

**HERBAL AND ALTERNATIVE MEDICINE UTILIZATION IN TANZANIAN
ADULTS ADMITTED WITH HYPERTENSION-RELATED CONDITIONS**

A Thesis

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Master of Science

By

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ABSTRACT

Background: Sub-Saharan Africa has the highest age-adjusted prevalence of hypertension of any region in the world. Herbal and alternative medicine use is also common in this region. Little is known about the utilization of herbal and alternative medicines specifically for hypertension (HTN) among African adults, particularly among inpatients.

Objective: The aim of these studies was to determine the pattern and correlates of herbal and alternative medicine use in hypertensive patients in Africa. We also investigated whether herbal or alternative medicine use was associated with antihypertensive medication non-adherence.

Methods: We conducted 2 studies. The first was a prospective, cross-sectional study of 213 consecutive Tanzanian adults admitted to a Tanzanian zonal hospital with hypertension-related conditions. Factors associated with herbal and alternative medicine use and treatment adherence were examined using ordered logistic regression. The second was a systematic review of the literature to determine what is currently known and not known about herbal medicine use among hypertensive adults in Africa.

Results: Herbal medicines had been consumed by 161 (75.6%) of study subjects. Sixty-nine (27.7%) had consumed herbal medicines specifically for HTN and 52 (24.4%) had consumed herbs in the past one-month before admission. Thirty-eight (17.8%) reported having stopped allopathic medicines for herbs and 47 (22.1%) had used herbs with allopathic medicines. Education level ($p=0.007$), occupation ($p=0.002$), lack of medical insurance ($p=0.001$) and prior stroke ($p=0.008$) were all significantly associated with herbal

medicine use in the last month. Neither utilization of herbs nor other alternative therapies were significantly associated with recent medication non-adherence. Many patients reported using foods as herbal medication.

In the literature from sub-Saharan Africa, the prevalence of THM use was 25-65% (average 38.6%). THM was the most common type of complementary and alternative medicines used by patients (86.7%-96.6%). Among THM users, 47.5% concomitantly used both allopathic medicine and THMs. Increased age ($p < 0.001$), male sex (RR 2.58), belief in a supernatural cause of hypertension (RR 2.11), and family history of hypertension (OR 1.78) were positively associated with THM use while belief that hypertension is preventable was negatively associated with a THM use (OR 0.57).

Conclusion: Herbal and alternative medicine use is common among Tanzanian men and women admitted with hypertension-related conditions and is associated with lower socio-economic status. Many adults reported stopping allopathic medicines to take herbs in the past. These studies highlight the need for healthcare workers in Africa to discuss herbal and alternative medicine use with all adults with hypertension and to do so in a way that promotes open dialogue about proper and improper utilization patterns.

BIOGRAPHICAL SKETCH

Anthony (Tony) Liwa was born in Tanzania in November 27, 1974. He obtained his medical degree from the Hubert Kairuki Memorial University (HKMU) in 2004. In December 2004 he joined Bugando Medical Centre (BMC) for a one year Internship program. After the Internship, he joined the then Bugando University College of Health and Allied Sciences (BUCHS), which later became Weill Bugando School of Medicine and Catholic University of Health and Allied Sciences (CUHAS).

He worked as a Tutorial Assistant in the Department of Clinical Pharmacology. In 2007 he went for graduate studies in the University of Stellenbosch, Cape Town, South Africa where he received a Bachelors degree with honors (BScMedSchHonns) and Masters of Medical Sciences in Pharmacology.

As part of his fellowship in Masters of Science degree in Clinical Epidemiology and Health Services Research, he has been studying the patient behavior towards the treatment of hypertension, specifically on the use of herbal and alternative medicine.

He is currently working in the department as an assistant lecture and he is a PhD (Medical Sciences) candidate at University of Calgary, Alberta, Canada.

To Hyasinta, Mary and Cuthbert

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CHAPTER 1

MANUSCRIPT 1

TITLE PAGE

**Herbal and alternative medicine utilization in Tanzanian adults admitted
with hypertension-related conditions**

ABSTRACT

Background: Sub-Saharan Africa has the highest age-adjusted prevalence of hypertension of any region in the world. Herbal and alternative medicine use is also common in this region. Little is known about the utilization of herbal and alternative medicines specifically for hypertension (HTN) among African adults, particularly among inpatients.

Objective: The aim of this study was to determine the pattern and correlates of herbal and alternative medicine use in patients admitted to a Tanzanian hospital due to HTN. We also investigated whether herbal or alternative medicine use was associated with antihypertensive medication non-adherence.

Methods: This was a prospective, cross-sectional study of 213 consecutive Tanzanian adults admitted to a Tanzanian zonal hospital with hypertension-related conditions. Factors associated with herbal and alternative medicine use and treatment adherence were examined using ordered logistic regression.

Results: Herbal medicines had been consumed by 161 (75.6%) of study subjects. Sixty-nine (27.7%) had consumed herbal medicines specifically for HTN and 52 (24.4%) had consumed herbs in the past one-month before admission. Thirty-eight (17.8%) reported having stopped allopathic medicines for herbs and 47 (22.1%) had used herbs with allopathic medicines. Education

level ($p=0.007$), occupation ($p=0.002$), lack of medical insurance ($p=0.001$) and prior stroke ($p=0.008$) were all significantly associated with herbal medicine use in the last month. Neither utilization of herbs nor other alternative therapies were significantly associated with recent medication non-adherence. Many patients reported using foods as herbal medication.

Conclusion: Herbal and alternative medicine use is common among Tanzanian men and women admitted with hypertension-related conditions and is associated with lower socio-economic status. Many adults reported stopping allopathic medicines to take herbs in the past. This study is highlighting the need for healthcare workers in Africa to discuss herbal and alternative medicine use with all adults with hypertension and to do so in a way that promotes open dialogue about proper and improper utilization patterns.

MANUSCRIPT TEXT

INTRODUCTION

The burden of hypertension (HTN) is rapidly increasing in sub-Saharan Africa (SSA) (**Twagirumukiza et al., 2011**). The age-standardized prevalence of HTN in SSA is the highest of any region in the world (**WHO Global Brief on HTN, 2013**). In one recent study, the age-standardized prevalence of hypertension among Tanzania adults was >35% in Tanzania (**Hendricks et al., 2014**). Tanzania has also been ranked among the lowest rates of BP control in SSA (**Kayima et al., 2013**). On the medical wards of our own hospital, hypertension is the second leading cause of admissions, accounting for nearly 20% of hospital admissions, in-hospital deaths and hospital days (**Peck et al., 2013**).

In our own, recent meta-analysis, we described the high prevalence of herbal and alternative medicine use among adults with hypertension in SSA. Herbal and alternative medicine use ranged from 25-65% in four studies (one in South Africa and three studies in Nigeria). In these studies, many study subjects were found to use herbal medicines concurrently with allopathic medicine (**Liwa et al., 2014**). Although many herbs can be harmless, some may potentially raise blood pressure or interact with allopathic medicines for hypertension (**Vora and Mansoor, 2005; Izzo and Ernst 2009**). Whether herbal medicines were used specifically for hypertension, which herbal medicines were used specifically for hypertension and the associations

between herbal medicine use for hypertension and adherence have not yet been reported.

Therefore, we conducted this cross-sectional study to test the hypothesis that herbal and alternative therapy use is common among Tanzanians admitted with hypertension-related diseases and is associated with non-adherence to allopathic medicines. The objectives of this study were to determine: 1) the prevalence and pattern of herbal and alternative medicine utilization among adult hypertensive inpatients; 2) factors associated with herbal medicine use for hypertension; and 3) if herbal medicine use for hypertension were associated with current non-adherence to allopathic medicines

METHODS

Study Site

This cross-sectional study was prospectively conducted between April 1 and October 1, 2014 in the adult medical wards of Bugando Medical Centre (BMC). BMC is a zonal hospital that serves the Lake Zone of northwestern Tanzania.

Study Population

The subjects for this study were consecutively selected from patients admitted at medical wards of Bugando hospital. Inclusion criteria included a diagnosis of

hypertension and age >18 years. Exclusion criteria included: altered mental status and planned discharge within 24 hours, both of which would make private patient interview impossible. Patients who met inclusion criteria were approached and invited to participate in the study.

Data Collection

A structured researcher-administered questionnaire with both closed ended and open-ended questions was used to collect data were from eligible patients. The questionnaire consisted of sections that assessed patient information such as age, gender, marital status, education level and duration of disease were obtained. Responses on patients' knowledge about hypertension disease, use of herbal and alternative medicine, reasons for herbal and alternative medicine use, sources of herbs and adherence to antihypertensive medications were obtained. Interviews were conducted by the primary investigator, took place in a private space on the medical wards and lasted approximately 15 minutes.

Adherence to anti-hypertensive medications was measured using a Morisky Medication Adherence Scale, the 4-item scale (MMAS-4). The MMAS-4 is a commonly used adherence-screening tool. It is composed of 4 yes/no questions about past medication use patterns and is thus quick and simple to use during drug history interviews. MMAS-4 was published by Dr. Morisky his

colleagues in 1986, and was first validated in a study demonstrating an association between MMAS-4 score and long-term blood pressure control among hypertensive adults. (**Morisky *et al.*, 1986**). It has since been used in a number of studies of hypertension in United States of America, New Zealand and Germany (**Tan *et al.*, 2014; Shalansky *et al.*, 2004**).

Data Analysis

Data were entered into Microsoft Excel 2010 software (Microsoft Corporation, Redmond, VA) and analyzed using STATA version 12 (StataCorp, College Station, Texas). The primary outcome was herb use in the past month before admission for hypertension. Secondary outcomes included medication adherence and other variables related to alternative and complementary medicine utilization. Categorical variables were described as proportions (percentiles) and continuous variables were described as medians [interquartile ranges]. To examine potential factors associated with the current use of herbs, univariate and multivariate logistic regression was conducted. Factors associated with adherence to allopathic anti-hypertensive medications were explored using ordinal logistic regression. The Brant test was used to assess the proportional odds assumption. $P < 0.05$ was considered significant. Since this was an exploratory analysis, we did not make any adjustment for multiple comparisons.

Ethical Issues

Ethical clearance for the study was obtained from the BMC Research Ethics Committee in Tanzania and the Institutional Review Board of Weill Cornell Medical College. All interviewed patients gave written informed consent. Consent to participate in this study did not affect the clinical care of the patients.

RESULTS

Enrollment

Between April 1 and October, a total of 1, 377 adults were admitted to the medical wards of Bugando Medical Centre with hypertension-related diseases. Of these, a total of 164 patients were excluded for the following reasons: 147 were either unable to give a reliable history due to altered mental status (mostly due to stroke, dementia or hypertensive encephalopathy), 9 decline to participate in the study and 8 were discharged within 24 hours (before interviews could occur). The remaining 213 adults consented and were enrolled.

Demographic characteristics

Among the 213 adult inpatients enrolled in our study, approximately half were female 112 (52.6%), the median age was 56 years [45-67], and 121 (56.8%) had not completed a primary school education. Most study subjects (162 (76.1%)) were aware of their hypertension before admission but 51 (23.9%) were newly diagnosed to have hypertension during the current hospital admission. Most (159 (74.7%)) had a previous history of using antihypertensive medications but only 103 (48.4%) were taking medications in the month before being admitted to the hospital. Of the 159 study subjects who reported prior use of antihypertensive medications, 35 (22.0%) reported high adherence, 38 (23.9%) reported medium adherent and 86 (54.1%) reported low adherence to antihypertensive medications. The average years of patient illness was 5 years [2-10]. Most (173 (81.2)) had at least 1 co-morbid condition: 54 (24.5%) had heart failure, 39 (18.4) had diabetes mellitus, 24 (11.3%) had kidney disease and 20 (9.4%) reported a history of stroke. The characteristics of the study population are presented in Table 1.1.

Table 1.1 Socio-demographic and clinical characteristics of 213 consecutive adults admitted to Bugando Medical Centre with hypertension-related diseases.

Variable	Value
Proportion (%)	(n=213)
Median [IQR]	
Female gender	112(52.6)
Age (years)	56[45-67]
Education level	
Not completed primary school	58(27.2)
Completed primary school	121(56.8)
Completed secondary school	34(16.0)
Occupation	
Farmer	78(36.6)
Small scale business	54(25.4)
Professional, Business, or Student	81(38.0)
Health Insurance	70(32.9)
Hypertension diagnosis	
New diagnosis	51(23.9)
Previously diagnosed	162(76.1)
Medication adherence (MMAS-4 Score)*	
High (0)	35(22.0)
Medium (1-2)	38(23.9)
Low (3-4)	86(54.1)

Systolic Blood Pressure	160[150-180]
Diastolic Blood Pressure	100[90-120]
Is hypertension curable (or is it a lifelong condition)?	
No (Hypertension is a lifelong condition)	95(44.6)
Yes (Hypertension is curable)	118(55.4)
Is there anything that can be done to prevent hypertension?	
Yes	54(25.4)
No	159(74.7)
Years since hypertension diagnosis	5[2-10]
Place of diagnosis	
Hospital	194(91.1)
Other	19(8.9)
History of hypertensive medication	159(74.7)
Currently on hypertensive medication	103(48.4)
Prevalence of co-morbid conditions	173(81.2)
Heart failure	54(24.5)
Diabetes mellitus	39(18.4)
Kidney disease	24(11.3)
Stroke	20(9.4)

*MMAS-4 refers to Morisky Medication Adherence Scale, a 4-Item scale.

Outcomes

Of the 213 Tanzanian adults inpatients with hypertension that participated in the study, 52 (24.4%) reported using herbs in the month before admission. A total of 161 (75.6%) reported using THM at some point in their life and 69 (27.7%) reported to have consumed herbal and other alternative remedies specifically to manage hypertension at some point in their life. Thirty-eight (17.8%) of the respondents admitted to have stopped allopathic medications for herbs and 47 (22.1%) reported to the concurrent use of herbs and allopathic medications. Only 20 (9.4%) reported having been asked about alternative and herbal medicine use by their admitting doctor. Alternative and herbal medicine use did not differ significantly by gender. The other outcomes related to the utilization of herbal, alternative and complementary medicine are presented in detail in Table 1.2.

Table 1.2 Alternative and herbal medicine utilization patterns in 213 consecutive adults admitted to Bugando Medical Centre with hypertension-related diseases (total and by gender).

Outcome	Total	Female	Male	p-value
Proportion (%)	(n=213)	(n=112)	(n=101)	
Median [IQR]				
Used Herbs in last month *	52(24.4)	26(23.2)	26(25.7)	0.67
Ever attended a traditional healer for any reason	144(67.6)	77(68.8)	67(66.3)	0.71
Ever attended traditional healer for hypertension (HTN)	59(27.7)	29(25.9)	30(29.7)	0.54
Ever used herbs for any reason	161(75.6)	35(31.3)	74(73.3)	0.46
Ever used herbs for hypertension	69(27.7)	38(33.9)	31(30.7)	0.61
Practiced religious healing for hypertension	30(14.1)	17(15.2)	13(12.9)	0.63
Using herbs in hospital	10(4.7)	5(5.0)	5(4.5)	0.87
Stopped allopathic medicines for herbs	38(17.8)	17(15.2)	21(20.8)	0.29
Used herbs with allopathic medicines	47(22.1)	28(25.0)	19(18.8)	0.28
Believes it is okay to use herbs with allopathic medicines	152(71.4)	76(67.9)	76(75.3)	0.24
Traditional healer have asked about allopathic medicines	20(9.4)	8(7.1)	12(11.9)	0.24
Doctors have asked about herbs	20(9.4)	11(9.8)	9(8.9)	0.82

*Primary study outcome.

Factors associated with herbal medicine use

Table 1.3 displays the results of our logistic regression analysis to determine factors associated with herbal medicine use for hypertension in the past month before admission. Variables significantly associated with herbal medicine use included: lower education level, occupation, knowledge regarding hypertension, lack of medical insurance and comorbid stroke. Patients with higher categories of education were less likely to consume herbs compared to their counterparts ($p < 0.007$; OR=0.49; CI 0.29-0.82). Professionals, businessman and government employees were also less likely to consume herbal and other alternative therapies compared to farmers ($p = 0.002$; OR=0.27; CI 0.11-0.61). Study subjects with medical insurance were also less likely to use herbal medicines ($p = 0.001$; OR=0.24; CI 0.10-0.57). Stroke as a co-morbid condition was also significantly associated with herbal medicine use ($p = 0.008$; OR=3.59; CI 1.40-9.21).

Table 1.3 Characteristics and factors associated with the current user of herbal medicine in comparison to non-herb user.

Variable	Herb user (n=52)	Herb non-users (n=161)	Odds ratio [95%CI]	p-value
Proportion (%)				
Median [IQR]				
Female gender	26(23.2)	86(76.8)	0.87[0.47-1.63]	0.67
Age category (years)				
≤ 45	13(21.7)	47(78.3)		
46-55	12(30.0)	28(7.0)	1.55[0.62-3.86]	
56-65	11(20.1)	43(79.6)	0.93[0.37-2.28]	
>65	16(27.1)	43(72.9)	1.35[0.58-3.12]	0.65
Education level				
Not completed primary school	21(36.2)	37(63.8)	0.49[0.29-0.82]	0.007
Completed primary school	27(22.3)	94(77.7)		
Completed secondary school	4(11.8)	30(88.2)		

Occupation

Farmer	25(32.1)	53(68.0)		
Small scale business	18(33.3)	36(66.7)	1.06[0.51-2.21]	
Professional, Business, or Student	9(11.1)	72(88.9)	0.27[0.11-0.61]	0.002
Health Insurance	7(10.0)	63(90.0)	0.24[0.10-0.57]	0.001
Hypertension (HTN) diagnosis				
New diagnosis	13(25.5)	38(74.5)		
Previously diagnosed	39(24.1)	123(75.9)	0.93[0.45-1.92]	0.84
Years of diagnosis				
≤1	16(32.0)	34(38.0)		
2-4	7(16.7)	35(83.3)	0.43[0.16-1.16]	
5-9	8(28.6)	20(71.4)	0.85[0.31-2.34]	
≥10	21(24.4)	72(77.4)	0.62[0.29-1.34]	0.34
Systolic Blood Pressure				
≤ 140	8(18.2)	36(81.8)		
141-160	17(27.9)	44(72.1)	1.74[0.67-4.50]	
161-180	16(29.6)	38(70.4)	1.89[0.72-4.97]	

> 180	11(20.4)	43(79.6)	1.15[0.42-3.17]	0.45
Currently on hypertensive medication	38(23.9)	121(76.1)	1.53 [0.81-2.89]	0.77
Is hypertension curable (or is it a lifelong condition)?				
No (Hypertension is a lifelong condition)	34(28.8)	84(71.2)		
Yes (Hypertension is curable)	18(19.0)	77(81.1)	0.58[0.30-1.11]	0.098
Is there anything that can be done to prevent hypertension?				
Yes	8(14.8)	46(85.2)	0.46[0.19-1.04]	0.06
No	44(27.7)	115(72.3)		
Place of diagnosis				
Hospital	47(24.2)	147(75.8)		
Other	5(26.3)	14(73.7)	1.12[0.38-3.27]	0.34
MMAS Question 1 (Ever forget to take medicines)	5(12.5)	35(87.5)	0.42[0.14-1.26]	0.12
MMAS Question 2 (Have problems remembering to take medicines)	5(14.3)	30(85.7)	0.54[0.18-1.63]	0.28

MMAS Question 3 (When feel better stops taking medicines)	12(21.8)	43(78.2)	1.21[0.46-3.18]	0.70
MMAS Question 4 (Stop taking medicines when feeling worse with medicines)	1(11.1)	8(88.9)	0.46[0.55-3.92]	0.44
Medication adherence (MMAS-4)[#] Score				0.85
High Adherence (0)	8(22.9)	27(77.1)	1.64[0.66-1.64]	
Medium Adherence (1-2)	9(23.7)	29(76.3)		
Low Adherence (3-4)	21(24.4)	65(75.6)		
Prevalence of co-morbid condition	44(25.4)	129(74.6)	1.36[0.59-3.18]	0.47
Individual co-morbid conditions				
Diabetes mellitus	9(23.1)	30(76.9)	0.9[0.40-2.10]	0.82
Kidney disease	7(29.2)	17(70.8)	1.32[0.51-3.38]	0.57
Stroke	10(50)	10(50)	3.60[1.40-9.21]	0.008
Heart failure	10(18.5)	44(81.5)	0.63[0.29-1.36]	0.24

[#]MMAS-

4 refers

to Morisky Medication Adherence Scale, 4-Item.

Variables associated with medication non-adherence

Table 1.4 displays our ordinal logistic regression analysis of factors associated with poor medication adherence. Higher education level was associated with better medication adherence ($p=0.04$; $OR=0.63$; $CI\ 0.40-0.99$ for lower adherence). Study subjects who knew that hypertension could not be cured with a short course of traditional or allopathic medicines also had better medication adherence ($p=0.001$; $OR=0.34$; $CI\ 0.18-0.63$ for low adherence). In addition, study subjects who were diagnosed with hypertension in places other than hospitals were more likely to be non-adherent to antihypertensive medications ($p=0.02$; $OR=3.80$; $CI\ 1.21-11.85$). Of note, neither alternative and herbal medicine use nor attendance to traditional healers was significantly associated with non-adherence. In fact, none of the variables for traditional medicine utilization were significantly associated with non-adherence.

Table 1.4 Factors associated with medication non-adherence by ordered logistic regression in 213 consecutive adults admitted to Bugando Medical Centre with hypertension-related diseases.

Variable	High-adherent (MMAS; 0) n=35(%)	Medium-adherent (MMAS; 1-2) n=38 (%)	Low-adherent (MMAS; 3-4) n=86(%)	Odds ratio [95% CI]	p-value
Proportion (%)					
Median [IQR]					
Female gender	23(28.1)	16(19.5)	43(52.4)	0.74[0.41-1.34]	0.31
Age category					
≤ 45	12(33.3)	9(25.0)	15(41.7)		
46-55	4(12.9)	10(32.3)	17(54.8)		
56-65	11(25.0)	7(15.9)	26(59.1)		
>65	8(16.7)	12(25.0)	28(58.3)	1.24[0.95-1.62]	0.12
Education level					
Not completed primary school	5(11.9)	9(21.4)	28(66.7)		
Completed primary school	25(27.5)	18(19.8)	48(52.8)		
Completed secondary school	5(19.2)	11(42.3)	10(38.5)	0.63[0.40-0.99]	0.04

Occupation

Farmer	14(25.9)	9(16.7)	31(57.4)		
Small scale business	5(14.3)	10(28.6)	20(57.1)		
Professional, Business, or Student	16(22.9)	19(27.1)	35(50.0)	1.20[0.53-2.74]	0.68

No Insurance

	21(21.2)	22(22.2)	56(56.6)	0.80[0.44-1.48]	0.47
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Systolic Blood Pressure

≤ 140	8(20.5)	14(35.9)	17(43.6)		
141-160	9(20.5)	7(15.9)	28(63.6)	1.78[0.78-4.08]	
161-180	7(20.0)	8(22.9)	20(57.1)	1.45[0.62-3.42]	
> 180	11(26.8)	9(22.0)	21(51.2)	1.09[0.48-2.45]	0.51

Is hypertension curable (or is it a lifelong condition)?

No (Hypertension is a lifelong condition)	23(28.8)	25(31.3)	32(40.0)		
Yes (Hypertension is curable)	12(15.2)	13(16.5)	54(68.4)	0.34[0.18-0.63]	0.001

Is there anything that can be done to prevent hypertension?					
Yes	6(12.8)	15(31.9)	26(55.3)		
No	29(25.9)	23(20.5)	60(53.6)	1.30[0.68-2.49]	0.43
Years of diagnosis					
1	12(24.0)	10(20)	28(56.0)		
≥2	8(19.1)	12(28.6)	22(52.4)		
≥5	8(28.6)	4(14.3)	16(57.1)		
≥10	7(18.0)	12(30.8)	20(51.3)	0.99[0.77-1.28]	0.93
Place of diagnosis					
Hospital	35(24.8)	34(24.1)	72(51.1)		
Other	0	4(22.2)	14(77.8)	3.80[1.21-11.85]	0.02
Ever used herbs for hypertension	14(20.6)	19(27.9)	35(51.5)	0.92[0.50-1.67]	0.77
Ever used herbs for any reason	24(20.7)	33(28.5)	59(50.9)	1.32[0.72-2.67]	0.44
Ever attended traditional healer	24(22.6)	28(26.4)	54(50.9)	1.36[0.72-2.60]	0.35

Stopped allopathic medications for herbs	7(20.6)	6(17.7)	21(61.8)	0.72[0.34-1.54]	0.40
Concurrent use of allopathic medications and herbs	8(21.1)	8(21.1)	22(57.9)	0.85[0.42-1.72]	0.64
Believes it is okay to use herbs with allopathic medicines	26(2.6)	27(23.5)	62(53.9)	1.06[0.54-2.05]	0.87
Prevalence of co-morbid conditions	30(22.2)	34(25.2)	71(52.6)	-0.33[-1.20-0.55]	0.46
Individual co-morbid conditions					
Diabetes mellitus	5(15.2)	13(39.4)	15(45.5)	-0.14[-0.4-0.56]	0.67
Kidney disease	6(33.3)	1(5.6)	11(61.1)	0.01[-0.1-1.02]	0.98
Stroke	2(10.5)	5(26.3)	12(63.16)	0.52[-0.43-0.47]	0.29
Heart failure	10(21.3)	10(21.3)	27(57.5)	0.17[-0.49-0.83]	0.61

MMAS-4 refers to Morisky Medication Adherence Scale, 4-Item.

Types of herbal medicines used

Of the 69 adults who reported using herbs specifically for hypertension, 42 (60.9%) reported that they were using “traditional herbs” but did not know the names of the herbs that they were consuming. The 27 study subjects who knew the names of the herbal remedies that they were taking for hypertension mentioned the wide range of remedies and 21 mentioned taking multiple herbs. The most frequently herbs reported were: Garlic (11), “Chinese herbs” (4), Ginger (3), Mronge seeds (*Moringa oleifera*) (2), Honey (2), Carrots (2), Avocado seeds (2), Bit roots (1), Wood charcoal (1), Papaya seeds (1), Lemons (1), Onions (1) and Aloe vera (1), Kuwarumbizo (Ikizu tribe) (1), Engeni tree (1) and Nyabururu (Sukuma tribe) (1), “Herbal Works” (1) and “Forever Living” health products (1). The 4 study subjects who reported using “Chinese medicines” were not able to give specific names. “Herbal Works” and “Forever Living” are both commercial products that are imported into Tanzania.

Reasons for herbal medicine use

The 69 study subjects who had used herbs specifically for the treatment of hypertension were asked to provide the reasons for herb use. Of these 69 subjects who had used herbs specifically for hypertension treatment: 22 (31.8%) patients claimed to do so because they still believe in traditional ways of treatment and customs of healthcare; 12 (17.4%) were convinced by friends or people who have

claimed to have been cured by herbs; 11 (15.9%) were looking for other options for treatment; 7 (10.2%) patients consumed herbs from a pressure from a spouse or family member; 5 (7.3%) used herbs and other alternative therapies because they didn't want to go to hospital because of uncaring attitude of hospital staff; 3 (4.4%) used because they didn't have funds to go to hospital; 3 (4.4%) patients wanted to reduce weight; 2 (2.9%) patients were convinced by radio advertisements; 2 (2.9%) patients claimed to have been bewitched to think traditional ways were the better option; 1 (1.5%) patient claimed that he was previously cured of hypertension with herbs; and 1 (1.5%) was advised by a local healer who knew the herbs.

DISCUSSION

Herbal and alternative medicine use is highly prevalent among Tanzanian adults admitted with hypertension-related conditions and many of those adults were using herbs specifically for hypertension. More than 75% of the adults in our study reported using herbal medicines in the past and nearly 70% had attended a traditional healer. More than 25% of adults were currently using herbs specifically for management of hypertension. This study is the first to describe the pattern of herbal and alternative medicine in African inpatients. This pattern is broadly similar to findings from hypertension clinics in South and West Africa (**Peltzer *et al*, 2004; Olisa *et al*, 2009; Kretchy *et al*, 2014; Amira and Okubadejo, 2007**), as well as community-based studies in East and West Africa (**Nuwaha and Musinguzi, 2013; Osamor and**

Owumi, 2010). In all of these settings, approximately one-quarter of African adults with hypertension reported the use alternative medicines and most of these were using herbal medicines. Because traditional herbs in particular are such an important part of hypertension self-management throughout Africa, collaboration with traditional healers should be explored a possible route for improving hypertension care (**Osamor and Owumi, 2010**).

Nearly 20% of adults reported stopping their allopathic medicines for herbs and >20% were concurrently using both herbs and allopathic medications. More than 70% of patients believed that there is no problem to use herbs together with allopathic medications. These findings are concerning. Although many herbs are harmless, concurrent use of some herbs could hamper the effectiveness of allopathic antihypertensive drugs such as the interaction between St. John's Wart and calcium channel blockers or the interaction between garlic and thiazide diuretics (**Izzo and Ernst 2009; Miller et al 1998**). Interactions between herb and cardiovascular drugs could also increase the toxicological effects of cardiovascular drugs such as the interaction between garlic and warfarin or the interaction between Ginseng and Digoxin (**Fugh-Berman, 2000; Mansoor, 2001; Kupiec and Raj, 2005**). Sodium-sparing herbal aquaretics such as dandelions, for example, may offset antihypertensive effects of thiazide diuretics (**Miller, 1998**). The use of ginseng with digoxin is associated with increased digoxin concentration in the blood and hence digoxin toxicity (**McRae, 1996**). Even garlic, which was the most commonly reported

herb in our own study has been shown to interact with warfarin leading to an increased risk of bleeding (**Fugh-Berman, 2000**) African adults with hypertension who are using herbs clearly require counseling not to stop their allopathic medicines for herbs as well as counseling as to possible interactions between the herbs they are using and their cardiovascular medications.

Factors that were significantly associated with the use of herbal medicines for hypertension included lower education level, non-professional occupation, lack of medical insurance and history of comorbid stroke. The lower education level was also found to be associated with the use of herbs Nigeria (**Olisa and Oyelola, 2009**). Occupation has also been shown to be associated with herbal medicine use in another study from West Africa (**Osamor and Owumi, 2010**). Inability to afford allopathic medicines was associated with herbal medicine use in Ghana (**Kretchy et al., 2014**). The association between herbal medicine use and stroke may be related to the cultural perception in Tanzania that stroke may have a magical origin, a perception that has been associated with herbal medicine use in other studies (**Osamor and Owumi, 2010**). These findings indicate that, in Africa, herbal medicine use may be associated with lower socioeconomic status and inability to pay for allopathic medications. Public health efforts designed to improve cardiovascular health in impoverished populations in sub-Saharan Africa should therefore carefully address the use of herbal medicines for hypertension in these populations,

particularly for hypertension related diseases that may be perceived to have a spiritual or magical origin.

Our patients commonly used traditional herbs, however they did not know the names of the majority of these herbs. Amongst the known herbs, garlic was the most frequently used herb. Garlic (*Allium sativum*) has been closely studied. Garlic has demonstrated multiple cardiovascular benefits that include lowering blood pressure, inhibiting platelet aggregation, enhancing fibrinolytic activity and reducing cholesterol and triglyceride levels. However, despite these evidence the routine use has not been advise because of methodological shortcomings of the published literature (**Mashaur et al., 1998**) and extreme caution is advised if garlic is taken concomitantly with CYP2E1 substrates (**Izzo and Ernst, 2009**) or in patients taking warfarin (**Miller, 1998**). Studies are needed to determine possible benefits and harms of native African herbs that are used by traditional healers for hypertension.

Over 90% of study subjects reported that their doctors did not ask them about the use of either herbs or other alternative therapies for hypertension. These findings are consistent with other studies from West Africa which indicate: 1) that the overwhelming majority of health care workers are not aware of the herbal medicine use of the hypertensive adults in their care (**Olisa and Oyelola, 2009; Kretchy et al., 2014**) and 2) that a leading reason for this are fear and lack of inquiry of the part of the healthcare worker (**Kretchy et al., 2014**). Of note, many of the herbs reportedly used by study subjects are foods that are likely not problematic to consume with

antihypertensive drugs i.e. ginger, onions, and honey. In addition, current use herbal medicines for hypertension were not associated with non-compliance to allopathic medicines, as it has been in prior studies (**Peltzer et al, 2004; Kretchy et al 2014**). It is therefore important that doctors not only ask about herbs and other alternative therapies among adults admitted with hypertension but also that they provide careful, specific and non-judgmental recommendations. The authors suspect that more patients will be willing to listen and follow advice if clinicians apply this careful, discerning approach.

CONCLUSION

A significant proportion of Tanzanian adults with hypertension-related conditions are using herbal and alternative remedies. Many adults reported stopping their allopathic medicines for herbs and/or using both allopathic medications and herbs concurrently. This brings the issue of efficacy, safety and drug-herb or herb-herb interactions because of lack of scientific data on herbal medicines. Factors significantly associated with the use of herbs in the last month before admission included education level, occupation, lack of medical insurance and certain comorbid conditions i.e. stroke. Majority of patients are not compliant to the prescribed medications. Of note, neither utilization of herbs nor other alternative therapies were associated with medication non-adherence. Alternative therapies ranging from herbs, food and vegetables to Chinese medicine has been used, however majority of herbs

users did not know what they were using. Most study subjects reported that their doctors did not ask them about the use of either herbs or other alternative therapies for hypertension. Doctors not only ask about herbs and other alternative therapies among adults with hypertension but also that they should provide careful, specific and non-judgmental recommendations. This will avoid disrupting doctor-patient relationship and possibly encourage medication compliance. More studies are necessary and should focus on safety, efficacy and drug-herb interactions as well as role and attitude of traditional healers towards hypertension and the timing of initiation of herbal and alternative therapy use.

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CHAPTER 2

MANUSCRIPT 2

TITLE PAGE

Traditional herbal medicine use among hypertensive patients in sub-Saharan Africa: a systematic review

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ABSTRACT

Background: Hypertension is increasingly common in sub-Saharan Africa, and rates of hypertension control are low. Use of traditional herbal medicines (THM) is common among adults in sub-Saharan Africa and may affect hypertension therapy.

Methods: We searched Ovid MEDLINE, Ovid EMBASE, and Web of Knowledge in June 2013 to find studies about THM use among hypertensive patients living in sub-Saharan Africa. Two independent reviewers evaluated titles and abstracts. Qualifying references were reviewed in full text. Data were extracted using a standardized questionnaire.

Results: Four hundred eighty-one references were retrieved, and 4 articles from 2 countries met criteria for inclusion. The prevalence of THM use was 25-65% (average 38.6%). THM was the most common type of complementary and alternative medicines used by patients (86.7%-96.6%). Among THM users, 47.5% concomitantly used both allopathic medicine and THMs. Increased age ($p < 0.001$), male sex (RR 2.58), belief in a supernatural cause of hypertension (RR 2.11), and family history of hypertension (OR 1.78) were positively associated with THM use while belief that hypertension is preventable was negatively associated with a THM use (OR 0.57).

Conclusion: More than a third of adults with hypertension in sub-Saharan Africa use THM. Half of these patients use THM concurrently with allopathic

medicine. Healthcare workers in sub-Saharan Africa must discuss THM use with their hypertensive patients. More research is urgently needed to define the impact of THM use on hypertension control and outcomes in sub-Saharan Africa.

INTRODUCTION

Although hypertension (HTN) was formerly rare in Africa [1–3], HTN prevalence is now rapidly increasing [4]. In one serial survey of Tanzanian adults 47-57 years old, the overall prevalence of hypertension increased from 25% to 40% between 1987 and 1998 alone [5–7]. According to the World Health Organization, the age-standardized prevalence of HTN in adults >25 years in Africa is now the highest in the world [8].

HTN-related complications are increasingly common in sub-Saharan Africa (SSA) [9,10]. The incidence of stroke in adults aged 30-69 in Tanzania is one of the highest rates in the world (120/100,000 person years) and is 6-10 fold higher than the US, UK and Canada [11]. At our own hospital in Western Tanzania, HTN-related diseases accounted for 15% of all medical admissions, deaths, and hospital days – second only to HIV – and half of these deaths occurred in adults < 65 years old [12]. The early onset of HTN-related complications has been attributed to low rates of diagnosis, treatment and control [13,14]. In one study, the authors summarized this problem as the rule of 1/6ths: among adults with HTN in Africa, only 2/6 are aware of their

diagnosis, of these only 1/6 are on treatment, and of these only 1/6 are controlled [15].

Traditional herbal medicine (THM), may have significant impact on HTN treatment and control in sub-Saharan Africa [16]. THM use is high among adults in SSA with a prevalence ranging from 38.5%-90% [17–20]. THM is commonly used around the world for both cardiovascular disease in general [21] and HTN specifically [22–24]. In our experience in Tanzania, adults admitted with complications of HTN frequently report prior THM use.

Therefore, we conducted a systematic review of the literature to collect and describe the currently available data regarding THM use among adults with HTN in SSA. In particular, we aimed to describe the prevalence of THM use, the timing and effects of THM use, reasons reported for THM use and factors associated with THM use.

METHODS

Literature Search

In June 2013 we searched Ovid MEDLINE (1946 to present) including in-process and non-indexed citations, Ovid EMBASE (1974 to present), and Web of Knowledge, for studies, which investigated the use of THM among hypertensive patients living in SSA. A detailed search using words, phrases, and controlled vocabulary was created by an information specialist (HABE)

with input from a clinical pharmacologist and two board certified internal medicine physicians. The search strategies were peer reviewed by a second information specialist to ensure high methodological quality. Key words and search terms for each database are provided in Appendix A. The search was not limited to a specific language, date, or publication status. Additional references were found through reviewing the reference lists and related articles of included studies.

Two independent reviewers sorted references based on title and abstract according to predetermined inclusion and exclusion criteria. Differences were resolved through discussion with a third reviewer. References marked for inclusion were obtained, read in full, and marked for inclusion or exclusion.

References were included if they enrolled participants aged 18 years old and above currently living in SSA who were suffering from arterial HTN and described the prevalence of THM use among hypertensive patients. References were excluded if they included pediatric data but did not report data separately for adults, if they included patients outside of SSA and did not report data separately for those living in SSA, or if they included less than 10 patients. References were also excluded if they were pharmacological studies, interventional trials, meta-analyses, reviews, editorial material, or guidelines. See Figure 1 for an explanation of how many references were retrieved and reasons for exclusion.

Data Extraction

Two reviewers used a predefined data questionnaire template independently. Any disagreements between the first two reviewers were resolved through independent review of a senior member of the research team. The following data points were extracted from each reference and included in the evidence table: sample size, average age \pm SD, age range, gender distribution, prevalence of HTN, prevalence of complementary and alternative (CAM) use, prevalence of THM use, source of THM prescription, types of THM used, factors associated with and reasons stated for THM use, timing of THM use, and effects of THM use. Risk of selection bias was scored on a three-point scale with 1 representing a randomly selected, representative sample of the population, 2 representing a non-random sample of the community, and 3 representing a hospital-based sample. Risk of measurement bias was also scored on a 3 point scale with 1 representing biologically confirmed THM use, 2 representing self-reported THM use, and 3 representing THM use reported by someone other than the patient.

RESULTS

Study Selection

For details of the study selection process, see Figure 1 for a PRISMA diagram. A systematic search of the literature revealed a total of 481 references: 58

from Ovid MEDLINE, 172 from Ovid Embase, and 251 from Web of Knowledge. An additional 4 references were found through hand searching reference lists. After removal of duplicates, 360 references remained. The titles and abstracts were reviewed, and 334 references were excluded. The remaining 26 were reviewed in full text and an additional 22 were excluded. Data extraction was completed on the remaining 4 references.

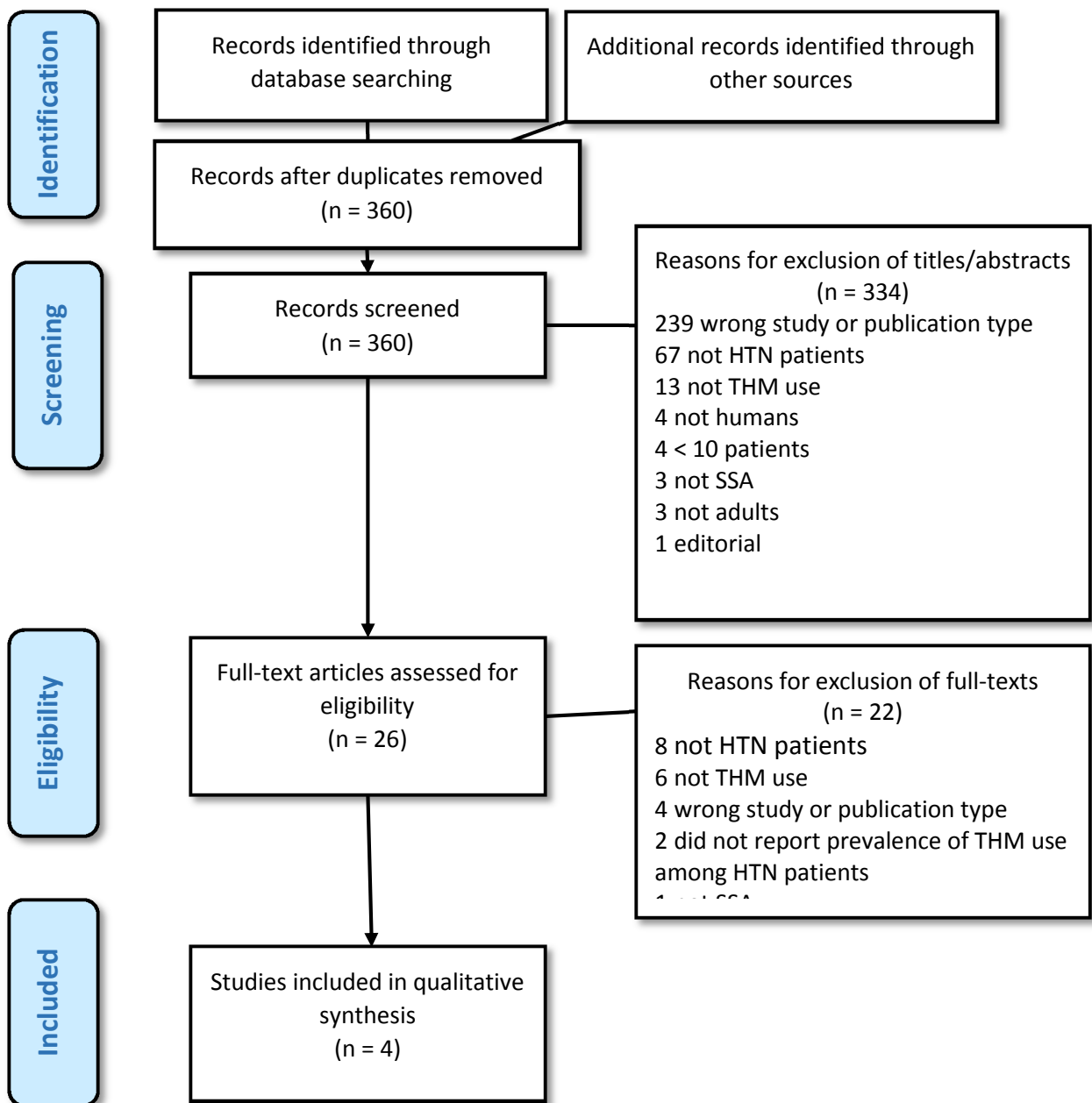


Figure 1 Flow diagram showing the description and selection process of studies included in the systematic review.

Characteristics of Selected Studies

For details of study characteristics, see Table 2.1. Of the 4 studies included, 1 was conducted in South Africa [16], and 3 were conducted in Nigeria [25–27]. The 3 studies from Nigeria all took place in an urban setting. Two were conducted in an urban hospital clinic [25,26], and 1 was conducted in an urban general population [27]. The 1 study from South Africa was conducted in a rural hospital clinic [16]. The sample size ranged from 100 to 480 participants. All 4 articles dealt exclusively with hypertensive patients [16,25–27]. The 3 references that included gender distribution reported a majority of respondents were female (60-67%)[16,25,27]. The average age of study participants was 55.1-60.7 years.

Table 2.1 Characteristics of included studies of THM use among adults with HTN in Sub-Saharan Africa.

Study	Country	Setting	Sample Frame	Sample Size	Average Age ± SD (years)	Female Gender (%)	Risk of Selection Bias (1-3)
Amira 2007	Nigeria	Urban	Hospital	225	55.1 ± 12.4	135/256 (60%)	3
Olisa 2009	Nigeria	Urban	Hospital	480	60.33 ± 16.33	NR	3
Osamor 2010	Nigeria	Urban	Population	440	60 ± 12	287/440 (65.23%)	1
Peltzer 2004	South Africa	Rural	Hospital	100	60.7 ± 9.8	67/100 (67%)	3

Key: SD: Standard deviation. IQR: Interquartile range. NR: Not reported. HTN: hypertension

Prevalence of CAM/THM Use

For details about the prevalence of CAM and THM use, see Table 2.2. The rate of CAM use (inclusive of THM) was reported by 3 studies and ranged from 29.1-75% [16,25,27], and the average was 47.7%. The rural study from South Africa reported a much higher rate of CAM use (75%) [16] than the 2 studies from Nigeria (29.1-39.1%) [25,27]. THM use in the 4 studies ranged from 25% to 65% with an average of 38.6%. The rural study from South Africa reported higher rate of THM use (65%) [16] than the 3 studies from Nigeria (25%-37.77%) [25–27]. In the three studies that reported both CAM use and THM use, THM use represented the overwhelming majority of CAM use (86.7%-96.6%) [16,25,27].

Table 2.2 The prevalence of CAM and THM use among adults with HTN in Sub-Saharan Africa.

Study	Patients Using CAM	Patients Using THM	THM use as a % of CAM use
Amira 2007	88/225 (39.1%)	85/225 (37.77%)	85/88 (96.6%)
Olisa 2009	NR	120/480 (25%)	NR
Osamor 2010	128/440 (29.1%)	118/440 (26.8%)*	118/128 (92.2%)*
Peltzer 2004	75/100 (75%)	65/100 (65%)†	65/75 (86.7%)

Key: CAM: Complementary and alternative medicine. THM: Traditional herbal medicine. HTN: Hypertension. NR: Not reported.

*Percentage is the sum of THM mentioned as being commonly used by all CAM users

†Sum of home remedies (39%) and traditional healing herbs (26%).

Categories were not mutually exclusive, so actual % may be lower.

Timing and Effects of THM Use

Results regarding the timing and effects of THM use are summarized in Table 2.3. Two studies specifically reported that patients with HTN used THM and allopathic medicines concurrently [25,26], although only one quantified the number of THM users who were also using allopathic medicines (47.5%) [26]. Only one study [25] compared the blood pressures between the patients who reported using allopathic medications alone and those who reported using both

allopathic and THM and reported no difference. The other three studies did not report any outcomes in those who were taking THM [16,26,27]. One study reported reasons for stopping THM among a small fraction of the study population (<5%) that had formerly used THM [26]. They found that 1.5% of their total study population stopped using THM due to inefficacy and 3% stopped using THM due to improvement of their disease.

Table 2.3 The timing and general effects of THM use

Study	Timing of THM use	General effects of THM
Amira 2007	Concurrent use of THM and allopathic (not quantified)	No change in BP control between THM+allopathic and allopathic alone.
Olisa 2009	Concurrent use of THM and allopathic 57/120 (47.50%)	Only reported in the 4.5% of patients who stopped using THM.

Key: THM: Traditional herbal medicine. BP: Blood pressure. NR: Not reported.

Reasons for THM use

For reasons provided and factors associated with THM use, see Table 2.4. One study [26] reported why patients used THM. These included 1) perceived failure of allopathic medicines (31.73%), 2) relatively high cost of allopathic medicines (23.08%), 3) social cultural practices and/or herbal knowledge (20.19%), 4) poor accessibility to medical facilities (19.23%), 5) safety concerns about allopathic medicines (9.62%), 6) uncaring attitudes of hospital staff (6.73%). Other reasons reported for THM use included prior phobia to hospitals, curiosity about using THM and pressure from herbal sellers.

Table 2.4 Associated factors and reasons for THM use

Study	Associated with THM Use among HTN Patients	Reasons for THM Use
Olisa 2009	<p>Higher THM Use: Increased age (p < 0.001)</p> <p>Lower THM Use: NR</p>	<ol style="list-style-type: none"> 1. Perceived failure of allopathic medicines (31.73%). 2. Relatively high cost of allopathic medicine (23.08%). 3. Social cultural practices/herbal knowledge (20.19%). 4. Poor accessibility to medical facilities (19.23%). 5. Safety concerns about allopathic medicines (9.62%). 6. Uncaring attitudes of hospital staff (6.73%). 7. Other: prior phobia of hospitals, curiosity about herbal medicines, and pressure from herbal sellers.
Osamor 2010	<p>Higher THM Use: 1. Male Sex: RR 2.58, CI 1.66-3.99, p < 0.0001 2. Belief in supernatural cause of HTN: OR 2.11, CI 1.18-3.78, p = 0.012 3. Family history of HTN: OR 1.78, CI 1.02-3.10, p = 0.042</p> <p>Lower THM Use: Belief that HTN is preventable: OR 0.57, CI 0.36-0.89, p = 0.014.</p>	NR

Key: CAM: Complementary and alternative medicine. HTN: Hypertension.

THM: Traditional herbal medicine. OR: Odds ratio. CI: Confidence interval. NR:

Not reported.

Factors Associated with THM Use

Factors which were statistically associated with THM use were reported by 2 studies [26,27]. One found that increased age was associated with THM use ($p < 0.001$) [26]. The other found that three factors were positively associated with increased THM use: 1) male sex, RR 2.58 (CI 1.66-3.99, $p < 0.0001$), 2) belief in a supernatural cause of HTN, OR 2.11 (CI 1.18-3.78, $p = 0.012$), and 3) a family history of HTN, OR 1.78 (CI 1.02-3.10, $p = 0.042$) [27]. Belief that HTN is preventable was associated with decreased THM use, OR 0.57 (CI 0.36-0.89, $p = 0.014$) [27].

Types and Sources of THM

For details of the types and sources of THM used, see Table 2.5. The three studies from Nigeria each asked study participants about the names of plants they used [25–27]. The list included “native herbs,” ginger, garlic, bitter leaf (*vernonia amygdalina*), aloe vera, azadirachta indica, allium sativa, tamarindus indica, hyenia thebacia, ocimum basil, carica papaya, adamsonia digitata, gacinia kola, zingiber officinalis, hymenocardia acida, melia azederach, mannix cymbopogon, piliostigma reticulatum, adeola herbal mixture, keys herbal mixture, herbal viagra, cassia alata, jatropha curcas, ximenis americana, moringa oleifera, kalms, and true man’s capsule. Only one study reported on the specific preparations used [26]. Patients reported using preformulated

THM from herb sellers, extracts that needed to be dissolved (in water, lime juice, or corn pap), steam inhalation, single herbs, and mixtures of herbs. Sources of THM were mentioned by 3 studies [16,26,27] and included open markets, friends, traditional healing homes, pharmacies, buses, spiritual pharmacies, traditional healers and faith healers.

Table 2.5 Plants, preparations used and the sources of THM

Study	Plants	Preparations	Sources
Amira 2007	Native herbs, ginger, garlic, bitter leaf (vernonia amygdalina), aloe vera	NR	NR
Olisa 2009	Azadirachta indica, allium sativa, aloe vera, tamarindus indica, hyenia thebacia, ocimum basil, carica papaya, adamsonia digitata, gacinia kola, zingiber officinalis, hymenocardia acida, melia azederach, mannix, cymbopogon, piliostigma reticulatum, adeola herbal mixture, Keys herbal mixture, herbal viagra, cassia alata, jatropha curcas, ximenis americana, moringa oleifera, kalms, true man's capsule, and garlic	<ol style="list-style-type: none"> 1. Preformulated from herb sellers. 2. Extracts that needed to be dissolved in water, lime juice, or corn pap. 3. Steam inhalation. 4. Single herbs. 5. Mixtures of herbs. 	Open markets, friends, traditional healing homes, pharmacies and buses
Osamor 2010	Herbs, garlic	NR	Traditional healers and spiritual pharmacies
Peltzer 2004	NR	NR	Traditional healers and faith healers

Key: THM: Traditional herbal medicine. HTN: Hypertension. NR: Not reported.

DISCUSSION

THM use is very common among adults with HTN in SSA. Among hypertensive adults enrolled in the 4 studies included in this systematic review, more than one third reported using THM at the time of the study [16,25–27]. Rates of THM use varied considerably by country with 65% of adults in rural South Africa reporting THM use compared to 30% of adults from urban Nigeria. In these populations, THM use was the dominant form of CAM, accounting for 86.7-96.6% of all CAM use. The rates of THM use among adults with HTN in SSA were higher than those reported in 2 recent studies from the UK [24] and India [23] that found a prevalence of 28.8% and 14.4% respectively. Several studies explore the types of THM used to treat hypertensive patients [28–30], but very few quantify the amount of THM use. The high prevalence of THM use among adults with HTN in all 4 of these studies highlights the importance of considering the possible effects of THM use on HTN treatment and control in SSA.

Lack of knowledge, traditional beliefs and health systems deficiencies are 3 important factors associated with THM use among adults with HTN in these studies. Perceived failure of allopathic medications was the most common reason reported for THM use according to 1 study [26], and belief that HTN is both unpreventable and has a supernatural cause were factors associated with hypertension in another study [27]. In order to improve knowledge about potential effects of THM, community education campaigns are needed [7,31].

In addition, healthcare workers should utilize every interaction with hypertensive adults to ask about THM use and to consider the effects of THM on HTN control. Finally, health systems strengthening is needed to reduce the relatively high cost of allopathic medications, increase access to medical facilities and counteract the perception of uncaring attitudes of hospital staff.

Concurrent use of THM and allopathic medications seems to be common among adults with hypertension in SSA. In 1 study, half of HTN patients who were taking THM were also taking allopathic medications [26]. The high prevalence of concurrent THM and allopathic medicine use has been documented in other chronic diseases such as HIV in SSA [32,33]. The potential for therapeutic interactions between allopathic medication and THM is high with concomitant use. THM are known to have an effect on both the cardiovascular system and on blood pressure control [34–37]. Interactions may include altered drug metabolism, exaggerated hypotensive effect, or decreased HTN control. Since adults in SSA rarely volunteer information about THM use to their physicians [38], careful and non-judgmental history taking is essential .

Despite the high prevalence of THM use among African adults with HTN, the authors were surprised to discover that little data exists regarding THM use among adults with HTN in SSA. Although recording THM use is part of the WHO STEPS instrument for NCD risk factor screening [39], it is not systematically reported in studies of HTN in SSA. Even among the 4 studies

that were included in this review, data regarding the prevalence, timing and reasons for THM use were not reported in a standardized manner. Physiologic outcomes (e.g. blood pressure measurements) were only reported in one study, and only 2 countries in SSA were represented by these 4 studies. Clearly there is an urgent need for more research regarding THM use among adults with HTN in SSA. Future studies should document the specific types of THM ingested by patients, physiologic effects of specific THM and any interactions with allopathic cardiovascular medications. Prospective cohort studies documenting the timing and impact of THM use on the natural history of HTN would be particularly valuable.

CONCLUSIONS

In conclusion, according to this systematic review of the current literature, >1/3 of adults with HTN in SSA use THM. Half of these patients use THMs concurrently with allopathic medicine. Major drivers of THM use are lack of knowledge regarding HTN, traditional cultural beliefs and weakness in the current health systems for HTN primary care in SSA. Health care workers in SSA should screen for THM use among adults with HTN. In addition, both community education and opportunistic patient education are needed to improve knowledge about interactions between THM and allopathic medications. Primary healthcare systems for HTN diagnosis and treatment need to be less expensive, more available and respectful. Finally, more

research is urgently needed to define the impact of THM use on HTN control and outcomes so that their beneficial effects can be leveraged and their negative effects avoided.

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APPENDICES

Database Search Strategy

Medline (OVID SP)

#1 exp africa south of the sahara/

#2 (africa* adj (central or east or eastern or west or western or south or southern)).mp

#3 (subsahara* or sub-sahara* or "sub sahara*").mp

#4 (cameroon* or central africa* republic or chad or chadian or congo* or democratic republic of the congo* or equatorial guinea* or gabon*).mp

#5 (burundi* or djibouti* or eritrea* or ethiopia* or kenya* or rwanda* or somalia* or sudan* or tanzania* or uganda*).mp

#6 (angola* or botswana* or lesotho* or malawi* or mozambique* or namibia* or south africa* or swaziland* or zambia* or zimbabwe*).mp

#7 (benin* or "burkina faso*" or "cape verde*" or "cote d'ivoire*" or "ivory coast" or gambia* or ghana* or guinea* or guinea-bissau* or "guinea bissau*" or liberia* or mali or malian or mauritania* or niger* or nigeria* or senegal* or "sierra leone*" or togo*).mp

#8 or/1-7

#9 exp hypertension/ or exp antihypertensive agents

#10 (hypertensi* or antihypertensi*).mp

#11 ((high or increased or elevated) adj blood pressure).mp

#12 or/9-11

#13 medicine, african traditional/ or medicine, traditional/

#14 (african traditional medicine or traditional healing or traditional healer* or african medicine or ethnomedicine* or native medicine or ethnopharmaceutical* or ethnobotanical* or natural remed*).mp

#15 or/13-14

#16 8 and 12 and 1

Embase (OVID SP)

#1 exp Africa south of the sahara/

#2 (africa* adj (central or east or eastern or west or western or south or southern)).mp

#3 (subsahara* or sub-sahara* or "sub sahara*").mp

#4 (cameroon* or central africa* republic or chad or chadian or congo* or democratic republic of the congo* or equatorial guinea* or gabon*).mp

#5 (burundi* or djibouti* or eritrea* or ethiopia* or kenya* or rwanda* or somalia* or sudan* or tanzania* or uganda*).mp

#6 (angola* or botswana* or lesotho* or malawi* or mozambique* or namibia* or south africa* or swaziland* or zambia* or zimbabwe*).mp

#7 (benin* or "burkina faso*" or "cape verde*" or "cote d'ivoire*" or "ivory coast" or gambia* or ghana* or guinea* or guinea-bissau* or "guinea bissau*" or liberia* or mali or malian or mauritania* or niger* or nigeria* or senegal* or "sierra leone*" or togo*).mp

#8 or/1-7

#9 exp hypertension/ or exp antihypertensive agent

- #10 (hypertensi* or antihypertensi*).mp
- #11 ((high or increased or elevated) adj blood pressure).mp
- #12 or/9-11
- #13 african medicine/ or herbal medicine/
- #14 traditional healer/ or traditional medicine/
- #15 (african traditional medicine or african medicine or native medicine or native remed*).mp
- #16 (tradition\$ adj3 (healing or healer* or healed)).mp
- #17 (ethnomedicine* or ethnopharmaceutical* or ethnobotanical*).mp
- #18 or/13-17
- #19 8 and 12 and 18

Web OF KNOWLEDGE (Thomson Reuters)

- #1 Topic=(cameroon* OR chad OR chadian OR congo* OR "central africa* republic" OR "democratic republic of the congo*" OR equatorial guinea* OR gabon*) OR Topic=(burundi OR djibouti* OR eritrea* OR ethiopia* OR kenya* OR rwanada* OR somalia* OR sudan* OR tanzania* OR uganda*)
Timespan=All years Search language=English
- #2 Topic=(angola* OR botswana* OR lesotho* OR malawi* OR mozambique* OR namibia* OR "south africa*" OR swaziland*) OR Topic=(zambia* OR zimbabwe* OR benin* OR "burkina faso*" OR "cape verde*" OR "cote d'ivoire*" OR "ivory coast") OR Topic=(gambia* OR ghana* OR guinea* OR

guinea-bissau* OR "guinea bissau*" OR liberia* OR mali OR malian)

Timespan=All years Search language=English

#3 Topic=(mauritania* OR niger* OR nigeria* OR senegal* or "sierra leone**")

Timespan=All years Search language=English

#4 Topic=((africa OR african) NEAR/2 subsahara*) Timespan=All years

Search language=English

#5 Topic=((africa OR african) NEAR/2 sub-sahara*) Timespan=All years

Search language=English

#6 Topic=((africa OR african) NEAR/2 "sub sahara**") Timespan=All years

Search language=English

#7 Topic=((africa OR african) NEAR/2 (central OR east OR eastern OR west

OR western OR south or southern)) Timespan=All years Search

language=English

#8 #7 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1 Timespan=All years Search

language=English

#9 Topic=(hypertensi* OR antihypertensi*) Timespan=All years Search

language=English

#10 Topic=(("blood pressure") NEAR/2 (high OR increased OR elevated))

Timespan=All years Search language=English

#11 #10 OR #9 Timespan=All years Search language=English

#12 Topic=(ethnobotanical* OR ethnopharmaceutical* OR ethnomedicine)

Timespan=All years

Search language=English

#13 Topic=(africa* NEAR/2 medicine) Timespan=All years Search language=English

#14 Topic=(native NEAR/2 (medicine OR remed*)) Timespan=All years
Search language=English

#15 Topic=(folk NEAR/2 medicine) Timespan=All years Search
language=English

#16 Topic=(traditional NEAR/2 (heal* OR medicine OR remed*))
Timespan=All years
Search language=English

#17 Topic=(natural NEAR/2 remed*) Timespan=All years Search
language=English

#18 #17 OR #16 OR #15 OR #14 OR #13 OR #12 Timespan=All years Search
language=English

#19 #18 AND #11 AND #8 Timespan=All years Search language=English