 56.9 per 100,000 doses administered for the Pfizer-BioNTech, 81.6 per 100,000 doses for the Moderna vaccine and 141.9 per 100,000 doses for the AstraZeneca/COVISHIELD vaccine. Furthermore, 29 reports of deaths plausibly associated with receipt of the COVID-19 vaccine have been filed and a causal relationship to any vaccine is still being investigated (7).

Despite the outstanding achievements in the development and rapid approval of the different vaccines, Africa is still at high risk of a likely long-time COVID-19 community spread, and hospitalisation mainly due to unwillingness of African to receive the vaccines (15) coupled with

the scarcity of vaccine and lack of infrastructure for vaccine production on the continent as well as paucity of funds. Also, there is dearth of information and lack of report for surveillance data on adverse events following COVID-19 vaccination in Africa. Hence this public health surveillance was designed to investigate adverse events associated with COVID-19 vaccination in the African population and the management options being employed by individuals reporting adverse events.

MATERIALS AND METHODS

Study Design and Participants

A descriptive cross-sectional, continent-based study was carried-out to monitor adverse events following COVID-19 vaccination in Africans living in Africa and diaspora between April – June 2021. An online survey instrument was deployed for data collection from consenting participants recruited using a convenience sampling method. Inclusion criteria were being an African regardless of location, 18 years of age and above, and having received any of the COVID-19 vaccines. Those who have not received the vaccines were excluded from the survey. Participants who met the inclusion criteria were only eligible if they had access to an electronic medium with an internet facility. Physical and paper-interviewer based questionnaires were avoided to reduce the risk of contracting and spreading SARS-CoV-2/COVID-19. An initial probable target of 50-100 respondents per country was planned to be recruited from North, Southern, West, and East Africa.

Questionnaire

A structured, multiple-choice pretested questionnaire was designed in English Language and translated into French and Arabic by native language experts to capture the specific and logical respondents' quantitative data in Arabic and Francophone speaking countries respectively. The

questionnaire was designed based on the WHO, FDA, and UK-NHS classification of common and uncommon COVID-19 vaccination reactions, to elicit information about respondents' socio-economic and demographic characteristics, health status and past medical history, adverse events following vaccination, and how it was managed. The questionnaire was uploaded to Google form (https://forms.gle/k9KYGp7wC4JNjZeL6, Alpha Inc., California, USA) for distribution and a one-time data collection process through various online social media platforms including WhatsApp, Facebook, Instagram, Telegram, Twitter, LinkedIn and emails. The questionnaire was earlier pretested among 30 respondents in different countries before its administration by research collaborators in various countries including Egypt, Ghana, Kenya, Morocco, Namibia, Nigeria, Rwanda, South Africa, Somalia and Sudan, among others. Continuous sharing was done on social media with sponsored advert on Facebook deployed as reminders to encourage participation.

Ethical consideration

Ethical approval for the study was obtained from various Institutional Review Committees of Nigeria (University of Ilorin), Egypt (Ahram Canadian University, Faculty of Oral and Dental Medicine) and Kenya (Kenyatta University). Guidelines and Code of Ethics for Human research were observed in line with the Declaration of Helsinki-Ethical Principles for Medical Research involving Human Subjects (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013). Participation in the study was voluntary, allowing any participant to quit at any stage without submitting the online form. All participants consented to the study by initially selecting an option to: "voluntarily agree or disagree to participate in the current study" leading to the study questionnaire or finished page as the case may be. Data collection was anonymous and respondents' information was kept highly confidential.

Data analyses and Statistics

The collated public health surveillance data on adverse vaccine events were retrieved from the Google form in excel format for sorting and coding. Categorical variables were presented as frequencies and proportions using descriptive statistics. Chi-square test (and Fisher's exact test for 2×2 tables) was used to test for statistical significance between variables and the demographic (independent) values. Variables considered include demographic characteristics such as age (categories), gender, educational attainment, community type (rural, urban, semi-urban), questionnaire items concerning adverse events and subsequent reactions following vaccination. All the vaccinated participants were included in the adverse events' data analyses irrespective of the number of COVID-19 vaccine doses or type received. The proportion of vaccinees who reported side effects post-vaccination were calculated. Differences between the severity of post-vaccination adverse events were compared to investigate the variability in different categories and between variables. The event of previous exposure to SARS-CoV-2/ COVID-19 and the consequence of adverse reaction was compared to the naive population.

No adjustments were made for missing data, and all analyses used complete case analysis. P-values were two-sided, and analyses were carried out at 95% confidence interval using Statistical Package for the Social Sciences (SPSS) software v.22 and the GraphPad Prism 9.0.0 (121).

RESULTS AND DISCUSSION

This is a report of the first pan-African findings on rare and fatal cases following COVID-19 vaccination among Africans, using the common vaccines administered in the continent. It also detailed past exposure to SARS-CoV-2 and hospitalisation following vaccination, how adverse events were treated by Africans, and how they were recommended for COVID-19 vaccination (Fig

1). The major strengths of this research include the fact that it is a population-based, and geographically diverse study over time (Klein *et al*., 2021).

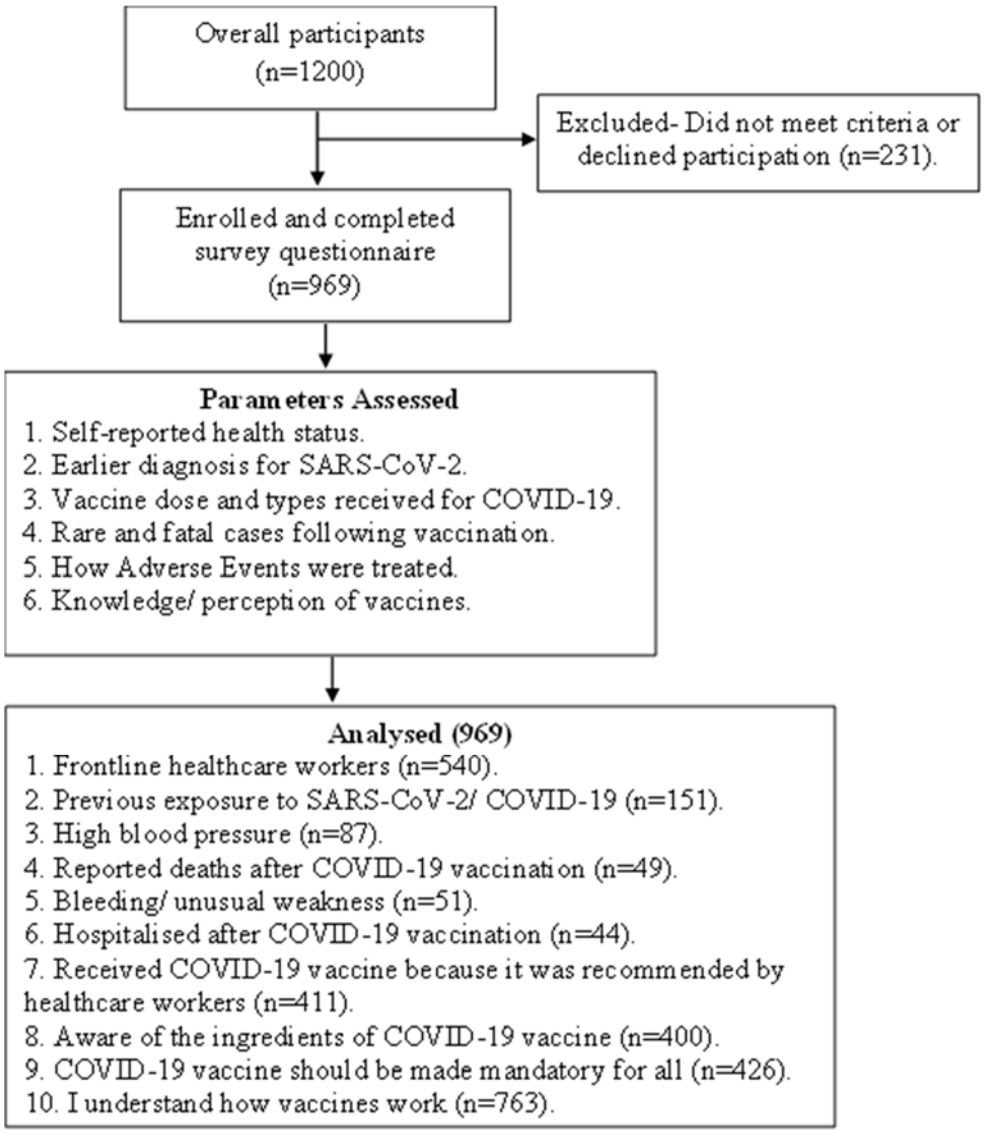
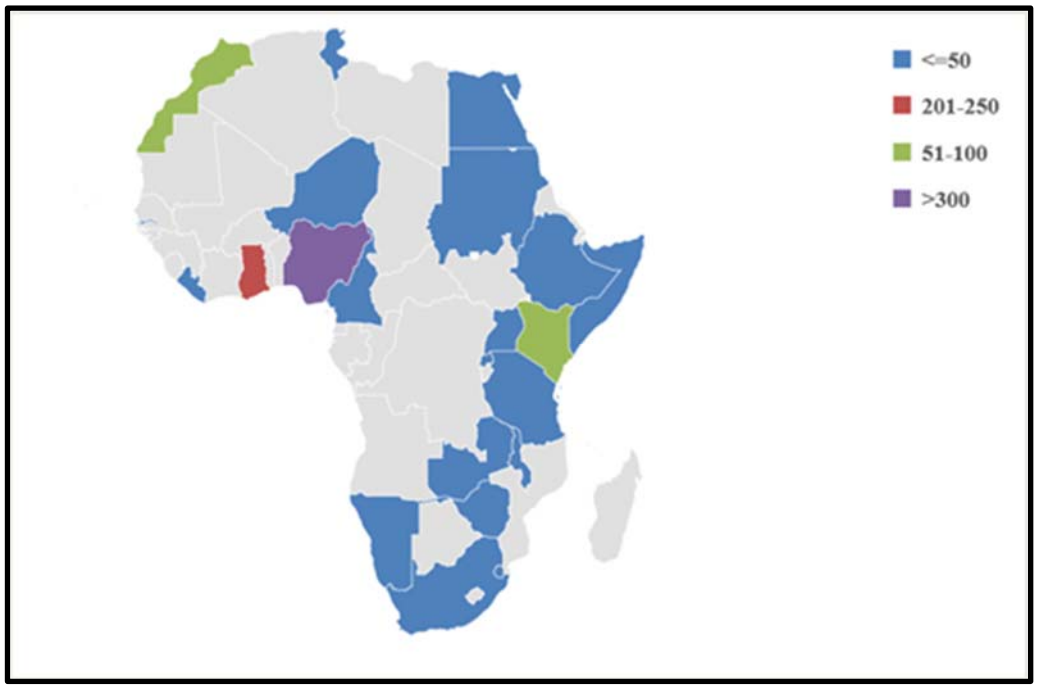


Fig 1. Flow chart of Participants on Adverse events following COVID-19 Vaccination in Africa.

Out of the overall participants (n = 1200), a total of 19.2% (n = 231) were excluded as they did not meet the study inclusion criteria or decline participation by not giving their consent while 80.8% (n= 969) reported different adverse events following COVID-19 vaccination from 35 countries

281 including 22 African countries: Cameroon, Egypt, Ethiopia, Gambia, Ghana, Liberia, Kenya,
282 Malawi, Morocco, Namibia, Niger, Nigeria, Rwanda, Somalia, South Africa, Tanzania, Tunisia,
283 Uganda, Swaziland, Sudan, Zambia, Zimbabwe (Fig 2)
284



285

286 Fig. 2: Distribution of respondents to questions on adverse events of COVID-19 vaccination in
287 African countries.
288

289 Participants from 13 countries (USA, UK, Saudi Arabia, Canada, UAE, Bahrain, Qatar, Brazil,
290 China, Finland, Ireland, Philippines, and Sweden) represent Africans who live in the Diaspora (Fig
291 3). Surveillance for adverse events following vaccination is crucial to ensure safety, maintain trust,
292 and guide policy-makers. This is further corroborated by several studies reported elsewhere
293 including in Asia (16-18), America (12, 19), and Europe (20, 21).
294

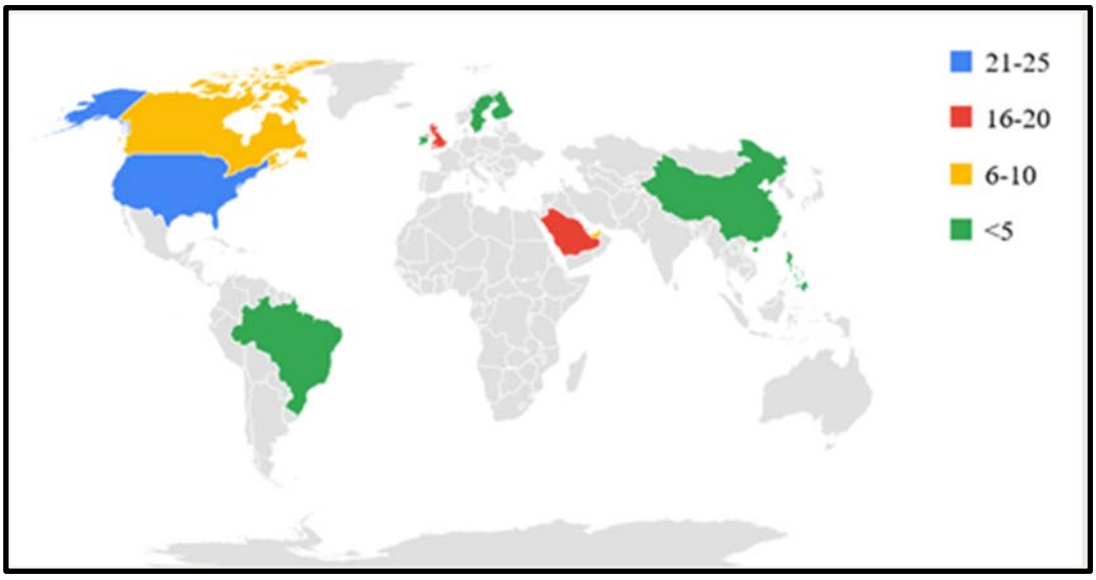


Fig. 3: Distribution of some Africans vaccinated against COVID-19 living in the Diaspora

Different demographic profiles of Africans vaccinated against COVID-19 were investigated with the highest 40.7% young (25-34 years) population who may be at a higher risk of blood clots (22) and other adverse events, and a decrease in the vaccinated population as the age increases except for the age category 18-24 years. This trend is in line with previous reports that youths are more willing to partake in vaccination compared to the older population (18, 23). Furthermore, Klein, Lewis (19) reported the largest number of doses (5124940) from vaccinees aged 18 to 49 years. It should however be noted that online questionnaire administration may also facilitate more inclusion of the youth group.

In this study, more than half of the vaccinated population are male (53.0%) (Table 1), this observation is similar to the finding of Sakinah, Nugraha (18) that found no significant statistical difference in AEFI reported based on gender, an implication of no correlation between gender and reactogenicity. The proportion of frontline healthcare workers that participated in the study was 55.7%, an unsurprising observation, because of the need to prioritise vaccination and proper

surveillance of AEFI among healthcare workers in order to reduce occupational hazard and the burden of hospitalisation associated with SARS-CoV-2/ COVID-19 infection.

Table 1: Demographic distribution of Africans Vaccinated for COVID-19

Category	Frequency	Percentage
Age		
18-24	84	8.7
25-34	394	40.7
35-44	268	27.7
45-54	123	12.7
55-64	69	7.1
>65	31	3.2
Gender		
Male	514	53.0
Female	455	47.0
Education		
Tertiary	804	83.0
Secondary	49	5.1
Primary	10	1.0

Others	89	9.2
None	17	1.8
Occupation		
Frontline Healthcare Workers	540	55.7
Frontline Non- healthcare Workers	127	13.1
Others	302	31.2
Community		
Urban	727	75.0
Semi-urban	149	15.4
Rural	93	9.6

A total of 15.6% (n=151) reported previous exposure to SARS-CoV-2/ COVID-19. Earlier investigators opined that prior exposure may alter the response of participants to COVID-19 vaccination. However, there is a need for further studies to unravel the effect and mechanism of immunological response of past exposure to SARS-CoV-2/COVID-19 and vaccination, especially among the African populace. About a quarter, 240/969 (24.8%) of vaccinated Africans reported different underlying conditions prior to COVID-19 vaccination. Cardiovascular diseases such as high blood pressure and heart diseases accounted for more than one-third (38.8%), followed by asthma (17.9%) and diabetes (12.9%), while glaucoma and arthritis of 0.2% each respectively were the least reported (Table 2). Although there is burgeoning data on the mystery and mechanistic roles surrounding the interference of these underlying health conditions in the general population,

including among Africans (24), they remain potential predictors of various adverse events following COVID-19 vaccination.

Table 2: African respondents earlier diagnosed positive for SARS-CoV-2 and underlying conditions before COVID-19 vaccination.

	Frequency (n=969)	**Proportion (%)**
Earlier diagnosed positive		
No	799	82.5
Yes	151	15.6
Missing	19	2.0
Underlying conditions		
No	729	75.2
Yes	**240**	24.8
CVD	93	38.8
Asthma	43	17.9
Diabetes	31	12.9
Obesity	26	10.8
Infectious Diseases	14	5.8
GIT Diseases	10	4.2

Haematological disorder	9	3.8
Cancer	5	2.1
Arthritis	2	0.8
Glaucoma	2	0.8
Others	5	2.1

Oxford-AstraZeneca remains the highest (77.8%) administered COVID-19 vaccine across different countries in Africa (Table 3) and elsewhere in the world, despite the fact that the African Union is now looking for alternatives to AstraZeneca with the possibility of Johnson and Johnson as a replacement for its planned 400 million doses for distribution among her states (22).

Table 3: Vaccine dose and types administered for COVID-19 in Africa

	Frequency n=969	Proportion %
Vaccine dose		
First dose	811	83.7
Complete dose	158	16.3
Vaccine Brand	Vaccinees	%
Oxford-AstraZeneca	754	77.8
Johnson & Johnson	5	0.5
Covaxin	9	0.9
Sinopharm-BBIBP	44	4.5
Moderna	17	1.8
Pfizer-BioNTech	88	9.1
CoronaVac	6	0.6
Sputnik V	7	0.7
Sinopharm-WIBP	5	0.5
Covi Vac	2	0.2
Others	32	3.3

These data showcased incidents of serious rare and fatal cases following COVID-19 vaccination, including bleeding/ unusual weakness 5.3% (n=51), reported number of deaths 5.1% (n=49), convulsion 4.3% (n =42), breathing difficulty 2.7% (n =26), and hearing/vision problem 2.2% (n = 21). It is probable that these may have been missed out in clinical trials despite the willingness of Africans 35.8% (n=347) to partake in clinical trials (Table 4). The serious rare and fatal cases reported amongst Africans agree with the adverse events and deaths reported by the European Medicines Agency (20) including the fatal cases, along with the blood, ear, eyes, and respiratory disorders following COVID-19 vaccination. However, it does not sufficiently prove that the vaccines caused the adverse events.

Although some of the adverse events were reported to resolve within a few days after vaccination, in actual fact, they may be the reaction of the immune system shortly after vaccination (also known as reactogenicity) (21, 25). The CDC recommends that individuals having severe allergic reactions immediately (within 4 hours) or some days after administration of the vaccine should refrain from getting a second shot of that type of vaccine that produced the event (26). Generally, the WHO, CDC, and major international organisations and experts in vaccinology agreed that the efficacy of the current COVID-19 vaccines at reducing the spread of SARS-CoV-2, disease complications and deaths far outweigh the likely risk of adverse events.

Table 4: Rare and fatal cases following COVID-19 Vaccination among Africans

	Frequency (n= 969)	Per cent (%)	P-value
Bleeding/ Unusual weakness			
No	918	94.7	<0.0001
Yes	51	5.3	
Died after vaccination			
No	920	94.9	<0.0001
Yes	49	5.1	
Seizure (convulsion) or high fever after hours or a few days			
No	927	95.7	<0.0001
Yes	42	4.3	
Breathing difficulty			
No	943	97.3	<0.0001
Yes	26	2.7	
Hearing/ Vision problem			
No	948	97.8	<0.0001
Yes	21	2.2	

Clinical trial			
No	622	64.2	<0.0001
Yes	347	35.8	

**The deaths were accounted for by the healthcare workers that attended to the vaccinees with adverse events leading to deaths, or the family members of the dead persons.*

We have determined some heterogenous adverse events to COVID-19 vaccine' administration in Africa. These heterogenous adverse events among Africans were statistically significant, and can be reported in three categories: uncommon, common, and very common signs. Reported uncommon signs include feeling dizzy 11.9% (n=116), abdominal pain 3.3% (n=32), itchy skin or rash 2.9% (n=28), enlarged lymph nodes 2.4% (n=23), and menstrual disorder 0.5% (n=5) (Table 5). Out of the common adverse events, fever 33% (n=320), injection site swelling, redness or lump 18.2% (n=176), and influenza-like symptoms 12.1% (n=117) were the most reported, while fatigue 40% (n=388), tenderness 39.2% (n=380), and headache 37.5% (n=363) represent the topmost very common signs. These adverse events among Africans reported here align with similar ones reported from other continents including dizziness, fever, and tenderness at the injection site remain recurrent, while abdominal pain and menstrual disorder were less reported in other populations (17, 20, 21).

Nonetheless, transient local inflammation signaling neutrophils and antigen presenting cells to the site of injection is expected after intramuscular administration of lipid nanoparticle-formulated mRNA vaccines. According to the CDC, following the administration of the first dose of the COVID-19 vaccine, if an itch, swollen or painful rash is observed, such person(s) should be treated with antihistamine or acetaminophen. If fatigue or pain is observed, treatment is equally

recommended before such candidates proceed for the second shot of the vaccine based on availability to affirm complete protection (26). In all cases, it becomes necessary to critically evaluate patients' previous medical histories and vaccine-associated allergies in detail; it is also important to monitor vaccinated persons for at least 30 minutes following COVID-19 vaccine administration to ensure that no immediate untoward effects are observed.

Table 5: Adverse events following COVID-19 Vaccination among Africans

	Frequency (n=969)	**Percentage**	**P-value**
I experienced uncommon signs including:			<0.0001
None	651	67.1	
Feeling dizzy	116	11.9	
Decreased appetite	62	6.4	
Excessive sweating	41	4.2	
Abdominal pain	32	3.3	
Itchy skin or rash	28	2.9	
Enlarged lymph nodes	23	2.4	
Menstrual disorder	5	0.5	
Hunger	4	0.4	
Increased libido	2	0.2	

I experienced common signs including:			
None	508	52.4	<0.0001
Fever	320	33.0	
Swelling, redness or a lump at the injection site	176	18.2	
Flu-like symptoms such as high temperature, sore throat, runny nose, cough and chills	117	12.1	
Being sick (vomiting)	44	4.5	
Diarrhoea	20	2.1	
Heaviness of the head	2	0.2	
Bone ache	1	0.1	
Lymph node enlargement	1	0.1	
I experienced very common signs including:			<0.0001
None	220	22.7	
Feeling tired/fatigued	388	40.0	
Tenderness, pain, warmth, itching or bruising where the injection was given	380	39.2	
Headache	363	37.5	
Generally feeling unwell	339	34.9	
Chills or feeling feverish	293	30.2	

Joint pain/ muscle ache	269	27.8
Feeling sick/ nausea	115	11.9
Deep sleep	5	0.5
Lymph in armpits	3	0.3
Mouth sores	1	0.1
Boil	1	0.1
Experienced lower sex drive	1	0.1
Diarrhoea	1	0.1
Ear pain	1	0.1
Chest pain	1	0.1
Vomiting	1	0.1
Blood (red) spot on left eye	1	0.1
Tender swollen tongue, loss of taste and appetite	1	0.1
Insomnia	1	0.1
Dry cough	1	0.1
Rhinitis	1	0.1
Numbness at neck and hand after 2nd dose for one night	1	0.1

419

In our survey, Nigeria recorded the highest number of participants (33.7%), followed by Ghana (23.3%) and Kenya (9.7%) respectively (Table 6). Whether this observation was due to willingness of the respondents to complete the questionnaire, the intensity of administration of the questionnaire, ability to access the questionnaires, or the effect of population distributions is unclear. However, the reasons for low participation in online surveys in Africa are obvious and multifaceted, including but not limited to the lack of power supply, poor access to or irregular internet and electronic gadgets, lack of motivation, perception of questionnaires as too burdensome or intrusive, unexplained context of the objectives, or ethical-related issues.

Table 6: Distribution in some African countries based on the number of willing participants

Country	Frequency	Proportion (%)
Nigeria	327	33.7

Ghana	226	23.3
Kenya	94	9.7
Diaspora	83	8.6
Morocco	52	5.4
Egypt	50	5.2
Somalia	49	5.1
Sudan	40	4.1
Rwanda	27	2.8

A large proportion of Africans 37% (n=361) with COVID-19 adverse events managed and treated the reactions at home without any visit to the hospital (Fig 3) while 1% (n=7) sought the option of traditional remedy. These observations agree with the review of Hernández, Calina (21) that only a limited proportion (typically less than 0.1% of the participants) who have serious adverse events elsewhere considered treatment. These may be a reflection of the following: 1) the under-resourced situation of most healthcare facilities in Africa; 2) the lack of healthcare service delivery where it is most needed among the poor, and 3) the costs associated with seeking healthcare in Africa, including the lack of health insurance for the majority of the populations. In addition, previous experiences of people seeking hospitalization including wrong or unfavorable evaluations and diagnoses by physicians, health care organisations, or the low perceived need to seek medical care with views that the illnesses or symptoms will improve over time, or time constraints to visit hospitals may also be major constraint (27).

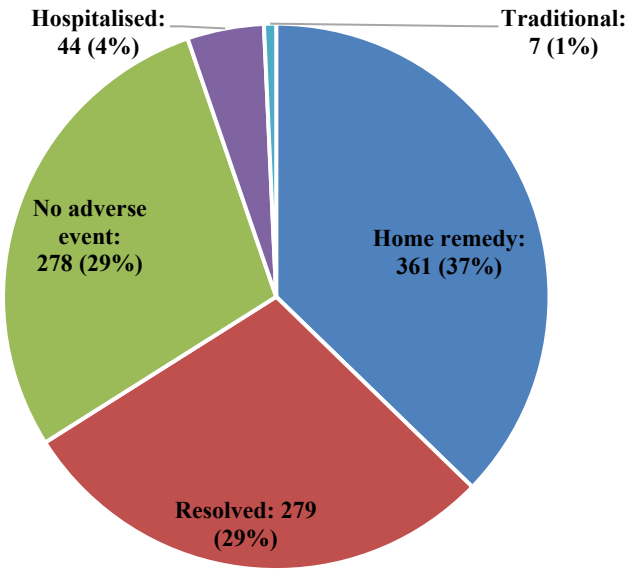


Fig. 3: How Adverse events of COVID-19 vaccination were treated among Africans

Study participants were vaccinated for COVID-19 significantly based on the recommendations given by healthcare workers (23.8%), various levels of governments (17.9%), personal research/ investigation (15.0%), public health organisations/ institutions (14.3%), and scientists (13.5%). These sources are about 5-10 times the enablers of COVID-19 vaccination compared to the least recommendations received from religious and community leaders (2.7%), social media (2.7%), not-for-profit organizations (NGOs) (0.8%), and celebrities (0.3%) (Fig 4). For the society to benefit from optimal coverage of COVID-19 vaccine administration, the proposal of Anjorin, Odetokun (15), on the use of multi-channel vaccination campaign strategy is apt in view of findings from this study.

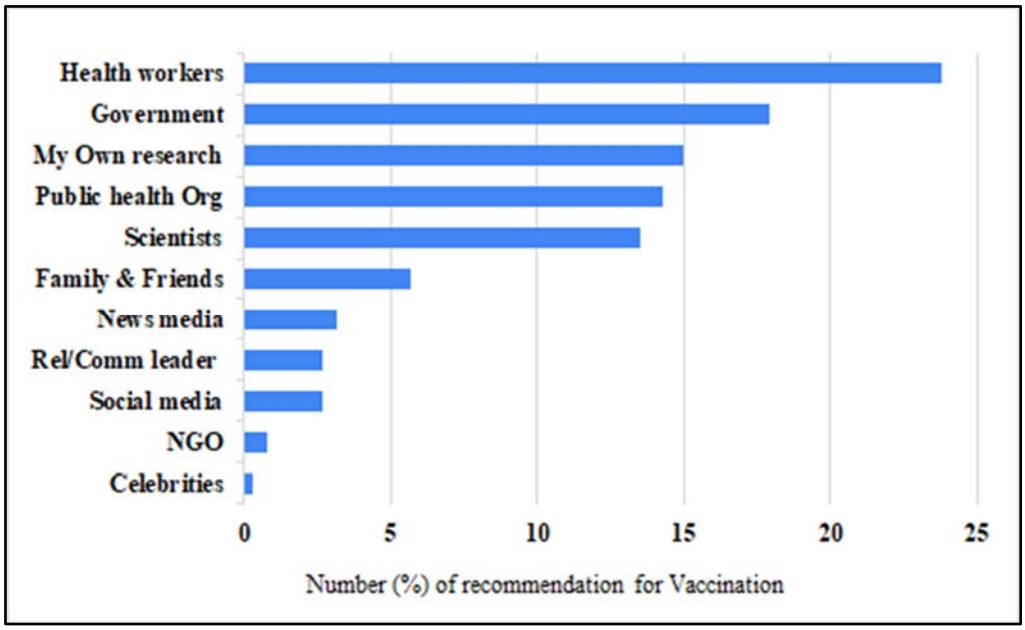


Figure 4: Distribution of recommendations that enhanced COVID-19 vaccination among Africans

In the new world, a reporting system such as the Vaccine Adverse Event Reporting System (VAERS) has been introduced by the CDC and US Food and Drug Administration (FDA) to record any adverse events known to occur in the future after vaccination. The system also proffers invaluable information to vaccinologists to guarantee safety (28). Whether the adoption of such technologies has wide adoption in Africa is doubtful. However, selected African countries are utilising similar technologies. This includes for instance, the Med Safety App, originally developed by the WEB-Recognising Adverse Drug Reactions (WEB-RADR), which was aimed to self-report suspected adverse events following vaccines or drugs for proper monitoring. In Nigeria, for instance, such monitoring is conducted by the National Agency for Food and Drug Administration and Control (NAFDAC) (https://www.nafdac.gov.ng/wp-content/uploads/Publications/Others/Events_PDF/how-to-download-the-med-safety-app-1-1.pdf), and in South Africa, the tool is equally applied (Med Safety App - SAHPRA

(https://medsafety.sahpra.org.za)). There is therefore a need to promote the utilisation of easy to access and report tools like the above, and encourage other African countries that are yet to voluntarily adopt and utilise such available reporting systems to join the league of adoptees for proper documentation and future informed decision making.

We have evaluated the adverse events following the use of COVID-19 vaccines in Africa and report our findings. However, our study is subjected to some limitations. One, since the study is based on a willingness to participate, it became difficult to get proportional representation per country or to get all the countries enrolled based on density of vaccination per country or other logical considerations. This may have affected the statistically empirical determination of expected number of participants per country, thus skewing the analyses, including for the outcomes that are less frequent. It should be noted that some variables and predictors of interest were not captured in this preliminary report, perhaps due to the intrusive nature of the associated questions which may discourage the participants from cooperating with filling the questionnaires.

CONCLUSIONS

We hereby report adverse events following COVID-19 vaccination from a total of 80.8% (n= 969) Africans in 35 different countries. Previous exposure to SARS-CoV-2/COVID-19 was reported by 15.6% (n=151) participants with various underlying diseases. Oxford-AstraZeneca remains the most (77.8%) administered COVID-19 vaccine across African countries. The most worrisome rare and fatal cases include bleeding/ unusual weakness 5.3% (n=51), reported number of deaths 5.1% (n=49), convulsion 4.3% (n =42), breathing difficulty 2.7% (n =26), and hearing/vision problem 2.2% (n = 21) while heterogenous adverse events were reported in three categories as uncommon,

common, and very common signs including abdominal pain 3.3% (n=32), enlarged lymph nodes 2.4% (n=23), and menstrual disorder 0.5% (n=5). Perhaps, an advanced, government based, more robust real-time online data capturing system for reporting continuous sentinel AEFI surveillance, instituted in different African countries, from which future data may be mined for analysis, may be necessary. Such a database may be managed by the Africa Union or its agency, the Africa Centres for Disease Control and Prevention on behalf of the member states, similar to databases that exist in other continents.

Ethics approval and consent to participate

Consent for publication

Availability of data and materials

Competing interests

Funding

Authors' contributions

Acknowledgements

Authors' information (optional)

Authors' contributions:

AAA: Conceptualization, and original draft; JBN, KSA, JE, HE: Part of manuscript draft; AAA, JE, KSA: Methodology; AAA, IAI, IO, JBN, HE, JE, GG, AMM, MFYM, EZM, TA, LN, MS, BLS, YR, NE, KOW, ZE, RM: Questionnaire design and data collection; AAA, IO, IAI, HE, JBN, AOM, YR, EZM, KOW, BLS, RM: Data merging, and coding; AAA, IO: Statistical analyses; AAA, FOF, IO, NE, KOW: Result interpretation; AAA, KOW, IO, NE, KSA, FOF: Writing review & editing; AAA, HE, EJ, KSA, JBN, RM: Reference collation.

REFERENCES

1. WHO. Vaccines and immunization: WHO; 2021 [Available from: https://www.who.int/health-topics/vaccines-and-immunization#tab=tab_1.
2. WHO. First COVID-19 COVAX vaccine doses administered in Africa 2021 [Available from: https://www.who.int/news/item/01-03-2021-first-covid-19-covax-vaccine-doses-administered-in-africa.
3. Understanding Adverse Events and Side Effects [Internet]. 2021 [cited 28/11/2021]. Available from: https://www.cdc.gov/vaccinesafety/ensuringsafety/sideeffects/index.html.
4. Konu YR, Gbeasor-Komlanvi FA, Yerima M, Sadio AJ, Tchankoni MK, Zida-Compaore WIC, et al. Prevalence of severe adverse events among health professionals after receiving the first dose of the ChAdOx1 nCoV-19 coronavirus vaccine (Covishield) in Togo, March 2021. Archives of Public Health. 2021;79(1):1-9.
5. Li X, Ostropolets A, Makadia R, Shoaibi A, Rao G, Sena AG, et al. Characterising the background incidence rates of adverse events of special interest for covid-19 vaccines in eight countries: multinational network cohort study. BMJ. 2021;373:n1435.
6. 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. The Lancet Infectious Diseases. 2021.
7. Adverse Events Following Immunization (AEFIs) for COVID-19 in Ontario: December 13, 2020 to January 23, 2021 [Internet]. 2020.
8. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. New England Journal of Medicine. 2020;383(27):2603-15.
9. Edmonds CE, Zuckerman SP, Conant EF. Management of unilateral axillary lymphadenopathy detected on breast MRI in the era of coronavirus disease (COVID-19) vaccination. American Journal of Roentgenology. 2021.
10. Klimek L, Novak N, Worm M, Hamelmann E, Werfel T, Wagenmann M. AeDA/DGAKI/GPA-Stellungnahme zu schweren allergischen Reaktionen nach COVID-19-Impfung mit dem Impfstoff von Pfizer/BioNTech in Großbritannien. Allergo J Int. 2021;10.
11. Renoud L, Khouri C, Revol B, Lepelley M, Perez J, Roustit M, et al. Association of Facial Paralysis With mRNA COVID-19 Vaccines: A Disproportionality Analysis Using the World Health Organization Pharmacovigilance Database. JAMA Internal Medicine. 2021.
12. CDC. Selected Adverse Events Reported after COVID-19 Vaccination 2021 [Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/adverse-events.html.
13. ECDC-Report. Suspected adverse reactions to COVID- 19 vaccination and the safety of substances of human origin Key facts. 2021.
14. MHRA. Coronavirus vaccine - weekly summary of Yellow Card reporting. Medicines & Healthcare products Regulatory Agency; 2021.
15. Anjorin A, Odetokun I, Abioye A, Elnadi H, Umoren M, Damaris B, et al. Will Africans Take COVID-19 Vaccination? . PLoS One. 2021.
16. Esba LCA, Al Jeraisy M. Reported Adverse Effects following COVID-19 Vaccination at a Tertiary Care Hospital, Focus on Cerebral Venous Sinus Thrombosis (CVST). Expert Review of Vaccines. 2021(just-accepted).
17. Jeon M, Kim J, Oh CE, Lee J-Y. Adverse events following immunization associated with coronavirus disease 2019 vaccination reported in the mobile vaccine adverse events reporting system. Journal of Korean medical science. 2021;36(17).
18. Sakinah EN, Nugraha MY, Qodar TS, Mulyono BW, Tohari AI. COVID-19 Vaccines Programs: adverse events following immunization (AEFI) among medical Clerkship Student in Jember, Indonesia. BMC Pharmacology and Toxicology. 2021;22(1):1-7.
19. Klein NP, Lewis N, Goddard K, Fireman B, Zerbo O, Hanson KE, et al. Surveillance for adverse events after COVID-19 mRNA vaccination. JAMA. 2021;326(14):1390-9.

20. EMA. Committee for Medicinal Products for Human Use (CHMP). Assessment Report EMA/707383/2020. 2021.
21. Hernández AF, Calina D, Poulas K, Docea AO, Tsatsakis AM. Safety of COVID-19 vaccines administered in the EU: Should we be concerned? Toxicology Reports. 2021;8:871-9.
22. Bhatia M, Putcha VR, Dwivedi LK, Singh D. Serious adverse events and fatal outcomes following COVID-19 vaccination in the UK: Lessons for other countries. The International Journal of Community and Social Development. 2021:25166026211053485.
23. Zhang Y, Zeng G, Pan H, Li C, Hu Y, Chu K, et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18–59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. The Lancet infectious diseases. 2021;21(2):181-92.
24. Anjorin A, Abioye A, Asowata O, Soipe A, Kazeem M, Adesanya I, et al. Comorbidities and the COVID-19 pandemic dynamics in Africa. Tropical Medicine & International Health. 2021;26(1):2-13.
25. Forni G, Mantovani A. COVID-19 vaccines: where we stand and challenges ahead. Cell Death & Differentiation. 2021;28(2):626-39.
26. CDC. What to Do if You Had an Allergic Reaction after Getting a COVID-19 Vaccine 2021 [Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/allergic-reaction.html.
27. Taber JM, Leyva B, Persoskie A. Why do people avoid medical care? A qualitative study using national data. Journal of general internal medicine. 2015;30(3):290-7.
28. CDC. Vaccine Adverse Event Reporting System (VAERS): Centers for Disease Control and Prevention; 2021 [updated November 2, 2021. Available from: https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/index.html.

APPENDIX

STUDY QUESTIONNAIRE

1. CONSENT STATEMENT: Do you agree to participate in the study?

I disagree with participating in the current study (0), end survey.

I voluntarily agree to participate in the current study (1), Continue……..

ADVERSE EVENTS FOLLOWING COVID-19 VACCINATION IN AFRICA

BIODATA

2. Have you been vaccinated against COVID-19?

Yes (1), proceed, or No (0), end of survey.

3. Age……18-24 (1); 25-34 (2); 35-44 (3); 45-54 (4); 55-64 (5); >65 (6)
4. Gender (M/F). Male (1) Female (2) Other.
5. Highest Level of Education Completed: None (0) Primary (1) Secondary (2) Tertiary (3) Other (4).
6. Country of residence…… A drop down of all countries.…….
7. Community setting (Urban/semi-urban/rural) Rural (1) Semi-urban (2) Urban (3). Dropdown menu to choose state.

8. Occupation……. Frontline medical/ healthcare worker (1) Frontline non-healthcare worker (2) Other (3).

SELF-REPORTED HEALTH STATUS

1. I have been diagnosed positive to SARS-CoV-2/ COVID-19 before? Yes/ No
2. I have received the COVID-19 vaccine…… First dose (0) Complete dose (1).
3. Date of first dose……
4. Date of Second dose……
5. I know the brand name of the COVID-19 vaccine I was administered. Dropdown menu to choose vaccine brand name
6. I experienced very common signs including:

Tenderness, pain, warmth, itching or bruising where the injection was given.
generally feeling unwell.
feeling tired/ fatigue.
chills or feeling feverish.
Headache.
feeling sick/ nausea.
joint pain/ muscle ache.
Dropdown menu to choose multiple common signs

7. I experienced common signs including:

swelling, redness or a lump at the injection site
fever
being sick (vomiting) or diarrhoea.
flu-like symptoms, such as high temperature, sore throat, runny nose, cough and chills.
Dropdown menu to choose multiple common signs.

8. I experienced uncommon signs including:

Feeling dizzy
decreased appetite
abdominal pain
enlarged lymph nodes
excessive sweating, itchy skin or rash.
Dropdown menu to choose multiple common signs.

Multiple choice questions (Yes/No):

9. I experienced unknown severe allergic reaction (anaphylaxis).
10. I experienced fever in 5-7 days following vaccination. Yes (1) No (0).
11. I had pain at the site of COVID-19 vaccine injection. Yes (1) No (0).
12. I experienced joint or muscle pain. Yes (1) No (0).
13. I experienced general rash 7 and 10 days after vaccination Yes (1) No (0).
14. I had seizure (black-out or convulsions) or high fever (after few hours or a few days) Yes (1) No (0).

15. I had problems with hearing or vision, Hives (other itching or irritation) Yes (1) No (0).
16. I experienced extreme drowsiness, and fainting. Yes (1) No (0).
17. I experienced bleeding, or unusual weakness. Yes (1) No (0).
18. I experienced difficulty in breathing or swallowing. Yes (1) No (0).
19. Please state any other adverse event/ sign or symptom you experienced following COVID-19 vaccination (if not already captured above). Yes (1) No (0).
20. How was the adverse event treated? …….. At home (1) Hospital (2) Traditional remedy (3) I did not treat it, it resolved spontaneously (4) I did not have any adverse effect (5). Other (6).
21. Have you ever had severe allergic reaction (anaphylaxis) following any other vaccination Yes (1) No (0).
22. I know somebody who died following COVID-19 vaccination complication? Yes (1) No (0).
23. Do you have any underlying disease(s)/ health challenge(s)? Yes (1) No (0).
24. Please state the underlying disease(s)/ health challenge(s) you had before taking the COVID-19 vaccine (Select all that apply).
25. Please state any other underlying disease(s)/ health challenge(s) you had before taking the COVID-19 vaccine (if not captured above).

KNOWLEDGE/PERCEPTION OF VACCINES AND ACCEPTANCE OF COVID-19 VACCINE

1. I understand how vaccines work. No (0), Yes (1).
2. I would be willing to participate in a clinical trial for a coronavirus vaccine. No (0), Yes (1).
3. Are you aware of the ingredients of COVID-19 vaccine? No (0), Yes (1).
4. Are you aware of the side effects of the COVID-19 vaccine? No (0), Yes (1).
5. I received the COVID-19 vaccine because it was recommended by religious leaders (1), community elders (2), NGO (3) Government (4) Healthcare workers (5), scientists (6), news media (7), social media (8), celebrities (9), schools (10), public health organizations (NCDC) (11), my own research (12), friends (13), family (14), Not applicable (15).
6. I got the COVID-19 vaccine jab because of the ease of my house/ office to the vaccination center. No (0), Yes (1).
7. To reach my nearest vaccination center, it took <15min (1), <30min (2), 1hr (3), <2hr (4), >2hr (5).
8. The COVID-19 vaccine should be made mandatory for all. No (0), Yes (1), Maybe (2).
9. For future cohort study, can we contact you through your email?

Yes (1), email: ……. , No (0), end survey.