TITLE **Prevalence and factors associated with traditional herbal medicine use among patients on highly active antiretroviral therapy in Uganda**

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INTRODUCTION

Worldwide, more than 40 million people are infected with HIV [1]. Since the AIDS epidemic began, more than 20 million deaths have been attributed to AIDS[2]. The introduction of ARVs has led to reduction in AIDS- related morbidity and mortality[3, 4]. With the number of global and regional initiatives towards improving access to HAART and the decrease in prices of antiretroviral medicines (ARVs) the numbers of people accessing HAART are on the rise.

Globally there were over 3 million people in low-middle income countries and 2 million in the Sub-Saharan Africa on HAART by 2002-2007[UNAIDS 2008]. In Uganda, there are over 1 million people with HIV. More than 312,000 HIV-1 infected persons need HAART, of which about 212,200 have access to the drugs and close to ¾ are buying the drugs [15]. However management of HAART adverse events is difficult in many resource limited setting [UNAIDS 2008 Report on the global AIDS epidemic]. In Africa, majority of the HIV patients rely on traditional herbal medicine (THM) for their primary health care needs [13].

World Health Organization (WHO) estimates that 80% of the world population use traditional medicines. few studies have reported large numbers of traditional health practices (THPs) in developing countries involved in the treatment of HIV/AIDS [5]. Herbal medicines are frequently used in conjunction with other medicines, and it is essential to understand the consequences of such combined use and monitor whether any adverse effects are arising [14]. The extent and factors associated with herbal medicines use among HIV/AIDs patients on antiretroviral therapy are not well documented. Consequently there are no clear guidelines on herbal medicine use among HAART patients. Drug interactions between herbs and HAART may lower the serum level of HAART or may decrease its effectiveness[9] moreover, there is a lack of effective communication on this subject at all levels from international to local This could worsen side-effects or reduce the suppression & possibly increase the cause drug resistance.

We conducted a study to determine the prevalence and factors associated with herbal medicine use among HAART patients in two TASO health care treatment centres a Ugandan setting.

Methods: A cross-sectional study was carried out in two TASO centres, Jinja and Entebbe with 401 randomly selected eligible participants, between January 2008 and March 2008. Herbal medicine use was assessed quantitatively using a pre-tested, interviewer-administered semi-structured questionnaire. STATA version 9.0 was used for analysis. Statistical significance was tested using p-values and 95% confidence intervals. Multivariate analysis was done using logistic regression

Data collection: Participant data were collected using a pre-tested interviewer-administered semi-structured questionnaire developed specifically for the research. The data were collected by trained research assistants under direct supervision of the principal investigator. Interviews were conducted at one-on-one basis before and after the participants had seen their doctor. Others were interviewed before and after, HAART was dispensed to them. Corresponding medical and/or counseling records were crosschecked for various predictor variables to minimize bias. The outcome variable was traditional herbal medicine use. This referred to someone who had ever used or was currently using THM that contain active ingredients of; parts of plants, or plant material or a combination of both while on HAART. The study was approved by the Makerere University College of Health Sciences Medicine Research and Ethics Committee. Confidentiality of the participants' information was ensured and the study included only patients that had given informed consent before data collection.

Statistical analysis: We computed sample size using the clientele load at each study site, we had 233 and 168 participants from Jinja and Entebbe TASO centres respectively. Descriptive statistics were used to summarize baseline characteristics and to determine the prevalence of herbal medicine use. Bivariate analysis was used to determine the association between herbal medicine use with each categorical independent variable using chi-square tests. A p-value less than 0.05, was considered significant. Logistic regression was used for multivariate analysis to determine the independent predictors of herbal medicine use and to assess for confounding and statistical interaction.. Confounding was determined by calculating the difference in the odds ratio.

RESULTS

The prevalence of THM use among HAART patients was high (n = 135, 33.7%, 95% CI: 33.38-34.02). THM use was more common among the female respondents (36.4%, 95% CI: 35.96 – 36.84), respondents who were 39 years old and above (41.6%, 95% CI: 41.00 – 42.20) and respondents that were not married (38.4%, 95% CI: 37.94 - 36.86). The prevalence at the two TASO centres was almost similar, Table 1.

Bivariate analysis

Among the HAART patients the older (39 – 78 years) respondents were less likely to use traditional herbal medicine compared to the younger respondents. Other factors were not significantly associated with herbal medicine use, table 2. Participants who had ever experienced side effects were two times more likely to use herbal medicine compared to those who did not experience side effects while participants who had been on HAART for ≤ 3 years were less likely to use herbs than those who were on HAART for four years and more, table 3. Those advised by parents and/or relatives to start using traditional herbal medicine while on HAART were more than two times likely to combine THM with HAART compared to those advised by friends (Table 4). On the other hand, patients who perceived the importance of HAART to their lives were less likely to combine THM and HAART.

Multivariate analysis

Old aged patients were not associated with Traditional herbal medicine use among HAART patients. Participants with HAART adherence levels > 95% were nine percent times less likely to use herbs compared to those whose HAART adherence level was ≤ 95% . Those who were on

HAART for 3years or less were more than five times likely to use THM compared to those who were on HAART for four years or more. The participants who experienced HAART side effects were about four times more likely to use THM compared to those who had not experienced any HAART side effects since their time of initiation. See table 5 below. With a 0.05 level of significance and at 4 degrees of freedom, we found no significant interaction between the independent factors associated with herbal medicine use (p value < 0.01).

DISCUSSION

The prevalence of traditional herbal medicine use among HAART patients in TASO Uganda was high. One in every three patients was using herbs alongside HAART. Findings were similar to other studies [7] that found prevalence ranging between 30% - 68% [8].

Our study was done in a setting where patients are sensitized on the dangers of combining conventional drugs like ARVS with THM. If this was done in other settings where patients are not sensitized the proportion would be higher. The prevalence of herbal medicine use found in this study is likely to be an underestimate because self reports were used. Some patients were not likely to report practices like herbal medicine use alongside HAART that have been discouraged by their health care providers. However, those who reported use could honestly be combining HAART with THM. This could possibly depict a true picture of THM use among HAART patients as well as patients with other health complications. The abundance of local herbs in Uganda, the perception and attitude of the patients to these local herbs are some of the factors that could lead to their extensive usage. Besides, training of local herbalists by WHO to promote

good practice of traditional herbal use among the communities across the country promotes herbal medicine use.

Sex of the participants was not significantly associated with combining THM and HAART. This could probably be due to the few male patients attending TASO services, plausibly because in Uganda and Africa in particular, men rarely assess health care services and this could have distorted our findings. The younger respondents between 18 and 38 years were more likely to use herbal medicine compared to the older respondents. This is plausible that the older respondents were more informed about THM and had possibly used it but in vain.

Patients who had been on HAART for a shorter time, that is three years or less were more than five times as likely to use to use traditional herbal medicine compared to those who had been on HAART for a longer time. It is possible that these patients have not yet been well sensitized about not using herbs alongside HAART or they may have been using them before they were on HAART and just continue to do so possibly because their belief in the HAART is not yet strong enough.

Most adverse drug reactions manifest after long time at least more than a year. ARV adverse effects among patients are the main reason of using THM. Those who had ever experienced ART side effects were more than three times as likely to use THM compared to those who had never experience any. This possibly was due to the facts given to the users by traditional herbalists that THM are natural foods without any toxic element and are a relief if eaten in good quantities. The findings were similar to other studies [8-10].

What participants had experienced before and after use of THM was improved health status and this was referred to as positive outcome due to herbal use. However, this improvement was self reported and could not clinically be assessed neither was the time the improvement was noticed. It could actually be true since the person reported what he felt but on the other hand improvement could be due to HAART and the positive living counseling obtained from the health care service providers. Individuals who could not tell if herbs or HAART had improved their health were found to use THM more than two times compared to those who perfectly knew THM improved their health. RCT in China reported promising effects from three herbal medicines[11]. Pharmacological investigations would be prudent to identify the potential risks, benefits, and interaction or non-interactions associated with HAART and local THM use in Uganda. Failure to do these studies may result in drug interactions, treatment failure, resistant HIV, and drug toxicities.

Patients whose HAART adherence level was below 95% were more likely to use THM concurrently with ARV drugs. This is similar to what Kiguba et at[6] found out in their study. In Zambia, pregnant women with low adherence half of them were as likely to adhere to NVP. The study had a limited sample size to generalize their findings [12]. This means that HAART adherence can be affected by use of traditional herbal medicine, compromising on the effectiveness of HAART. Over 63% of the data on adherence was missing in the database that we could not compare it with our respondents' self report. This could be higher in a different setting where individuals even to this HAART era still hide while taking ARV drugs. This stigma can lead to low ART adherence. We however can not rule out that our results should therefore be interpreted with caution because our study had few respondents on adherence. We therefore need to provide adherence counseling to our patients and integrate traditional herbalist

in the health care system. As observed in herbalist clinics, Traditional healers can play an important role in delivering an AIDS prevention message and some may be able to offer treatment for opportunistic infections.

Sexually active respondents were more likely to use THM while on HAART patients. Most of the respondents were married. HAART is attributed to activating the sexual urge of many patients who might end up getting pregnant, where in most cases THM is commonly used to avoid pregnancy complications in Uganda. It is plausible that this increased use of THM alongside HAART. Although we did a comprehensive search, the majority of published studies did not have some of the factors our study looked at and this hindered our comparisons. Only one study [6] could be comparable to our study but it had very small sample size.

Conclusions

The prevalence of THM use among HAART patients was high. The main reason of THM use was to relieve HAART adverse events. This raises clinical and pharmacological concerns that need attention by the health care service providers.

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Table 1: The prevalence of traditional herbal medicine use among HAART patients in TASO Uganda, during 2008

Variable	Number	Herbal users	Prevalence of THM use	95% CI
Sex				
Male	121	33	27.3	26.12 - 28.48
Female	280	102	36.4	35.96 - 36.84
Age (categorized at median age)				
18 – 38	211	56	26.5	25.82 - 27.18
39 - 78	190	79	41.6	41.00 - 42.20
Religion				
Christian	328	120	36.6	36.22 - 36.98
Moslem	73	15	20.5	18.37 - 22.63
Marital Status				
Not married	263	101	38.4	37.94 - 36.86
Married	138	34	24.6	23.53 - 25.67
Highest education level attained				
Primary	204	69	33.8	33.16 - 34.44
Secondary	130	45	34.6	33.61 - 35.59
Tertiary	13	4	30.8	20.36 - 41.24
None	54	17	31.5	29.01 - 33.99
Occupation				
Employed	263	83	31.6	31.09 - 32.11
Not employed	138	52	37.7	36.81 - 38.59
Location				
Urban	206	74	35.9	35.29 - 36.51
Rural	195	61	31.3	30.61 - 31.99
Site				
Entebbe	168	57	33.9	33.13 - 34.67
Jinja	233	78	33.5	32.94 - 34.06
Overall herbal use	401	135	33.7	33.38 - 34.02

Table 2: Bivariate analysis of socio-demographic factors and herbal medicine use among HAART patients at TASO Uganda, during 2008

Variable	Used herbal N=135(%)	Not used herbal N=266 (%)	Unadjusted OR (95%CI)	P- value
Sex				
Male	33 (24.4)	88 (33.1)	1.00	**0.084**
Female	102 (75.6)	178 (66.9)	0.65 (0.41 – 1.05)	
Age (categorized at median age)				
18 – 38	56 (41.5)	155 (58.3)	1.00	
39 – 78	79 (58.5)	111 (41.7)	0.51 (0.33 – 0.77)	**0.002**
Religion				
Catholic	42 (31.11)	67 (25.19)	1.00	
Protestant	49 (36.30)	83 (31.20)	1.06 (0.63 – 1.79)	0.822
Muslin	15 (11.11)	58 (21.80)	2.42 (1.20 – 4.89)	0.010
Pentecost	24 (17.78)	53 (19.92)	1.38 (0.74 – 2.58)	0.303
Other	5 (3.70)	5 (1.88)	0.63 (0.17 – 2.23)	0.480
Marital Status				
Married	34 (25.2)	104 (39.1)	1.00	
Not married	101 (74.8)	162 (60.9)	1.91 (1.20 – 3.02)	**0.006**
Highest education level attained				
Primary	69 (51.11)	135 (50.75)	1.00	
Secondary	45 (33.33)	85 (31.95)	0.97 (0.61 – 1.54)	0.882
Tertiary	4 (2.96)	9 (3.38)	1.15 (0.34 – 3.88)	0.822
None	17 (12.59)	37 (13.91)	1.11 (0.58 – 2.12)	0.746
Occupation				
Self employed	62 (45.93)	133 (50.00)	1.00	
Salaried employed	21 (15.56)	47 (17.67)	1.04 (0.57 – 1.90)	0.889
None	30 (22.22)	53 (19.92)	0.82 (0.48 – 1.41)	0.481
Peasant	22 (16.30)	33 (12.41)	0.70 (0.38 – 1.30)	0.256
Site				
Jinja	78 (57.8)	155 (58.3)	1.00	
Entebbe	57 (42.2)	111 (41.7)	1.02 (0.67 – 1.55)	1.000

Table 3 Association between herbal medicine use and drug related factors among HAART patients in TASO using traditional herbal medicine, during 2008

Variable	Used herbal N=135(%)	Not used herbal N=266 (%)	Unadjusted Odds ratio (95%CI)	P- value
Duration on HAART				
4 years and more	25 (18.5)	33 (12.4)	1.00	**0.048**
3 years or less	110 (81.5)	233 (87.6)	1.79 (1.00 – 3.20)	
Ever experienced side effects				
No	50 (37.0)	146 (54.5)	1.00	**0.001**
Yes	85 (63.0)	121 (45.5)	2.04(1.33 – 3.12)	
Adherence level in the last 3 months*				
> 95%	56 (94.9)	79 (86.8)	1.00	0.163
75% – 95 %	3 (05.1)	12 (13.2)	0.35 (0.10 – 1.31)	
Respondent knows his/her CD4 counts				
No	46 (34.1)	93 (35.0)	1.00	0.912
Yes	89 (65.9)	173 (65.0)	1.04 (0.77 – 1.37)	
Respondent ever changed ART drug regimen				
Yes	130 (96.3)	62 (23.3)	1.00	
Can not tell	5 (3.7)	18 (9.0)	0.84 (0.16 – 4.46)	0.840
Perception of ARVs on wellbeing since initiation				
Not better due to complaints	35 (25.9)	52 (19.5)	1.00	
Better with improved weight gain	100 (74.1)	214 (80.5)	0.69 (0.43 – 1.13)	0.143
Dose of herbal medicine				
Half to 1 cup/glass	87 (64.44)	51 (19.17)	1.00	
1 – 2 spoons	39 (28.89)	21 (07.89)	0.92 (0.49 – 1.73)	0.793
No measurements	9 (06.67)	8 (03.01)	1.52 (0.55 – 4.20)	0.420
Duration on herbs while on HAART				
< 6 months	30 (22.22)	35(13.16)	1.00	
6 – 12 months	35 (25.93)	16 (6.02)	0.39 (0.18 – 0.86)	**0.016**
More than a year	70 (51.85)	29 (10.9)	0.35 (0.18 – 0.70)	**0.002**

Table 4 Individual factors associated with herbal medicine use among HAART patients in TASO using traditional herbal medicine, during 2008

Variable	Used herbal N=135(%)	Not used herbal N=266 (%)	Unadjusted OR (95%CI)	P- value
Disclosure of Status				
Yes	119 (88.1)	207 (77.8)	1.00	**0.014**
No	16 (11.9)	59 (22.2)	2.12 (1.17 – 3.85)	
Knowledge of ART				
Yes	134 (99.3)	262 (98.5)	1.00	0.667
No	1 (0.7)	4 (01.5)	2.05 (0.23 18.49)	
Ever changed regimen				
Yes	39 (28.89)	45 (16.92)	1.00	
No	96 (71.11)	221 (83.08)	2.00 (1.21 – 3.28)	**0.005**
Who advised you to start on herbs				
Friend	71 (52.59)	29 (10.90)	1.00	
Parents/ relatives	38 (28.15)	33 (06.77)	2.13 (1.11 – 4.06)	**0.020**
Own decision	26 (19.26)	18 (69.92)	1.69 (0.80 – 3.58)	**0.16**
Sexually active patients*				
Yes	100 (74.60)	120 (62.50)	1.00	
No	34 (25.40)	72 (37.50)	0.57 (0.35 – 0.92)	**0.023**
Patient's belief/perception of usefulness of ARVs				
ARVs not yet helpful	7 (5.20)	5 (1.90)	1.00	
ARVs helpful	128 (94.80)	261 (98.1)	0.35 (0.11 – 1.13)	0.116
Familiar with herbs				
Yes	135 (100)	218 (82.0)	1.00	**P < 0.001**
No	0	48 (18.0)	0.62 (0.577 – 0.67)	
Outcome expectation of Herbs				
Yes	135 (100)	62 (77.5)	1.00	**P < 0.001**
No	0	18 (22.5)	0.32 (0.25 – 0.39)	

*Missing values

Table 5 **Multivariate model for factors associated with herbal medicine use among HAART patients at TASO, during 2008**

Variable	Adjusted OR	95% CI	P-value
Age categorized (median)			
18 – 38	1.00		
39 –78	0.26	0.08 – 0.83	0.023
ART Adherence level			
75% – 95 %	1.00		
>95%	0.09	0.01 – 0.65	0.017
Herbs improved health			
Yes	1.00		
Can not tell	2.40	1.62 – 3.55	0.001
Duration on HAART			
4 years and more	1.00		
3 years or less	5.98	1.13 – 31.73	0.036
Ever experienced side effects			
No	1.00		
Yes	3.66	1.15 -11.68	0.028
Sexually active participant*			
Yes	1.00		
No	0.26	0.08 – 0.90	0.033

*Missing values