

Consumption and adverse reaction reporting of herbal medicines among people living with HIV at University teaching hospitals in Blantyre, Malawi and Ibadan, Nigeria

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Abstract

Background

Consumption of herbal medicines among people living with HIV is a common practice in Sub-Saharan Africa. The utilization of herbal medicines was at 17.5% and 67.9% in Malawi and Nigeria, respectively. There is inadequate data on use and adverse reactions (ADRs) reporting of herbal medicines among people living with HIV (PLWHIV). This study was designed to investigate use and ADRs reporting of herbal medicines among PLWHIV at the University Teaching Hospitals in Blantyre, Malawi and Ibadan, Nigeria.

Methodology

A cross-sectional study was conducted among PLWHIV attending Antiretroviral Therapy (ART) clinic at Queen Elizabeth Central Hospital, Blantyre, Malawi and University College Hospital, Ibadan, Nigeria. A structured questionnaire was administered to 360 and 370 participants in Blantyre and Ibadan respectively, through face-to-face interviews after obtaining their informed consent.

Results

The prevalence of herbal medicines use among PLWHIV in Malawi and Nigeria was at 80.6% and 55.7% ($p < 0.001$), respectively. The most frequently used herbal medicines in Malawi were *Aloe vera* (14.0%), *Moringa oleifera* (14.0%), *Zingiber officinale* (13.0%) and *Allium sativum* (7.0%). Likewise, in Nigeria, the most commonly used herbal medicines were *Zingiber officinale* (15.0%), *Vernonia amygdalina* (14.0%), *Moringa oleifera* (9.0%), and *Allium sativum* (11.0%). The major reason for herbal medicines' use in Malawi was ready availability (42.1%) and perception that it boosts immunity (44.6%) in Nigeria. The PLWHIV reported experiencing suspected herbal medicine ADRs in Malawi (3.9%) and in Nigeria (8.0%).

Conclusion

A higher percentage of people living with HIV are using herbal medicines in Malawi as well as in Nigeria. In both countries, a few participants reported experiencing suspected ADRs related to herbal medicines.

Keywords: Adverse reactions, Herbal medicines, Pharmacovigilance, People living with HIV

Introduction

Globally there were over 39 million people who were living with HIV (PLWHV) in 2021¹. Sub-Saharan Africa accounts for almost 80.0% of all PLWHIV in the world with Malawi representing 4.0% and Nigeria 13.0% respectively². Malawi had an HIV prevalence of 9.2% in 2018 which was among the countries with the highest prevalence of HIV in Africa³. The prevalence was reflected in the proportion of the adult population aged 15 to 49 years that were living with HIV³. The HIV epidemic had contributed to the reduction of the country's life expectancy to as low as 57 years for men and 60 years for women by 2015. It was also reported that 66.0% of all PLWHIV in Malawi were on treatment and 59.0% of all PLWHIV were virally suppressed^{3,4}. The national prevalence of HIV in Nigeria was estimated at 1.4% among persons aged 15 to 49 years and an estimated 1.9 million PLWHIV

in 2018⁵. The origin and popularity of the consumption of herbal medicines by PLWHIV is the fact that for many years, there was no treatment for HIV, furthermore, antiretroviral therapy (ART) became available until the 1990s whereas HIV was reported in the 1980s and therefore herbal medicine was the available option for managing HIV⁶. The World Health Organization (WHO) defines herbal medicines to include herbs, herbal materials, herbal preparations, and finished herbal products that contain, as active ingredients, parts of plants, other plant materials, or combinations thereof^{7,8}. Malawians have been using herbal medicines since time immemorial for assistance in a variety of social and health challenges⁸, for example, traditional healers had herbal medicines sold with claims to treat, prevent, and manage diseases⁹, including those with claims to treat HIV¹⁰, for example, herbal products like Garani MW1 powder¹¹, Teras

juice, Moyowathanzi powder, CICA powder and Hope wonderful drug syrup in Malawi¹². Most of these herbal medicinal products were prepared from *Allium sativum* L., *Aloe vera* (L.) Burm. f., *Artemisia annua* L., *Amaranthus cruentus* L., *Azadirachta indica* A. Juss., *Moringa oleifera* Lam.¹³, *Cannabis sativa* L., and *Adansonia digitata* L.¹⁴ while in Nigeria most herbal medicinal products with claims to treat HIV were derived from *Nigella sativa* L.¹⁵. Ninety percent of Malawians rely on herbal medicines for consumption and trading¹⁶ while in Nigeria 67.9% had used herbal medicines in the past and 47.8% were taking herbal medicines concurrently with conventional medicines¹⁷. The PLWHIV preferred to use herbal medicines rather than conventional medicines to manage opportunistic infections and antiretroviral medicines adverse reactions (ADRs)^{18,19}. Studies on the prevalence of herbal medicines use among PLWHIV have been reported in some African countries. For example, the prevalence of herbal medicines use ranged from 98.2% in Zimbabwe²⁰, 70.8% in Ethiopia¹⁸, 71.6% in Uganda²¹, 70.1% in Kenya²² and 51.0% in South Africa²³. Reports indicate that Malawi and Nigeria registered low prevalence in the region, 17.5% and 4.2% of herbal medicine consumption among PLWHIV, respectively^{24,25}. However, higher prevalence rates were reported at the State level in Nigeria, with Jos and Gombe States at 41.8% and Kano at 28.0%²⁶.

Despite the reported prevalence of herbal medicine use by PLWHIV, there is inadequate data on reports of potential ADRs associated with herbal medicine consumption. The monitoring of herbal medicines ADRs is the mandate of the national regulatory authorities through their pharmacovigilance centers^{27-29,30}. Herbal medicine pharmacovigilance is in its infancy in most countries in the African region. WHO defines herbal medicine pharmacovigilance as encompassing all activities relating to the detection, assessment, understanding, and prevention of ADRs or events related to the use of herbal medicines or their derived products^{31,32}. ADRs are defined as unintended consequences suspected to be related to the use of medicinal products, including herbal medicines^{31,33-35}. Herbal medicine ADRs are of concern because they can harm the patient or interfere with treatment outcomes through drug-herbal medicine interactions^{18,36,37}. The adverse reaction (ADR) associated with herbal medicine use may be due to predictable side effects, overdose, over duration, misuse and abuse, hypersensitivity, allergic and idiosyncratic reactions, and subacute and chronic toxicity effects³⁸. The challenges of reporting herbal medicine ADRs include underreporting, the complex nature of herbal medicines, and lack of information on the toxicity profiles of herbal medicines^{39,40}. The challenge of underreporting in the spontaneous ADR reporting system is not only experienced with conventional medicines but also with herbal medicines⁴¹. The factors that contribute to underreporting include lack of association between herbal medicine and potential ADRs, the patients stopping using herbal medicines when they feel unwell, doctor/patient unaware of herbal medicine ADRs reporting, and doctor's unawareness of herbal medicines consumption by the patients^{38,42,43}.

Herbal medicine safety is monitored through spontaneous reporting systems using standardized forms for reporting suspected ADRs by medical practitioners and consumers^{27,29}. The spontaneous reports work well where herbal medicines are well-regulated, prescribed, and dispensed by well-informed medical practitioners and the existence of the

pharmacovigilance system³⁸. Both Malawi and Nigeria have well-functioning pharmacovigilance systems that were set to gather safety reports on medicines and herbal medicines⁴⁴. There is currently no regulation for herbal medicines in Malawi while Nigeria has a well-regulated system for listing herbal medicines^{45,46,24}, however, the consumption of unregulated and unmonitored use of herbal medicines among PLWHIV put the lives at risk due to lack of safety and quality, and potential interactions that may lead to suspected ADRs^{47,48}. With the challenge of inadequate data on the consumption of herbal medicines, and reporting of ADRs associated with its use, this study was designed to investigate herbal medicines consumption, its associated factors and experiences of ADR reporting among PLWHIV at the University Teaching Hospitals in Blantyre, Malawi and Ibadan, Nigeria. The findings from this study will assist the policymakers, regulators, researchers, PLWHIV, and other stakeholders in making informed decisions on the safety of herbal medicine consumption and ADR reporting.

Methods

Study design

A hospital-based cross-sectional study was conducted where interviews were done using structured questionnaires among PLWHIV between July 2020 and January 2021.

Study setting and population

The study was conducted on PLWHIV who visited the Light House Umodzi clinic, Queen Elizabeth Central Hospital (QECH), a tertiary teaching hospital of the Kamuzu University of Health Sciences (KUHS) in Blantyre and the Infectious Disease Institute Clinic, University College Hospital (UCH), a tertiary facility in Ibadan in Nigeria.

Inclusion and exclusion criteria

All patients who were living with HIV and receiving antiretroviral therapy, aged 18 years and above, and those who gave consent were recruited into the study. Those who did not give consent were excluded from the study.

Study population, sample size determination, and recruitment

All adults (more than 18 years) PLWHIV who had been diagnosed with HIV/AIDS and who took antiretroviral therapy before recruitment were taken as our source population while those patients who visited the outpatient clinic at QECH and UCH for consultation and medication refill during the data collection period were taken as the study population¹⁸. Client numbers issued during the clinic consultations were shared with the principal investigator and were used to generate random numbers. Using these numbers, a simple random sampling technique was used to select study participants until the final sample sizes were reached. The following formula was used to calculate the sample size of patients⁴⁹: $n = Z^2P(1-P)/d^2 = 340$ { Z = confidence level interval at 95.0%, P = prevalence rate (33.0%)^{50,51}, d = precision at 5% (0.05). The 10 percent non-response ($n=34$) was added to the sample size giving the final sample size of 374 per site. A total of 374 participants attending a clinic in each country were approached to participate in the study, 14 declined at QECH in Blantyre, Malawi while only 4 declined at UCH, in Ibadan, Nigeria, representing 96.3% and 98.9% response rates, respectively.

Data collection method and tool

A structured questionnaire was used for data collection during interviews. The data collection tool was created by adapting items in the previously used instruments^{18,25}. The questionnaire contained sections that explored participants' demographic and clinical characteristics, knowledge of potential herbal medicine ADRs, experiences with the consumption of herbal medicines, length of herbal medicine use, sources of herbal medicines, names, part used, duration of treatment, outcomes of use, consultation with the doctor on the use of herbal medicines, reasons for using herbal medicines, experience and reporting of herbal medicine ADRs. The questionnaire was first prepared in English and later translated into Chichewa for Blantyre participants and Yoruba for Ibadan participants and back-translated to English to ensure that it retains its intended meaning and aids understanding of the questions. The questionnaire items were reviewed for relevance by a team of experts including experienced pharmacists, doctors, and public health professionals. The questionnaire was validated by pretesting on 10 PLWHIV at the same facility in Malawi and in Nigeria but these participants were not included in the study⁵². The structured questionnaires were administered by a team of four trained research assistants including the principal investigator. The research assistants' training content included: project objectives and methods, interview and communication skills, process of getting informed consent, use of informed consent forms, and use of questionnaires during interviews. The questionnaire was administered in the form of face-to-face guided interviews in a consultation room isolated for this purpose away from the clinical staff and other participants at the facility to ensure privacy.

Data approach, management, and analysis

All the data variables collected and their responses were organized, coded, and entered into the Microsoft Access software package in preparation for data analysis. Data were imported into Stata 15 (StataCorp, Texas, USA) from Microsoft Access.

Analysis approach

Analysis was done using R (R Core Team, 2015). Summary statistics were computed for continuous variables using mean and standard deviation (SD) after examining and confirming normal distribution by plotting histograms and formally testing using the Shapiro-Wilks test for normality. Unpaired t-tests were used to compare means of continuous variables between Malawi and Nigeria whereas Chi-squared tests were used to examine differences in frequencies between categorical variables and the countries (Malawi and Nigeria). P-values from all tests were considered statistically significant if less than 0.05 on a two-sided test.

Ethical considerations

Approvals in Malawi and Nigeria were obtained through the College of Medicine Research and Ethics Committee (COMREC) in Malawi with approval number P.02/20/2932 and the University College Hospital Ethics Committee (UI/EC) with approval number NHREC/05/01/2008a in Nigeria, respectively. Written informed consent was obtained from participants who were literate while verbal consent was obtained among non-literate participants who used their thumbprint in the informed consent form. The informed consent process involved explaining the purpose of the project and the benefits of the study in knowledge

contribution. The process emphasized participant's freedom to either participate or not participate in the interviews. The participants' time was compensated with a token of appreciation in the form of money for transportation. All questionnaires were anonymous to ensure anonymity.

Results

Demographic and clinical information characteristics of the study population

The study participants were mostly females in both Malawi, 67.5% (n=243) and Nigeria, 65.1% (n=241). The majority of the participants were Christians 63.6% (n=229) and 63.2% (n=234), married 63.6% (n=229) and 71.9% (n=266), secondary school educated 49.2% (n=177) and 38.6% (n=143), urban residents 43.6% (n=157) and 80.3% (n=297) and doing business 35.0% (n=126) and 70.0% (n=259), $p < 0.001$, in Malawi and Nigeria, respectively (see Table 1). The participants were mostly on the first-line antiretroviral therapy, 90.3% (n=325) and 81.9% (n=303), and concurrently taking other medicines along with antiretroviral therapy, 90.0% (n=323) and 57.8% (n=214) in Malawi and Nigeria, respectively. Cotrimoxazole was the most commonly prescribed medicine taken along with antiretroviral therapy, in Malawi, 96.0% (n=310) and Nigeria 69.8% (n=150) as shown in Table 2.

Use of herbal medicines and associated factors

Overall, the majority (67.9%) of PLWHIV that had used herbal medicines in both countries, 80.6% (n=290) were from Malawi while 55.7% (n=206) were from Nigeria as shown in Table 3. The most frequently mentioned herbal medicines in Malawi were *Aloe vera* (L.) Burm.f. (14.0%), *Moringa oleifera* Lam. (14.0%), *Zingiber officinale* Roscoe (13.0%), and *Allium sativum* L. (7.0%). Furthermore, in Nigeria, the most commonly used herbal medicines were *Zingiber officinale* Roscoe (15.0%), *Vernonia amygdalina* Delile (14.0%), *Moringa oleifera* Lam. (9.0%), and *Allium sativum* L. (11.0%) (see Figures 1 and 2).

The participants' reasons for consuming herbal medicines concurrently with ARVs included the fact that herbal medicines were readily available, 42.1% (n=115), and perceived to boost immunity, 44.6% (n=91) in Malawi and Nigeria, respectively as shown in Table 4. Participants confirmed that the use of herbal medicine improved their health condition in Malawi (58.1%, n=250) and in Nigeria (41.9%, n=180). Less than half (43.8%) and 50.2% of PLWHIV from Malawi and Nigeria, respectively had used herbal medicines for over one year. The common source of herbal medicinal products used by PLWHIV was through the market sellers, 52.8% (n=151) in Malawi and 35.9% (n=133) in Nigeria as described in Table 3.

Herbal medicine ADR reporting

More PLWHIV in Malawi, 90.6% (n=326) than in Nigeria, 54.6% (n=202), $p < 0.001$, reported that doctors did not ask them about herbal medicine use during history taking (Table 4). Patients in both Malawi, 91.8% (n=145) and Nigeria 81.3% (n=109) mentioned that fear of being shouted at was the reason for not revealing herbal medicine use to the doctor. Fewer patients in Malawi, 3.9% (n=12), and in Nigeria, 8.0% (n=18), reported having experienced herbal medicine ADRs and about 50.0% (n=5, n=8) of those who experienced ADRs in both countries did not know what to do as reflected on Table 5.

Table 1: Demographic information of people living with HIV (n=730)

Description	Level	Overall (%)	Malawi (%)	Nigeria (%)
Sex	Male	246 (33.7)	117 (32.5)	129 (34.9)
	Female	484 (66.3)	243 (67.5)	241 (65.1)
Age (mean±SD)	Years	43.65±11.65	41.19±10.92	46.04 ±11.86
Religion	Christian	565 (77.4)	331 (91.9)	234 (63.2)
	Muslim	162 (22.2)	29 (8.1)	133 (35.9)
	Other	3 (0.4)	0 (0.0)	3 (0.8)
Marital status	Married	495 (67.8)	229 (63.6)	266 (71.9)
	Divorced	50 (6.8)	31 (8.6)	19 (5.1)
	Widowed	116 (15.9)	57 (15.8)	59 (15.9)
	Unmarried	69 (9.5)	43 (11.9)	26 (7.0)
Education	None	42 (5.8)	16 (4.4)	26 (7.0)
	Primary school	203 (27.8)	126 (35.0)	77 (20.8)
	Secondary school	320 (43.8)	177 (49.2)	143 (38.6)
	College and above	165 (22.6)	41 (11.4)	124 (33.5)
Employment	Full time	338 (46.3)	101 (28.1)	237 (64.1)
	Part time	27 (3.7)	26 (7.2)	1 (0.3)
	Unemployed	365 (50.0)	233 (64.7)	132 (35.7)
Residence	Urban	454 (62.2)	157 (43.6)	297 (80.3)
	Suburban	188 (25.8)	122 (33.9)	66 (17.8)
	Rural	88 (12.1)	81 (22.5)	7 (1.9)
Occupation	House wife	14 (1.9)	11 (3.1)	3 (0.8)
	Unemployed	127 (17.4)	104 (28.9)	23 (6.2)
	Employed	175 (24.0)	108 (30.0)	67 (18.1)
	Pensioner	23 (3.2)	11 (3.1)	12 (3.2)
	Student	5 (0.7)	0 (0.0)	5 (1.4)
	Business	385 (52.7)	126 (35.0)	259 (70.0)
	Other	1 (0.1)	0 (0.0)	1 (0.3)

Table 2: Clinical information of people living with HIV (n=730)

Description	Level	Overall (%)	Malawi (%)	Nigeria (%)	p-value [¶]
Time diagnosed HIV	<1 year	47 (6.4)	24 (6.7)	23 (6.2)	0.011
	1-2 years	52 (7.1)	36 (10.0)	16 (4.3)	
	>2 years	631 (86.4)	300 (83.3)	331 (89.5)	
ART type	First line ^{¶ ¶}	628 (86.0)	325 (90.3)	303 (81.9)	<0.001
	Second line ^{¶ ¶ ¶}	101 (13.7)	35 (9.7)	66 (17.8)	
	Other	1 (0.3)	0 (0)	1 (0.3)	
Taking ART with other medicines	Yes	537 (73.7)	323 (90.0)	214 (57.8)	<0.001
	No	192 (26.3)	36 (10.0)	156 (42.2)	
Type of other medicines	Cotrimoxazole	460 (85.5)	310 (96.0)	150 (69.8)	<0.001
	Fluconazole	3 (0.6)	2 (0.6)	1 (0.5)	
	Anti TB medicines	16 (3.0)	2 (0.6)	14 (6.5)	
	Other medicines	59 (11.0)	9 (2.8)	50 (23.3)	

* Statistically significant at $p < 0.05$ and $p < 0.001$.

** First line: TDF/3TC/DTG, TDF/3TC/EFV, ABC/3TC/DTG, ABC/3TC/EFV.

*** Second line: TDF/3TC/ATVr, TDF/3TC/LPVr, ABC/3TC/ ATVr, ABC/3TC/LPVr.

TDF, Tenofovir Disoproxil Fumarate. 3TC, Lamivudine. DTG, Dolutegravir. EFV, Efavirenz. ABC, Abacavir. ATV, Atazanavir. r, ritonavir. LPV, Lopinavir.

Table 3: Use of herbal medicines among PLWHIV (n=730)

Variable description	level	Overall (%)	Malawi (%)	Nigeria (%)	p-value
Used herbal products	Yes	496 (67.9)	290 (80.6)	206 (55.7)	<0.001
	No	234 (32.1)	70 (19.4)	164 (44.3)	
Length of herbal use	Currently	186 (37.7)	83 (28.8)	103 (50.2)	<0.001
	Up to 6 months	129 (26.2)	57 (19.8)	72 (35.1)	
	Over 6 months to 1 yr.	32 (6.5)	22 (7.6)	10 (4.9)	
	Over 1 yr.	146 (29.6)	126 (43.8)	20 (9.8)	
Source of herbal medicines	Pharmacy shop	2 (0.3)	1 (0.3)	1 (0.3)	<0.001
	Herbalist clinic	22 (3.4)	21 (7.3)	1 (0.3)	
	Market vendor	284 (43.3)	151 (52.8)	133 (35.9)	
	Friends/family	34 (5.2)	25 (8.7)	9 (2.4)	
	Garden/wild	149 (22.7)	88 (30.8)	61 (16.5)	
Dosage form	Powder	2 (0.6)	2 (1.2)	0 (0.0)	<0.001
	Tablets	1 (0.3)	0 (0.0)	1 (0.5)	
	Capsules	252 (70.0)	146 (85.9)	106 (55.8)	
	Liquid	104 (28.9)	21 (12.4)	83 (43.7)	
	Other	1 (0.3)	1 (0.6)	0 (0.0)	
Herbal medicine duration of use per course	Up to one week	144 (60.2)	74 (25.9)	70 (34.3)	<0.001
	>1 week-1 month	51 (14.7)	37 (17.5)	14 (10.4)	
	>1 month-3 months	21 (6.1)	16 (7.5)	5 (3.7)	
	>3 months-6 months	5 (1.4)	4 (1.9)	1 (0.7)	
	>6 months	2 (0.6)	1 (0.5)	1 (0.7)	
	Unlimited	266 (76.9)	153 (72.2)	113 (84.3)	

Statistically significant at $p < 0.001$.

Table 4: Factors associated with the use of herbal medicines among people living with HIV (n=730)

Description	level	Overall (%)	Malawi (%)	Nigeria (%)	p-value
Doctor asked about herbal medicine use	Yes	201 (27.5)	34 (9.4)	167 (45.1)	<0.001
	No	528 (72.3)	326 (90.6)	202 (54.6)	
Revealed to doctor about herbal use	Yes	531 (99.8)	334 (100.0)	197 (99.5)	0.791
	No	1 (0.2)	0 (0.0)	1 (0.5)	
Reasons for revealing to doctor	To know more about herbals	14 (51.9)	3 (25.0)	11 (73.3)	0.036
		12 (44.4)	8 (66.7)	4 (26.7)	
	Had side effects	1 (3.7)	1 (8.3)	0 (0.0)	
Reasons for not revealing to doctor	Fear of being shouted at	254 (87.0)	145 (91.8)	109 (81.3)	0.028
	It is not important	28 (9.6)	9 (5.7)	19 (14.2)	
	They don't care	10 (3.4)	4 (2.5)	6 (4.5)	
Reasons for using herbal medicines	Readily available	151 (31.7)	115 (42.1)	36 (17.6)	<0.001
	Part of culture	93 (19.5)	70 (25.6)	23 (11.3)	
	They don't have side effects	19 (4.0)	17 (6.2)	2 (1.0)	
	Help alleviate ART side effects	6 (1.3)	1 (0.4)	5 (2.5)	
	Perceived to boost immunity	149 (31.2)	58 (21.2)	91 (44.6)	
	Improve appetite	4 (0.8)	2 (0.7)	2 (1.0)	
	Other	55 (11.5)	10 (3.7)	45 (22.1)	

* Statistically significant at $p < 0.05$ and $p < 0.001$.

Table 5: Herbal medicine knowledge and ADRs reporting among people living with HIV (n=730)

Description	level	Overall (%)	Malawi (%)	Nigeria (%)	p-value
Experienced ART ADRs	Yes	240 (33.4)	123 (34.9)	117 (31.9)	0.429
	No	479 (66.6)	229 (65.1)	250 (68.1)	
Action on experiencing ART ADRs	Did nothing	29 (13.2)	16 (14.7)	13 (11.7)	0.005
	Reported to hospital	181 (82.3)	93 (85.3)	88 (79.3)	
	Other	10 (4.5)	0 (0.0)	10 (9.0)	
Experienced herbal medicine ADRs	Yes	30 (5.6)	12 (3.9)	18 (8.0)	0.066
	No	503 (94.4)	296 (96.1)	207 (92.0)	
Action on experiencing herbal medicine ADRs	Did nothing	13 (50.0)	5 (50.0)	8 (50.0)	0.794
	Reported to hospital	7 (26.9)	2 (20.0)	5 (31.2)	
	Other	6 (23.1)	3 (30.0)	3 (18.8)	
Knowledge of where to report ADRs	Yes	653 (89.7)	333 (92.8)	320 (86.7)	0.011
	No	75 (10.3)	26 (7.2)	49 (13.3)	

* Statistically significant at p<0.05

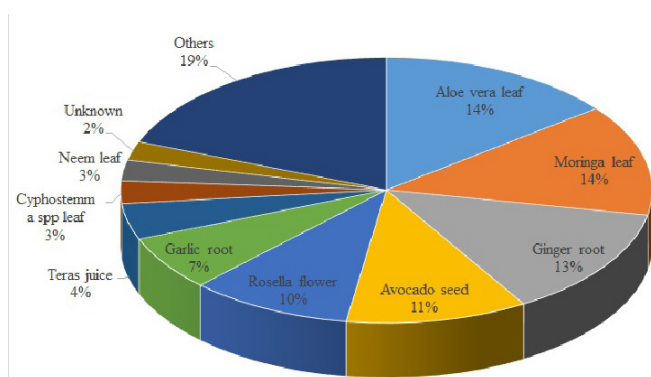


Figure 1: Herbal medicines used among people living with HIV in Malawi (n=435)

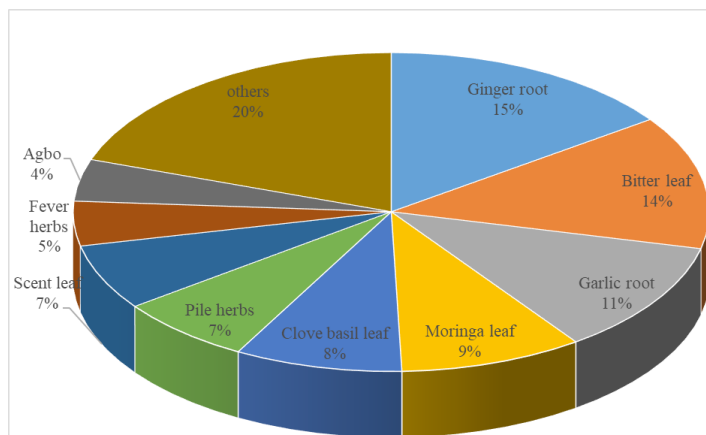


Figure 2: Herbal medicines used among people living with HIV in Nigeria (n=376)

Discussion

This study aimed to investigate herbal medicine consumption, its associated factors, and experiences of ADR reporting among PLWHIV at the University Teaching Hospitals in Blantyre, Malawi, and Ibadan, Nigeria. The extent of herbal medicine use among PLWHIV ranges between 50.0% and 95.0% according to various studies¹⁹. The study shows a possible increase in the prevalence of herbal medicine use in Blantyre compared with the previous reports²⁴. The increase in herbal medicine use may be attributed to ready availability, accessibility, and attractive therapeutic claims used in marketing the herbal medicines^{24,53,54,55}. Furthermore,

in Nigeria, this may be the highest prevalence and probably the first to be reported in Ibadan (55.7%) as compared with the prevalence in other states cities such as in Lagos 8.2% and 42.7% in 2012⁵⁶ and 2017⁵⁷, respectively, in Calabar 33.6%⁵¹ and 43.0% collectively in Katsina, Gombe, Lafia, and Jos⁵⁴. The Nigerian prevalence is comparable to that of the Republic of South Africa (24.0%)⁵⁸, Kabarole, Uganda (63.5%)⁵⁹ while that of Malawi is comparable to that of Kenya at 70.1%⁶⁰ and Ethiopia at 70.8%¹⁸. The pattern of the use of the following herbal medicines: *Aloe vera* (L.) *Burm.f.*, *Allium sativum* L., *Zingiber officinale* Roscoe, *Vernonia amygdalina* Delile, and *Moringa oleifera* Lam. or herbal medicinal products derived thereof, among PLWHIV is consistent reports from elsewhere^{18,24,57,59-63,64}. These findings are consistent with reports that an increase in the use of herbal medicine in developing countries was due to availability⁵⁵, accessibility^{63,65}, and immune supplementation²².

This study was conducted during the COVID-19 disease outbreak before vaccines were developed. The majority of people who were reportedly at risk of being infected by COVID-19 were those with immune suppression including PLWHIV who resorted to using herbal medicine concoctions that comprised of *Azadirachta indica* A. Juss., *Allium sativum* L., *Zingiber officinale* Roscoe to prevent or manage the pandemic^{66,67}. The COVID-19 pandemic may have contributed to the increase in the prevalence of herbal medicines use among PLWHIV in Malawi and Nigeria during the period the study was conducted^{66,68}. The participants from Malawi and Nigeria reported improved health conditions through herbal medicine consumption. This is in agreement with the Uganda report⁵⁹. This implies that Ministries of Health and the National Regulatory Agencies across the region including Malawi and Nigeria need to consider and familiarise themselves with the current role of herbal medicines and its future possibilities within the conventional healthcare system⁶⁹. The study findings imply that most PLWHIV are consuming herbal medicines. In Malawi, these herbal medicines are not regulated and the market is replete with these products of questionable quality, safety, and efficacy⁷⁰. The Pharmacy and Medicines Regulatory Authority (PMRA) is yet to introduce the regulations and guidelines for the registration

herbal medicines^{30,71}. In Nigeria, herbal medicines are well regulated through listing by the National Agency for Food and Drug Administration and Control (NAFDAC)^{72,73}. Despite the availability of a registration system, there remain illegal herbal medicine vendors in the streets of Ibadan due to a lack of enforcement of regulations^{57,73,74}. The lack of herbal medicine regulations in Malawi and inadequate enforcement of such regulations in Nigeria may further endanger the health of the public including those PLWHIV as the market continues to be flooded with herbal products with unproven claims and testimonies of curing HIV and other diseases of public health importance.

The present study established the fact that the majority of PLWHIV were from urban areas and were able to afford to purchase well-packaged herbal medicines from herbal medicine vendors and supermarkets. This is contrary to findings that showed that herbal medicine users were rural dwellers whose source were friends and family^{8,24,69,75}. However, this shows diversity in the demand for herbal medicines from rural and urban participants and their perception of herbal medicines use in the management of opportunistic infections and ADRs associated with ART. Consumption of herbal medicines in urban areas was associated with the promotion of healthy lifestyles, and prevention of chronic diseases like hypertension, diabetes, and HIV-related illnesses^{76,55,75}. Other studies reported that combined use of herbal medicines with ART may encourage non-adherence to ART^{77, 78}. However, Mbali²⁴ reported that concurrent use of herbal medicines with ART did not affect non-adherence to ART. The combined use of herbal medicines with ART may increase the potential for drug-herbal interactions specifically pharmacokinetic and pharmacodynamics interactions^{79,80}. For example, the most commonly used herbal medicine *Moringa oleifera* Lam. in both Malawi and Nigeria was reported elsewhere to interact with nevirapine pharmacokinetically without any clinical significance^{81,82,78}. Furthermore, the herbal medicine *Ginkgo biloba* L. was reported to interact with efavirenz^{78,83} efavirenz is one of the key drugs in the first line of HIV treatment in both countries^{5,84-86}. Since the study sample sizes obtained from the teaching hospitals were limited and could not be used to generalize the use of herbal medicines among PLWHIV, therefore, further larger studies are required to investigate potential drug-herbal interactions between the frequently consumed herbal medicines and ART in both countries⁸⁷. The study has shown the importance of screening all PLWHIV by clinicians and medical doctors of herbal medicine use to avoid potential ADRs due to interaction with ART.

The study has shown that doctors did not inquire about herbal medicine use by PLWHIV during history taking and this is consistent with the Trinidad report⁶³. These behaviors may reflect authority and power dynamics between doctors and patients because in many countries patients do not consider it appropriate to challenge the doctors' decisions or ask questions⁸⁸. PLWHIV mentioned fear of being shouted at by the doctor as the reason for not revealing herbal medicine use. The results from this study agree with reports that doctors admitted not asking participants regarding concurrent herbal medicine use with ART^{18,22,62}. Fewer PLWHIV reported herbal medicine ADRs experiences. Inadequate knowledge of pharmacovigilance and rational use of herbal medicines among PLWHIV and doctors may have contributed to underreporting⁶⁹. It was routine

for patients to report any conventional medicine ADRs including ART. The challenge of low herbal medicine ADR reporting was common in practice and this agrees with other reports⁶³. Despite the low figures on the herbal medicine ADR reporting, it was an indicator of the urgent need for herbal medicine pharmacovigilance to monitor these ADRs, some of which may be life-threatening to patients. The importance of herbal medicine pharmacovigilance on patients on antiretroviral therapy has been emphasized⁵⁹. Despite that few patients reported the herbal medicine ADRs, this study did not classify or characterise their severity. Therefore it was not possible to describe the severity of ADRs including death⁴⁸. The reported ADRs may require further investigations to establish a causal relationship with herbal medicine use. Larger studies with representative sample sizes are recommended for all ART clinics in both countries to establish national prevalence, reporting, and severity of ADRs associated with the herbal medicine use. Awareness training on the use and herbal medicine ADR reporting for PLWHIV and doctors are recommended to the Ministries of Health and the Medicines Regulatory Agencies.

Study strengths and limitations

This may be the first study to report on the use of herbal medicines and ADR reporting among PLWHIV both in Blantyre, Malawi, and Ibadan, Nigeria. The sample sizes for the study participants were large enough to represent PLWHIV at the teaching hospitals.

Participants' interviews were done at the clinic premises and this might have affected their responses in ways that they perceived would not affect the services they received on the day of the interviews. In mitigation to this challenge, no staff from the clinic were involved in interviewing the patients. The study did not collect the types and severity of ADRs hence if the few reports were characterised could probably be significant. The study was conducted in ART clinics so those who reject ART and only use herbal medicines were systematically excluded based on the design.

Conclusion

Most people living with HIV in Blantyre, Malawi, and Ibadan, Nigeria are using herbal medicines while on ART. The combined use of herbal medicines and ART may have potential drug-herbal interactions. Similar herbal medicines are being used in both countries despite different geographical locations. Most doctors are not inquiring about the use of herbal medicines during history taking in both countries. Fewer herbal medicine ADR experiences are reported by PLWHIV in both countries. More studies are being recommended to investigate potential herbal-ART interactions and evaluate the severity of herbal medicine ADRs among PLWHIV.

Abbreviations

ADRs: Adverse Reactions, ADR: Adverse Reaction, AIDS: Acquired Immunodeficiency Syndrome, ARVs: Antiretroviral drugs, ART: Antiretroviral therapy, HIV: Human Immunodeficiency Virus, MOH: Ministry of Health, NAFDAC: National Agency for Food and Drug Administration and Control, NNRTIs: Non-Nucleoside Reverse Transcriptase Inhibitors, NRTIs: Nucleoside Reverse Transcriptase Inhibitors, PMRA: Pharmacy and Medicines Regulatory Authority, PLWHIV: People Living with HIV, QECH: Queen Elizabeth Central Hospital, UCH: University College Hospital, UI/EC: University of Ibadan

Ethics Committee. WHO: World Health Organization.

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Contribution of Authors

The study was conceptualized, developed, and conducted by John Samson Mponda (JSM) under the supervision of Professor Jones Moody (JM), Professor Ademola Ajuwon (AA), and Professor Adamson Muula (AM). Dr. Augustine Choko (AC) provided statistical support for the study and interpretation of results. JSM drafted the initial manuscript and the manuscript was further reviewed and edited by JM, AA, and AM. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study received ethical approval from the College of Medicine Research Ethics Committee in Malawi (COMREC) with approval number P.02/20/2932 and the University College Hospital Ethics Committee (UI/EC) with approval number NHREC/05/01/2008a in Nigeria, respectively. All participants gave their consent to participate in the study. Participant identity was kept anonymous and their opinions were not shared by anyone outside the study team.

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Conflict of interest

There was no conflict of interest expressed by the authors.

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