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ORIGINAL RESEARCH

Ethnobotanical Survey of Medicinal Plants Used in Breast Cancer Treatment by Traditional Health Practitioners in Central Uganda

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Purpose: The study aimed to document the existing knowledge and practices related to breast cancer recognition and treatment using medicinal plants by traditional health practitioners in Central Uganda.

Methods: This cross-sectional exploratory survey, conducted between February and August 2020, applied a mixed methods research approach. A semi-structured questionnaire was administered to 119 traditional health practitioners (THPs) in Kampala, Wakiso and Mukono. Content analysis of qualitative data was done. Quantitative ethnobotanical survey indices, namely user reports (Nur), percentage of respondents with knowledge (PRK), informant consensus factor (Fic), fidelity level (FL), preference ranks (PR) and direct matrix ranking (DMR) were determined.

Results: Most THPs recognized breast cancer by breast swelling (n=74, 62.2%) and breast pain (n=29, 24.4%). They cited 30 plants from 30 genera in 23 families (Fic 0.75 on breast cancer). Asteraceae, Apocynaceae, Euphorbiaceae, Fabaceae, Lamiaceae and Rutaceae were the predominant families. The ten most cited plants were *Annona muricata* L. (Nur=24), *Rhoicissus tridentata* (L.f.) Wild & R.B.Drumm (Nur =19), *Erythrococca bongensis Pax (*Nur=11), *Ficus* sp. (Nur=10), *Cannabis sativa* L. (Nur=8), *Ipomoea wightii* (Wall.) Choisy (Nur=7), *Erythrina abyssinica* DC. (Nur=5), *Leucas martinicensis* (Jacq.) R.Br. (Nur=4), *Abelmoschus esculentus* (L.) Moench (Nur=4) and *Zanthoxylum chalybeum* Engl. (Nur=3). *Annona muricata* L. was highly preferred by THPs (PR 1), Ficus sp. had highest fidelity level (FL=77%) and *Zanthoxylum chalybeum* Engl. ranked as the highest multipurpose plant (DMR 1). Herbs (n=14, 47%) were the most commonly used life forms besides trees (n=11, 37%) and shrubs (n=5, 16%). THPs mostly used leaves (46%), prepared decoctions (82%) and applied residues on the breast.

Conclusion: THPs in Central Uganda recognized breast cancer by symptoms. Medicinal plants applied in its folk treatment have been documented and the claims of cure by THPs merit further investigation.

Keywords: breast tumors, ethnomedicine, herbal medicine, indigenous knowledge

Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer-related deaths among women; it accounts for 23% of total cancer cases and 14% of annual cancer deaths globally.[1] Breast cancer incidence of 22:100,000 with 5-year survival rate at 56% in Uganda has been reported, and the burden is expected to double in 2030 due to changes in risk factors and population growth.[2,3]

Chemotherapy, radiotherapy and surgery are the main breast cancer treatment modalities. However, only 25% of Ugandan breast cancer patients can access such care due to the limitations of poor nursing care and surgery, inadequate access to radiotherapy, poor availability of basic and modern systemic therapies translating into lower survival rates.[3] In Uganda, a mean delay to seek treatment by breast cancer patients of 13 months and majority of patients presenting

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with clinical stages IV (88.5%) and III (9.4%) have been reported.[4] The delay could be due to the fact that many breast cancer patients, particularly in rural Ugandan settings, are unable to access the only public health facility for specialized cancer treatment.[5] Furthermore, while 92.7% of the cost of medicines used at the Uganda Cancer Institute is covered by the government of Republic of Uganda,[6] the drugs are out of stock most of the time and patients have to buy them. Those who cannot afford these medicines discontinue treatment because of the economic burden. Like other cancer patients (up to 60%), breast cancer patients often resort to herbal concoctions prepared at home or by traditional health practitioners.[5]

Additionally, the anti-breast cancer drugs in clinical use exert toxicities and require long-term use, posing adherence challenges and the gradual resistance of cancer cells against these drugs.[7] This justifies the need to improve current therapeutic responses by additional novel approaches.[7,8] Whereas plants are important sources of modern anti-cancer drugs like Paclitaxel, Vincristine, Vinblastine and plant remedies used by breast cancer patients, with even claims of cure, the traditional treatment practices and plants used by the communities in Uganda and many other developing countries to treat breast cancer and the theories that explain their continued use are not well documented.[9–12] The responsible active compounds in these plants and their anti-breast cancer activity profiles are not known, and hence patients are at risk of using non-validated remedies.[11–13] This has hindered development of potential useful medicinal plants into modern pharmaceutical dosage forms for possible use in the battle against cancers.[13] The study aimed to document the existing knowledge and practices related to breast cancer recognition and treatment using medicinal plants by traditional health practitioners in Central Uganda.

Materials and Methods

Research Design

A cross-sectional exploratory survey was conducted between February and August 2020. A mixed methods research approach was adopted to enable the research team to assess knowledge of traditional health practitioners (THPs) on breast cancer (BC) to address the questions of community knowledge and practices in treating breast cancer by traditional health practitioners, what medicinal plants were used to treat breast cancer from the perspective of traditional health practitioners and how the plants were prepared and administered to patients over the past 5 years (January 2015–August 2020).

Study Area

The study was conducted in the districts of Kampala (0.347° N, 32.5825°E), Wakiso (0.3987° N, 32.4793°E) and Mukono (0.3549° N, 32.752°E). These districts are among the top ten most populated districts in Uganda. They are located in the central region, popularly known as Buganda region and neighbourhood of Uganda Cancer Institute.[14] They are accessible by road and well known in Uganda for their use of traditional medicine in the treatment of diseases and the local language spoken is Luganda.[15]

Study Population

There are no recent estimates of THPs in Uganda. The Ugandan government has enacted a law that seeks to regulate the practice of THPs and hopes to have THPs registered (not yet done as time of this study). However, as per the World Bank IK series, there is at least one traditional health practitioner for nearly 290 people in Uganda.[16] The population of THPs in the study area was therefore obtained by dividing the sum of the population aged 18 years and above as reported in the national population and housing census on area specific data for the districts by 290.[14–16] Accordingly, the study targeted 7457 THPs who were aged 18 years and above. In this study, THPs were defined as individuals who hold indigenous knowledge in traditional methods of treatment; they prepare, prescribe and/or administer herbal medicines to others within the community.

Sample Size Estimation and Selection

Sample size was estimated using Equation 1:

$$n = \frac{Np(1-p)}{(N-1)\left(\frac{d}{Z\alpha}\right)^2 + p(1-p)} \quad (1)$$

Where n=approximate sample size; N=population size under study; p=proportion of population considered; d=limit to error estimate; α=level of significance considered; $Z_{\alpha/2}$=value obtained from the table of standard normal distribution.[17,18] The study considered a population size of 7457 (N=7457), as earlier explained, confidence coefficient of 95% ($Z_{\alpha/2}$= 1.96), sampling error of 0.05 (d=0.05) and a proportion of 0.5 (p=0.5) was assigned due to nonexistence of previous information for this value to arrive at total estimated sample size of 366. The study population was divided into 20 strata-termed communities (Table 1), as guided by a method of determining sample size for ethnobotanical studies by Espinosa, Bieski and Martin.[18,19]

Each constituency was a stratum, "a community" for study, and it represented the number of households sampled per community, considering an informant (THP) per household. To estimate sample size for each community as shown in Table 1, we multiplied the sample fraction by the total sample size (366). For calculation of sample fraction, we divided the number of households in that community by the total number of households for the entire study area, which was 1,060,029 households.[14,17–20] An absolute minimum sample of four individuals within each category is indispensable for any statistical analysis.[20]

Sampling Techniques and Procedure

Each community, as indicated in Table 1, formed a stratum. We randomly sampled one THP per household from each stratum. The contacts for THPs were obtained from leaders of traditional healer associations in Buganda. THPs in each community were mapped, consented and interview schedule planned. A list of THPs in each stratum was generated, randomized by Microsoft Excel and the required number of THPs was obtained by simple random sampling. All THPs who did not treat breast cancer and those who did not use herbs in treatment of patients were excluded.

In order to maximize community co-operation, the study team was introduced to one chairperson of each area's local council. A researcher administered questionnaire was administered to the respondents by the principal investigator and four trained research assistants who were conversant with the language and cultures of the local people in the study area. This made it easy to extract information from respondents as desired. The leaders of traditional healer associations in Buganda region, respondents and local council authorities assisted the researchers to identify study respondents in the study districts.

The plants mentioned in the study were identified in the field using their local names, based on their taxonomic characters and the voucher specimens collected for confirmation at Makerere University Herbarium. Herbarium specimens were prepared, assigned voucher numbers and deposited at Makerere University herbarium and the Pharmacognosy Laboratory in the Department of Pharmacy Makerere University. Plant names have been checked with scientific plant databases at https://wfoplantlist.org/plant-list and https://plants.jstor.org/.

Data Collection Instruments

Primary data was collected using a semi-structured questionnaire constructed by the principal investigator and two senior researchers. This helped to improve the number and accuracy of responses to the survey.[21,22] A Luganda version of the questionnaire was used on participants who had low English literacy, but were fluent in Luganda. The questionnaire used can be accessed at Supplementary Information to this publication.

Data Quality Control

Validity of the questionnaire was established by determining its content validity index (CVI); three experts scored the relevance of the questions in the questionnaire in relation to the study variables. A content validity index of 0.7 or more was acceptable and a Likert scale analysis of each question by the experts was done as very relevant (4), quite relevant (3), somewhat relevant (2), and not relevant (1).

Reliability was established by a pilot testing of the questionnaire to ensure consistency, dependability and its ability to tap data that would answer the objective of the study. The pilot testing of the questionnaire was done in Nakasongola District (1.3490° N, 32.4467° E), one of the districts in Central Uganda. The results were subjected to reliability analysis (data available on request).[22]

Table 1 Distribution of 20 Communities in the Study Districts Including Sample Fractions

Community	Total Population Aged 18 Years and Above	Population of THPs Aged 18 Years and Above in Each Community	Households	Sample Fractions	Sample Size
Kampala District					
Central division constituency	48,167	166	23,142	0.0218	08
Kawempe division North constituency	123,229	425	58,806	0.0555	20
Kawempe division South constituency	66,656	230	35,396	0.0333	12
Makindye division East constituency	90,507	312	42,319	0.040	15
Makindye division West constituency	135,361	467	65,678	0.0620	23
Rubaga division North constituency	108,272	373	53,290	0.0503	18
Rubaga division South Constituency	107,118	369	51,922	0.0490	18
Nakawa Division constituency	182,733	630	83,853	0.0791	29
Wakiso District					
Kira municipality constituency	180,258	622	82,520	0.0778	28
Entebbe municipality constituency	37,208	128	17,859	0.0168	06
Makindye-Ssabagabo municipality constituency	149,099	514	70,780	0.0668	24
Nansana municipality constituency	182,724	630	90,742	0.0856	31
Kyadondo County East constituency	71,694	247	34,552	0.0326	12
Busiro County South constituency	124,816	430	64,659	0.0610	22
Busiro County North constituency	52,237	180	29,083	0.0274	10
Busiro County East constituency	225,376	777	111,268	0.1050	38
Mukono District					
Mukono municipality constituency	80,315	277	38,406	0.0362	13
Mukono County North constituency	46,619	161	24,137	0.0228	08
Mukono county South constituency	65,910	227	36,928	0.0348	13
Nakifuma county constituency	84,788	292	44,689	0.0422	18
TOTAL 2,163,087		7457	1,060,029	1	366

Data Organization and Analysis

Data Organization

Filled questionnaires were cross-checked by each data collector for completeness immediately after filling in the last response so that any missing information was collected before ending the interview. Data was organized using Microsoft Excel 2003 then analysed using SPSS V.18.0. The responses obtained from open-ended questions were grouped into categories according to similarities in the responses. Both theoretical and practical individual ethnobotanical knowledge of informants was analysed. Theoretical or passive knowledge refers to intellectual ability, such as the ability to name plants. Practical ethnobotanical knowledge refers to the practical dimension, for example ability to put knowledge into practice.[23]

Percentage of Respondents Having Knowledge

The percentage of respondents having knowledge (PRK) regarding the use of a plant species in the treatment of breast cancer was estimated using Equation 2:

$$PRK(\%) = \left(\frac{Np}{Nt}\right) * 100 \quad (2)$$

where Np is the total number of informants who are claiming to use a plant species to treat breast cancer and Nt is the total number of individuals interviewed.[24]

Informant Consensus Factor

Informant consensus factor was calculated to analyse individual ethnobotanical knowledge and indicate quality of information using Equation 3:

$$Fic = \frac{Nur - Ntaxa}{Nur - 1} \quad (3)$$

where *Nur* is the number of use reports and *Ntaxa* is the number of species in each use category [17].

Fic values range between 0 and 1, where "1" indicates the highest level of informant consent. Within a community, Fic points to the extensively used plants and helps in the selection of important medicinal plants for further pharmacological and phytochemical studies.[25]

Fidelity Level (FL)

Fidelity level indicates the importance of a certain plant species for a particular purpose. All reported ailments are grouped into major classes for calculation of FL values. In this study, FL values were estimated using Equation 4:

$$FL = \left(\frac{Ip}{Iu}\right) * 100 \quad (4)$$

where Ip is the total number of informants who claimed to use a plant species to treat breast cancer and Iu is the total number of respondents who mentioned the same plant for any ailment. The assumption is that plant species that are used frequently by most respondents for the same disease category are more likely to be biologically active plants.[26]

Preference Ranking (PR)

Rank values were assigned by 12 key informants to ten medicinal plants used for treating breast cancer in the study. The 12 key informants were randomly selected from among THPs who had treated at least five breast cancer patients and claimed cure of at least two of them in their settings over the past five years.

Direct Matrix Ranking

Direct matrix ranking (DMR) is used to gather data on use diversity of multipurpose medicinal plants. Target selection method was employed to identify 12 informants among interviewed THPs selected to rank the purposes of the cited plants beside their medicinal value in the community. DMR was determined for the top 10 plants.

Results

Demographic, Social and Economic Characteristics of Respondents

We interviewed 119 out of the 366 targeted traditional health practitioners (THPs) in Central Uganda, who came from Kampala 57(47.9%), Wakiso 41(34.5%) and Mukono 21(17.6%). The rest of the targeted participants were excluded as they did not treat breast cancer (n=150) and others did not use herbs in treatment of patients (n=97). Majority of the interviewed THPs (n=81, 72.3%) were male. The age of the respondents ranged between 30–73 years, with a mean of 54.61 years (SD=12.56) and had household members ranging between 1–11 (mean=4.97 members/household, SD=1.76); 81 (68.1%) THPs were married, 66 (55.5%) had attained primary education, 22 (18.5%) had no formal education, 24 (20.2%) had secondary education and only 7 (5.9%) had attained tertiary education.

The respondents were Baganda (62%), Banyankore (16%) and Bakiga (12%). Other ethnic groups in the study area were Basoga (5%), Langi (3.5%) and Lugbara (1.5%). THPs held religious beliefs. Participants disclosed their religions as Christians (56%), Muslims (24%), traditionists (7%), atheists (3%) and others (10%) did not disclose their religion.

Business and farming were the major economic activities of 65% and 30% of respondents, respectively. Only 5% were civil servants; 55% of THPs practised both farming and business as their source of livelihood.

Traditional Knowledge About Breast Cancer

Breast cancer in the study area is locally referred to as *Kokoolo wa mabere*. THPs commonly recognized breast cancer as a disease by looking for symptoms that included breast swelling (n=74, 62.2%), breast pain (n=29, 24.4%), colour changes in the nipple (n=7, 5.9%), pus from breast (n=6, 5%), and wounds on breast (1, 0.8%) or by asking for hospital documents (n=1, 0.8%).

Treatment Practices and Plant Species Used by THPs for Breast Cancer Patients in Central Uganda

Breast cancer was classified as a rare disease by THPs. Over the past 5 years (January 2015-–August 2020), the 119 THPs had treated a total of 4760 breast cancer patients. The number of patients treated by each THP per year ranged between 1–6 patients, with a mean of 3.76 (SD=1.59). Majority (n=108, 90.8%) of the THPs interviewed claimed that their herbal medicine had cured the patients they treated. However, only 3 (2.5%) of the interviewed THPs provided the first names and contacts of the patients treated for confirmation purposes. The rest of THPs (n=116, 97.5%) reported ignorance of the names and addresses of their patients, claiming it was the patients who sought their services and hence no need to keep their particulars, eg, "I don't keep their phone numbers; they always call me. I don't call them" (PID 050).

Some THPs (n=10, 8.4%) freely reported death of their patients: "I don't have those details but the last patient to treat passed away after a few months because medication was strong for her since the cancer was in its last stages" (PID-071). Another respondent stated: "I have treated one patient and he died after one year for breast cancer otherwise I treat all cancers similarly" (PID-070).

Whereas majority of THPs (n=117, 98.3%) treated BC patients based on symptoms, a few THPs (n=2, 1.7%) reported to have sent patients to the laboratory to confirm diagnosis. Some THPs (n=3, 2.5%) claimed to have a laboratory to diagnose breast cancer, but when the research team asked to confirm existence of such a laboratory, they were not shown any. Patient monitoring was done based on symptoms to assess progress of those on treatment.

In case of treatment failure, 61 (51.3%) THPs reported change to another herbal medicine for the patient, 28 (23.5%) referred to the government health facility and only 6 (5%) THPs reported having abandoned the patients. Alternative ways of handling treatment failure included buying western medicine for the patient (n=6, 5%), discharging the patient (n=5, 4.2%), giving same medicine but adding another plant (n=4, 3.4%), consulting qualified medical doctor (n=3, 2.5%), referring to another THP (n=3, 2.5%) or changing dose (n=1, 0.8%). Only 2 (1.7%) THPs reported never having had any of their herbal medicines failing to cure a breast cancer patient.

A respondent who believes in both traditional medicine and allopathic medicine stated, in the case of patients not responding to their herbal medicine: "I encourage the patient to persist on my medication as they also seek treatment from the hospital" (PID 071).

Over 99.2% (n=118) of referrals of breast cancer patients to other care facilities (other THPs, government health facility or clinic) were verbal. Only 1 THP claimed to make written referrals, although no such copy was available for verification. There were no written notes about breast cancer patients and herbal medicines given to them by all the THPs interviewed. A THP remarked: "We stopped treating so we discarded the records" (PID 057).

None of the THPs admitted to adding western medicine to herbal products for treatment of breast cancer in order to make them stronger. However, 117 (98.2%) THPs admitted to supplying herbal medicines to breast cancer patients in government hospitals and clinics.

Follow up of patients was also reported. In the study, 51 (42.8%) THPs interviewed reported following up their patients after they return to their homes or go to government health facilities and clinics.

THPs held a number of opinions about western medicines used to treat breast cancer. Majority of them stated they have side effects (n=67, 56.3%). Some believed they do not work (n=31, 26.1%), they just relieve symptoms (n=16, 14%). Other opinions reported by THPs included they work (n=1; 0.84%), they work but for a few (n=1, 0.84%), they work but have a lot of side effects (n=1, 0.84%), they work but require herbs to supplement (n=2,1.68%).

One respondent stated: "There is no cure for breast cancer. Western medicine just relieves the symptoms for some time" (PID 057). Another THP stated: "They come with side effects" (PID 085). Another cast doubt on efficacy of modern anti-breast cancer medicines and stated as follows: "I think those drugs don't work because those patients keep using herbal medicine" (PID 050).

THPs reported advertising on radio (n=32, 26.9%), vending in buses (n=27, 22.7%) and advertising on television (n=21, 17.6%) as means through which breast cancer patients came to know about their services. Others means of access to THP services are indicated in Table 2.

Medicinal Plants for Treatment of Breast Cancer by THPs

We documented 30 plants used to treat breast cancer by traditional health practitioners in Kampala, Wakiso and Mukono. The plants were distributed over 30 genera and 23 families; predominant families were Asteraceae, Apocynaceae, Euphorbiaceae, Fabaceae, Lamiaceae and Rutaceae. The families Annonaceae (n=24, 20.2%), Vitaceae (n=19, 16%) and Euphorbiaceae (n=11, 9.2%) contributed majority of the species. The most known plants in folk use against breast cancer were *Annona muricata* L. (Annonaceae), *Rhoicissus* tridentata (L.f.) Wild and R.B.Drumm (Vitaceae), *Erythrococca bongensis* Pax (Euphorbiaceae), *Ficus sp* (Moraceae) and *Cannabis sativa* L (Cannabaceae) with PRK values of 20.7%, 15.97%, 9.24%, 8.41% and 6.72% respectfully. Other top mentioned plants were *Ipomoea wightii* (Wall.) Choisy, *Erythrina abyssinica* DC, *Leucas martinicensis* (Jacq.) R.Br., *Abelmoschus esculentus* (L.) Moench and *Zanthoxylum chalybeum* Engl.

We found an informant consensus factor of 0.75 based on the 119 user reports on breast cancer for the 30 plants documented in the study area. *Annona muricata* L. had the highest number of user reports on breast cancer. The plants were also used to treat diseases other than breast cancer, as indicated in Table 3.

Fidelity Levels of Medicinal Plants Cited for Treatment of Breast Cancer by THPs

For the 30 cited plant species, a fidelity level was calculated to quantify their importance in treating breast cancer. *Ficus sp* had the highest fidelity level, 77%, followed by *Annona muricata* L. (62%) and *Leucas martinicensis* (Jacq.) R.Br.

Table 2 How Breast Cancer Patients Come to Know About Services of THPs in Uganda

Means by Which THP Services are Known by Patients	Frequency	Percent
Vending in buses	33	27.7
Advertising on radio	32	26.9
Advertising on television	21	17.6
Referral from past customers	17	14.3
Advertising in newspapers	8	6.7
Marketing agents	6	5.0
Referral by other traditional medicine practitioners	1	0.8
Vending in markets	1	0.8
Total	119	100.0

Table 3 Medicinal Plants Used to Treat Breast Cancer by Traditional Health Practitioners in Central Uganda

Family, Scientific Name	Nur[a] n=119	Voc. No[b]	PRK[c] (%)	Local Name/ Dialect[d]	Part Used[e]	Life Form[f]	Status[g]	Preparation and Administration of Breast Cancer Treatment	Other Conditions Treated by Mentioned Medicinal Plant/User Report
Annonaceae									
Annona muricata L*.	24	LS 001; LS 012	20.17	Ekitaferi (Lug); Soursop (Eng.)	Fr/Sd/ L	T	W	Decoction drunk	Diabetes (Nur=7), head and neck cancer (Nur=8)
Apiaceae									
Steganotaenia araliacea Hochst	1	LS 008	0.84	Kinulaŋombe/ Kimulyangimbe (Lug); Kibundubundu/ Ndujule (Lus)	L/R	T	W	Decoction drunk	Hemorrhoids (Nur=1)
Apocynaceae									
Mondia whitei (Hook.f.) Skeels;	1	LS. 011	0.84	Omulondo (Lug); Kimukombe (Gishu)	R	H	W	Decoction drunk	Erectile dysfunction (Nur=1), appetite (Nur=1), immune booster (Nur=1)
Catharanthus roseus (L) G.Don	2	LS 015	1.64	Yosefu ne maria (Runy/Ruk); Madagascar periwinkle (Eng)	L/Fl	H	W	Decoction drunk	Worms (Nur=2), hypertension (Nur=2), ulcers (Nur=2), diabetes (Nur=2), cancer (Nur=2)
Asteraceae									
Crassocephalum vitellinum (Benth.) S. Moore	1	LS 016	0.84	Esunuunu (Runy/ Ruk); Ekitonto (Lug)	Fl	H	Fm	Decoction drunk	Syphilis (Nur=1), diabetes (Nur=1), candidiasis (Nur=1), diarrhoea (Nur=1), headache (Nur=1), fever (Nur=1), ghonorrhea (Nur=1)
Vernonia amygdalina Dell.	1	LS 009	0.84	Omululuza (Lug)	L	S	W	Decoction drunk	Malaria (Nur=1), diarrhea (Nur=1), stomach ache (Nur=1), Covid-19 (Nur =1)
Balanites aegyptiaca (L.) Delile	1	LS 027	0.84	Mutete (Run); Liggwa limu(Lug)	L/R/B	T	W	Decoction drunk	Diabetes mellitus (Nur=1), measles (Nur=1), diarrhea (Nur=1), Flu (Nur=1), uterine fibroids (Nur=1)
Canellaceae									
Warburgia ugandensis Sprague	1	LS 002	0.84	Abasi (Lug)	B/L	T	W	Decoction drunk	Measles (Nur=1), cough (Nur=1), syphilis (Nur=1), aphrodisiac (Nur =1)
Cannabaceae									
Cannabis sativa L.	8	LS 021	6.72	Njaye /Njaga (Lug)	L/Fl/F	T	C	Decoction drunk	Measles (Nur=3), body pain (Nur=1), diarrhea (Nur=5), syphilis (Nur=4)
Caricaceae									
Carica papaya L.	1	LS 017	0.84	Papaali (Lug); Pawpaw (Eng)	L	H	SW	Decoction drunk	Intestinal worms (Nur=1), migraine (Nur=1), dyspepsia (Nur=1), snake bites (Nur=1), ulcers (Nur=1), cough (Nur=1), impotence (Nur=1)
Convolvulaceae									
Ipomoea wightii (Wall.) Choisy	7	LS 028	5.88	Ekihububa (Ruk)	L	H	W	Decoction drunk	Cough (Nur=4), leprosy (Nur=3), stomach ache (Nur=7)
Euphorbiaceae									
Euphorbia tirucalli L.	1	LS 005	0.84	Nkoni (Lug); Naked lady (Eng)	B	T	W	Decoction drunk	Snake bites (Nur=1), pimples (Nur=1), intestinal worms (Nur=1), warts (Nur=1)

(*Continued*)

Table 3 (Continued).

Family, Scientific Name	Nur[a] n=119	Voc. No[b]	PRK[c] (%)	Local Name/ Dialect[d]	Part Used[e]	Life Form[f]	Status[g]	Preparation and Administration of Breast Cancer Treatment	Other Conditions Treated by Mentioned Medicinal Plant/User Report
Erythrococca bongensis Pax.	11	LS 026	9.24	Omugoshora (Ruk)	L	T/H	W	Decoction drunk and residue rubbed on the paining area	Cough (Nur=5), diarrhoea (Nur=6), tonsilitis (Nur=9), hemorrhoids (Nur=4), Tape worms (Nur=5), East coast fever (Nur=6)
Fabaceae									
Albizia coriaria Oliv.	2	LS 007	1.68	Omugavu (Lug); Ayekayek (Luo)	B	T	W	Decoction drunk	Snake bites (Nur=1), diarrhea (Nur=2), syphilis (Nur=1), cough (Nur=2)
Erythrina abyssinica DC*.	5	LS 004, LS 032	4.20	Ejirikiti (Lug); Uganda coral (Eng)	B/L	T/S	W	Decoction drunk/ Residue applied on breast	Malaria (n=4), toothache (n=2), dysentery (3), syphilis (n=1), Skin infections (4)
Lamiaceae									
Leucas martinicensis (Jacq.) R.Br.	4	LS 010	3.36	Mbumbula (Run); Ekiyashura(Ruk)	L	H	W	Infusion drunk and residue applied on affected breast	Diarrhoea (gur=1), rheumatism (Nur=1), migraine headache (Nur=1)
Plectranthus hadiensis (Forssk.) Schweinf. Ex Sprenger;	1	LS 025	0.84	Kibwankulata (Lug)	L	H	W	Decoction drunk	Syphilis (Nur=1), Gonorrhea (Nur=1), diarrhea (Nur=1), fibroids (Nur=1), typhoid fever (Nur=1)
Liliaceae									
Allium sativum L.	1	LS 020	0.84	Katunguluccumu (lug)	Bu	H	C	Decoction drunk	Athletes feet (Nur=1), high cholesterol levels (Nur=1), Convulsions (n=1)
Lythraceae									
Punica granatum L.	1	LS 014	0.84	Nkomamawanga (Lug); Pomegranate (Eng.)	F	T/S	C	Decoction drunk	Cough (Nur=1),tapeworms (Nur=1), urinary tract infections (Nur=1)
Malvaceae									
Abelmoschus esculentus (L.) Moench	4	LS 022	3.36	Otigo(Lang), Bamia (Lus); Okra (Eng))	Sd	H	C	Decoction drunk	Weight loss (n=3), hypertension (n=2), gonorrhea (n=2)
Moraceae									
Ficus sp.	10	LS 031	8.41	Muwo (Lug)	B	T	W	Decoction drunk	Malaria (Nur=3)
Myricaceae									
Morella kandtiana (Engl.) Verdc. and Polhill	1	LS 023	0.84	Nkikimbo (Lug)	R/L	S	W	Decoction drunk	Fallopian tube blockage (Nur=1), anemia (Nur=1), HIV/AIDS (Nur=1), flu (Nur=1)
Pedaliaceae									
Sesamum calycinum subsp. Angustifolium (Oliv.) Ihlenf. and Seidenst;	1	LS 024	0.84	Lutungotungo (Lug)	L	H	W	Decoction drunk	Erectile dysfunction (Nur=1), diarrhea (Nur=1), vaginal dryness (Nur=1)
Plantaginaceae									
Plantago palmata Hook.f.	2	LS 013	1.68	Oruhigura (Ruk)	L	H	W	Decoction drunk / paste applied on breast	Diarrhea (Nur=1), intestinal worms (Nur=2), burns (Nur=1), joint pains (Nur=1)

(*Continued*)

Table 3 (Continued).

Family, Scientific Name	Nur[a] n=119	Voc. No[b]	PRK[c] (%)	Local Name/ Dialect[d]	Part Used[e]	Life Form[f]	Status[g]	Preparation and Administration of Breast Cancer Treatment	Other Conditions Treated by Mentioned Medicinal Plant/User Report
Polygalaceae									
Securidaca longipedunculata Fresen.	1	LS 018	0.84	Omukondwe (Lug);; Violet tree (Eng)	L	T	W	Decoction drunk	Syphilis (Nur=1), diarrhea (Nur=1), ulcers (Nur=1)
Polypodiaceae									
Microgramma sp	1	LS 029	0.84	Kukumba (Lug)	R/L	H	W/C	Decoction drunk	HIV/AIDS (Nur=1), anemia (Nur=1), flu (Nur=1)
Rosaceae									
Rubus apetalus Poir	1	LS 030	0.84	Encherere (Runy), Enkenene (Lug)	L/Fl	H	C	Paste applied on breast	Boosts immunity (Nur=1), cleanses the body of toxins (Nur=1)
Rutaceae									
Toddalia asiatica (L.) Lam.	1	LS 019	0.84	Kawule (Lug); Wait-a-bit thorn (Eng.)	R/L/B	S	W	Decoction drunk	Diabetes (Nur=1), menstrual cramps (Nur=1), snake bites (Nur=1)
Zanthoxylum chalybeum Engl.	4	LS 006	3.361	Ntaleyedungu(Lug); Mitala irundu (Soga); Outiku (Lugb)	R/L/B	T	W	Decoction drunk	Wounds (Nur=3), ulcers (Nur=3), malaria (Nur=4), sickle cell anaemia (Nur=4)
Vitaceae									
Rhoicissus tridentata (L.f.) Wild & R.B. Drumm.	19	LS 003	15.97	Omumara (Ruk)	L/Fr	S	W/C	Decoction drunk and residue applied on paining area	Labour induction (Nur=8), infertility (Nur=10)

Abbreviations: [a]Nur, Number of user reports, ie frequency of citations by the THPs interviewed; [b]Voc. No, Collector's/voucher number assigned by the collector in the field when collecting data; [c]PRK, Percentage of respondents who had knowledge regarding use of the mentioned species in the treatment of breast cancer; [d]Lug, Luganda; Ruk, Rukiga; Runy, Runyankore, Runy/Ruk, Runyankore/Rukiga; Lugb, Lugbara; Run, Runyoro; Lus, Lusoga; Lang, Lango; [e]L, Leaf; B, Bark; R, Root; Fr, Fruit; Fl, Flower; Sd, Seed; [f]H, herb; S, shrub; T, tree; [g]C, cultivated; SW, semi-wild; W, wild.

(57%). *Rhoicissus* tridentata (L.f) Wild & R.B.Drumm and *Steganotaenia araliacea* Hochst had similar fidelity levels, of 51% and 50%, respectively. High fidelity levels for these species point to their outstanding preference for treating breast cancer by THPs (Table 4).

Preferred Medicinal Plant for Breast Cancer Treatment

Annona muricata was highly ranked and regarded the most important in the treatment of breast cancer by the THPs. Table 5 shows rankings of ten most important plant species according to the key informants, together with scores assigned by each informant.

Direct Matrix Ranking

DMR results showed that all ten preferred plant species for treatment of breast cancer by THPs have a variety of other non-medicinal uses. *Zanthoxylum chalybeum* Engl was ranked the highest multipurpose species among the preferred plants for breast cancer treatment by THPs in Central Uganda. Other species utilized for food, construction, fodder, fuel/ fire wood beside their medicinal value were *Erythrina abyssinica* Lam Ex Dc, *Erythrococca bongensis, Annona muricata* and *Ipomoea wightii* (Table 6).

Table 4 Fidelity Levels of Medicinal Plants Used in Breast Cancer Treatment by THPs in Central Uganda

Plant Species	Ip	Iu	FL %
Ficus sp	10	13	77
Annona muricata L.;	24	39	62
Leucas martinicensis (Jacq.) R.Br.	4	7	57
Rhoicissus tridentata (L.f) Wild&R.B.Drumm.	19	37	51
Steganotaenia araliacea Hochst	1	2	50
Cannabis sativa L.	8	21	38
Abelmoschus esculentus (L.) Moench	4	11	36
Ipomoea wightii (Wall.) Choisy	7	21	33
Rubus apetalus Poir	1	3	33
Plantago palmata Hook f.	2	7	29
Erythrina abyssinica DC.	5	19	26
Albizia coriaria Oliv.	2	8	25
Mondia whitei (Hook f.) Skeels	1	4	25
Allium sativum L.	1	4	25
Punica granatum L.	1	4	25
Sesamum calycinum subsp. Angustifolium (Oliv.) Ihlenf. and Seidenst	1	4	25
Securidaca longipedunculata Fresen.	1	4	25
Microgramma sp	1	4	25
Toddalia asiatica (L.) Lam.	1	4	25
Erythrococca bongensis Pax.	11	45	24
Zanthoxylum chalybeum Engl.	3	18	22
Vernonia amygdalina Dell.	1	5	20
Warburgia ugandensis Sprague	1	5	20
Euphorbia tirucalli L.	1	5	20
Morella kandtiana (Engl.) Verdc. and Polhill	1	5	20
Catharanthus roseus (L) G.Don	2	12	17
Balanites aegyptiaca (L) Delile	1	6	17
Plectranthus hadiensis (Forssk.) Schweinf. Ex Sprenger;	1	6	17
Crassocephalum vitellinum (Benth.). S Moore	1	8	13
Carica papaya L.	1	8	13

Abbreviations: Ip, Number of informants who suggested use of the species for treatment of breast cancer; Iu, Total number of informants who mentioned the plant for any use; FL, Fidelity level.

Table 5 Preference Ranking of Ten Medicinal Plants Used to Treat Breast Cancer

Medicinal Plant	Key Respondents (R_1 –R_{12})												Total Score/120	Rank
	R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9	R_{10}	R_{11}	R_{12}		
Annona muricata L.	9	8	10	10	9	9	8	9	7	9	6	10	104	1st
Ficus Sp	8	10	8	9	9	8	8	7	10	6	10	8	100	2nd
Cannabis sativa L.	6	7	8	10	9	8	7	10	8	10	7	9	99	3rd
Erythrina abyssinica DC.	8	8	6	7	8	7	8	10	5	8	10	8	93	4th
Leucas martinicensis R. Br.	10	10	8	10	7	8	9	6	6	4	8	5	91	5th
Zanthoxylum chalybeum Engl.	8	9	8	7	8	9	9	6	5	8	7	5	89	6th
Erythrococca bongensis Pax.	4	9	9	8	7	6	5	7	8	10	8	7	88	7th
Rhoicissus tridentata (L.f) Wild & R. B.Drumm.	7	10	9	4	8	7	10	6	5	8	6	7	87	8th
Abelmoschus esculentus (L.) Moench	10	7	8	6	6	8	2	6	8	5	8	4	78	9th
Ipomoea wightii (Wall). Choisy	6	5	9	4	6	5	8	5	7	6	5	5	71	10th

Notes: Table scores indicate ranks given to medicinal plants based on their efficacy. Higher number (10) given for the medicinal plant which informants thought was most effective in treating breast cancer and the lowest number (1) for the least effective plant.

Table 6 Direct Matrix Ranking of Preferred Medicinal Plants for Breast Cancer Treatment in Uganda

Medicinal Plant	Score Out of 5 /Rank per Use Category					Total Score/25	Rank
	Use Category Scores						
	Food	Construction	Fodder/ Foliage	Fuel/ Firewood	Medicinal Value		
Zanthoxylum chalybeum Engl.	5	4	4	5	5	23	1st
Erythrina abyssinica DC.	3	3	5	4	5	20	2nd
Erythrococca bongensis Pax.	4	2	4	4	5	19	3rd
Annona muricata L.	3	1	4	3	5	16	4th
Ipomoea wightii (Wall.) Choisy	3	2	3	2	5	15	5th
Abelmoschus eschulentus (L.) Moench	4	0	3	3	4	14	6th
Rhoicissus tridentata (L.f)R.B. Drumm.	4	0	4	0	5	13	7th
Ficus sp	0	4	0	3	5	12	8th
Cannabis sativa L.	2	0	2	2	5	11	9th
Leucas martinicensis R. Br.	3	0	2	0	5	10	10th

Notes: Scores are the stress degrees based on a scale of 0–5 where 5=best; 4=very good; 3=good; 2=less used; 1=least used; and 0=not used.

Life Forms, Management Status and Plant Parts

The most commonly used life forms were herbs (n=14, 47%) followed by trees (n=11, 37%) and shrubs (n=5, 16%). Majority of these plants occur in the wild (n=23, 72%). Only 25% of plants were cultivated and 3% were semi-wild in

their management status. The THPs mentioned the leaves (46%) as the most commonly used plant part in breast cancer treatment, followed by roots (13%), fruits (10%) and flowers (8%), while the rest were used occasionally.

Preparation and Administration of Herbal Remedies

THPs prepared herbal remedies mainly as decoctions (82%) and infusions (3%) that are administered orally. The residues of these preparations were applied on the affected breasts (9%). Some THPs (6%) prepared a paste.

Availability Status and Source of Plants

Most (94.1%) THPs reported that plants used to treat breast cancer were scarce, 5% indicated that the plants were rare and 2% did not know. Despite this, only 6% of THPs reported owning a medicinal garden and only 3.3% had plans to establish such a garden. More than half (52.1%) of THPs collected the plants from the wild source. Other sources of plants were markets (47.1%) and gardens (0.8%).

Discussion

Ethnobotanical surveys have been reported to help scientists identify plants whose medicinal properties may be useful in the development of new drugs for further research.[17] In this study, we conducted an ethnobotanical survey to document the existing knowledge and practices related to breast cancer recognition and treatment using medicinal plants by traditional health practitioners (THPs), commonly referred to as herbalists, in the management of breast cancer in the Central Ugandan districts of Kampala, Wakiso and Mukono.

THPs in Central Uganda recognized breast cancer by mainly symptoms of breast swelling and pain. Whereas these are some of the symptoms of breast cancer, they are not conclusive as other diseases such as mastitis can also cause these symptoms. In a Ghanaian study, traditional practitioners are reported to have identified cancers by symptoms of advanced disease such as masses that are visible, fungating lesions, ulceration and bleeding.[13] Diagnosis of breast cancer based on symptoms by THPs is not adequate. This can lead to misdiagnosis and wrong treatments given by THPs. There is a need to build capacity of THPs to be able to recognize all the common signs and symptoms of breast cancer in its early stage, as indicated in the established national cancer treatment guidelines, and refer the patients for proper diagnosis by oncologists. This will minimize the number of cases that present to hospitals in advanced stages of the disease and deaths that occur as a result of such advanced disease and wrong treatments given to patients.[27,28]

Majority of THPs in Central Uganda did not refer patients to biomedical laboratories to confirm diagnosis. In contrast and without specifying the type of cancer, cancer patient referral by THPs to biomedical facilities has been reported in Northern Uganda.[29] Non-referral by THPs in Central Uganda implies that they treated unconfirmed breast cancer, and this could account for reported high mortality attributed to breast cancer in Uganda. Studies indicate that THPs cannot properly define cancer.[30,31] Elsewhere, some THPs have wrongly defined cancer as having high cholesterol or abscess accumulation.[32] Furthermore, there are breast cancer molecular profiles like triple negative breast cancer and HER2 positive breast cancer that have been reported to be significant determinants of advanced stage diagnosis.[33] These cannot be diagnosed by simply looking at symptoms, as observed in this study. Therefore, THPs should be sensitized to refer patients to biomedical laboratories for proper diagnosis.

About half of the study participants reported changing to another herbal medicine for patients in case of treatment failure. Only a quarter of the THPs in the study referred the patients to a government health facility in case of treatment failure. This implies that THPs in Central Uganda are hesitant to refer patients to modern health workers. Accordingly, this results in patient delays and late diagnosis as herbalists keep on attempting to cure the breast cancer with different herbal medicines. In contrast, Australian herbalists are reported to be aware of the value of medical diagnosis and inter-referrals, are well informed about patient medications and initiate closer working relationships with the medical community.[34] The claims by some THPs that their herbal medicines had cured patients, though there was lack of documentation in place to back up these claims, and fear of losing the patients to modern health care facilities could account for the hesitancy in referring patients.

THPs denied ever adding western medicine to their herbal products for breast cancer in order to make them stronger. This means that THPs treating breast cancer are aware of dangers of adulteration or feared disclosing the practice of

adulteration. However, the possibility of adulteration should not be ignored because some THPs reported buying western drugs for patients in case of treatment failure. Accordingly, it can be deduced that THPs can access some of the anti-breast cancer medicines on the market. Studies have shown that some THPs tend to adulterate their herbal products to sustain the claims at expense of patient safety occasioned by compromise in quality and efficacy of products.[35–40] Adulteration of herbal products can occur during production or at point of sale, and is in violation of acceptable standards and is a serious standardization problem which affects the quality and reliability of these products.[41] There is a need to employ analytical chemistry methods and DNA meta barcoding to rule out adulteration of herbal products supplied by THPs.[42,43]

When asked about how breast cancer patients came to know about their services, THPs reported vending in buses and advertising on radio and television as the main means. This implies that educational programs like breast cancer screening campaigns targeting breast cancer patients and the general population can be passed on through these channels. Furthermore, the regulatory framework in regard to herbal medicine promotion through advertising by THPs needs to be strengthened. This will ensure delivery of complete, true and unbiased information to the public in regard to herbal medicines for breast cancer treatment and national prevention and treatment guidelines for not only breast cancer but also other health conditions.

THPs in the study area reported using 30 plants belonging to 23 families to treat breast cancer in Central Uganda. Predominant families were *Asteraceae*, *Apocynaceae*, *Euphorbiaceae*, *Fabaceae*, *Lamiaceae* and *Rutaceae*. The ten most commonly mentioned plants were *Annona muricata L., Rhoicissus* tridentata (L.f.) Wild & R.B.Drumm, *Erythrococca bongensis Pax*, *Ficus sp, Cannabis sativa L*., *Ipomoea* wightii (Wall.) Choisy, *Erythrina abyssinica* DC., *Leucas martinicensis* (Jacq.) R.Br., *Abelmoschus esculentus* (L.) Moench and *Zanthoxylum chalybeum* Engl. In contrast, 25 plant species belonging to 17 families have been identified for management of breast cancer by traditional medical practitioners in North East Nigeria.[44] This finding confirms folk use of medicinal plants in traditional treatment of breast cancer in different countries, including Uganda.

Furthermore, whereas family Asteraceae had highest number of plant species reported to treat breast cancer, the mentioned plants in the study had low user reports on breast cancer by the THPs. This means one was more likely to find a plant species in the family Asteraceae; however, THPs did not frequently use plants in this family against breast cancer as compared to plant species from the other plant families. Asteraceae is one of the most abundant plant families, with more than 23,600 species of plants spread across 1620 genera and 13 subfamilies that occupy all continents except Antarctica.[45,46] Accordingly, occurrence of plant species from Asteraceae in the study area was more likely. Low use reports of plants from the family Asteraceae against breast cancer could relate to the effectiveness of plants or scanty documentation of plants within the study area as regards use of these plants for breast cancer. There is a need to explore further the reasons for the observed low use reports of plant species from Asteraceae family for folk treatment of breast cancer. Previous works indicate plant extracts of some species like *Senecio graveolens* Wedd., *Ageratum conyzoides* L., and others belonging to family Asteraceae exhibit significant anti-breast cancer activity.[47,48] Therefore Asteraceae should be investigated further to document plants with potential anti-breast cancer activities.

An informant consensus factor (IFC) is one of the quantitative indices used to express the benefits, importance and coverage of ethnomedicine.[26] In this study, an IFC on breast cancer of 0.75 was observed. This took into account the total number of use reports for breast cancer and total number of species of plants used to treat breast cancer. In contrast, an IFC of 0.96 has been reported in West Bank Palestine.[49] A high IFC close to 1, the maximum IFC value, means the mentioned plants in the study are being used extensively within the community and are thus important medicinal plants that can be considered for future pharmacological investigation.

Additionally, the high fidelity levels obtained and preference ranks assigned by THPs indicated that *Annona muricata L*., *Ficus sp*, *Cannabis sativa L*, *Erythrina abyssinica Dc and Leucas martinicensis R. Br* are considered the most important plants by THPs in Central Uganda in treating breast cancer. *Ficus dawei* Hutch has previously been reported to be in folk use against breast cancer in Uganda, but quantitative ethnobotanical indices were not reported.[50] The other plants are being reported for the first time for breast cancer treatment in the study area. This calls for focusing research efforts on documenting medicinal plants used to treat specific cancers, as there exist more than 277 different types of cancer, with different aetiologies, risk factors, clinical courses and management approaches.[51–53]

Whereas *Annona muricata* L has been reported to contain annonaceous acetogenins (Annopentocin A-C, Annomuricin D and Annomuricin E) which account for its anti-breast cancer activity, *Ficus* sp, though having highest fidelity level and

ranked second in terms of preference by the THPs in this study, like many plants mentioned in folk treatment of breast cancer remains uninvestigated, hence the need to generate scientific evidence to justify their continued folk use.[54–57] Further research on the plants may lead to isolation of important lead compounds that can be developed into useful drugs for breast cancer treatment. Reports indicate that the anti-breast cancer activity of plants is attributed to presence of important phytochemical compounds, namely, alkaloids, flavonoids, coumarins, phenolic compounds and terpenoids, among some of which their chemical structures have been elucidated.[48,58,59] Additionally, there is a likelihood of phytochemical variation that could arise from changes in environmental factors, biophysical limits, part of plant used, extraction methods, age of the plant and other factors, and hence the need to standardize the herbal products made from these plants such that patients are not exposed to unsafe, poor quality and non-efficacious remedies which can worsen their quality of life.

Medicinal plants reported in the study have non-medicinal uses as well. These were used in determining the direct matrix rank (DMR) of each of the preferred plants. *Zanthoxylum chalybeum* Engl had the highest DMR, calculated based on use category scores assigned by the THPs. This was followed by *Erythrina abyssinica* DC, *Erythrococca bongensis* Pax, *Annona muricata* L. and *Ipomea wightii* (Wall.) Choisy. The high DMRs of these plants point to the stress placed on them arising from their multipurpose nature in relation to their use and management practices within the community.[23] This was the first time DMRs were determined in Uganda for the mentioned plants. Given the high DMR values, these plants are likely to be harvested more by THPs and other community members. There is a need to protect such plants, their natural habitats and promote sustainable use and conservation, in order to not threaten their existence. Such plants may help to offer alternative and complementary treatments for breast cancer patients, based on the fact that conventional anti-cancer medicines are not affordable, the Covid-19 pandemic interrupted the healthcare system and presence of other perceived barriers to health seeking in Uganda.[60–62]

Limitations of the Study

Besides being time consuming to fill the questionnaires and analyse the data, respondents could have had a recall bias. Many of them had no records of patients treated and hence difficult to recall and verification of the responses difficult. In addition, the length of practice of each THP was not captured during data collection; the findings of this study are limited to Central Uganda and cannot be generalized. The study was cross sectional and data collected during covid-19 pandemic that interrupted in health services delivery due to lock downs.[60–62]

Conclusions

THPs in Central Uganda recognized breast cancer by symptoms. Medicinal plants applied in its folk treatment have been documented and the claims of cure by THPs merit further investigation. We underscored the need for documentation of such medicinal plant folk knowledge in the context of traditional diagnosis and management of breast cancer by the herbalists. Future works should focus on providing scientific validation of the documented plants in terms of chemical profiling, preclinical pharmacological testing against specific breast cancer cell lines and clinical evaluation. Promotion of good agricultural practices for sustainable utilization of the mentioned plants is warranted.

Ethics Approval and Informed Consent

The study was approved by Mbarara University Faculty of Medicine Research Committee (Ref DMS6), Gulu University Research and Ethics Committee (GUREC-016-19) and registered with the Uganda National Council of Science and Technology (HS405ES). Participants' informed consent included publication of anonymized responses.

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Disclosure

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