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ORIGINAL RESEARCH

Predictors of non adherence to antiretroviral therapy at an urban HIV care and treatment center in Tanzania

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Raphael Z Sangeda[1,2]
Fausta Mosha[3]
Said Aboud[4]
Appolinary Kamuhabwa[5]
Guerino Chalamilla[6,†]
Jurgen Vercauteren[2]
Eric Van Wijngaerden[7]
Eligius F Lyamuya[4]
Anne-Mieke Vandamme[2,8]

[1]Department of Pharmaceutical Microbiology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; [2]Department of Microbiology and Immunology, Rega Institute for Medical Research, Clinical and Epidemiological Virology, KU Leuven – University of Leuven, Leuven, Belgium; [3]Ministry of Health, Community Development, Gender, Elderly and Children, Dar es Salaam, Tanzania; [4]Department of Microbiology and Immunology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; [5]Department of Clinical Pharmacy and Pharmacology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; [6]Management and Development for Health (MDH), Dar es Salaam, Tanzania; [7]Department of General Internal Medicine, University Hospitals, KU Leuven – University of Leuven, Belgium; [8]Center for Global Health and Tropical Medicine, Unidade de Microbiologia, Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Lisbon, Portugal

[†]Dr Guerino Chalamilla passed away in November 2015

Correspondence: Raphael Z Sangeda
Department of Pharmaceutical Microbiology, Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania
Email sangeda@gmail.com

Background: Measurement of adherence to antiretroviral therapy (ART) can serve as a proxy for virologic failure in resource-limited settings. The aim of this study was to determine the factors underlying nonadherence measured by three methods.

Patients and methods: This is a prospective longitudinal cohort of 220 patients on ART at Amana Hospital in Dar es Salaam, Tanzania. We measured adherence using a structured questionnaire combining a visual analog scale (VAS) and Swiss HIV Cohort Study Adherence Questionnaire (SHCS-AQ), pharmacy refill, and appointment keeping during four periods over 1 year. Overall adherence was calculated as the mean adherence for all time points over the 1 year of follow-up. At each time point, adherence was defined as achieving a validated cutoff for adherence previously defined for each method.

Results: The proportion of overall adherence was 86.4% by VAS, 69% by SHCS-AQ, 79.8% by appointment keeping, and 51.8% by pharmacy refill. Forgetfulness was the major reported reason for patients to skip their medications. In multivariate analysis, significant predictors to good adherence were older age, less alcohol consumption, more advanced World Health Organization clinical staging, and having a lower body mass index with odds ratio (CI): 3.11 (1.55–6.93), 0.24 (0.09–0.62), 1.78 (1.14–2.84), and 0.93 (0.88–0.98), respectively.

Conclusion: We found relatively good adherence to ART in this setting. Barriers to adherence include young age and perception of well-being.

Keywords: self-report, appointment keeping, pharmacy refill, adherence barriers, resource-limited settings, AIDS

Background

Global funding programs on antiretrovirals (ARVs) have greatly helped resource-limited countries to reduce morbidity and mortality among HIV-infected individuals.[1] Furthermore, combination ARV therapy scale-up was accelerated by the availability of cheap generic ARVs in Brazil, India, Indonesia, Thailand, and other countries.[2]

However, therapy failure may occur because of lack of potency of combinations, insufficient drug adherence, interrupted ARV supply chains, transmission of drug-resistant virus, and development of resistance on therapy.[3–5] The emergence of HIV drug resistance (HIVDR) often confers cross resistance to other or all drugs of the same class[3] further complicating the epidemiology and transmission patterns of HIV especially in resource-limited settings. In such situations, optimizing adherence early on ensures better immunologic recovery and long-term virologic suppression.[6] In the perspective of HIV care continuum cascade, ART adherence plays a major role and is

placed after retention in HIV care stage. ART adherence is the primary determinant of viral suppression, consequently reducing the chance that persons living with HIV will transmit the virus by 96% and therefore prevent the development HIVDR.[7]

Adherence is defined as taking medications correctly and timely according to prescription by the health practitioner. The methods for assessing adherence and the level of adherence depend on the location, culture of the target population, and the method of adherence measurement used.[8]

Higher adherence levels have been shown repeatedly to correlate with longer efficiency of first-line regimens.[9–12] In sub-Saharan Africa, there are indications of higher or similar levels of adherence to ARV therapy (ART) regimens compared to developed countries.[13] In resource-limited countries, levels of self-reported adherence range between 78% and 96%,[14–16] and in some high-income countries they range from 44% to 66%.[7] Despite these high adherence levels, there are barriers to adherence levels that vary according to local circumstances. In Tanzania, patients with HIV and AIDS are known to interrupt ART because of poverty, stigmatization, poor access to ARVs, and traditional beliefs, which make patients seek alternative treatment from unregistered herbalists and traditional healers.[17,18] Moreover, patients not in free ART programs can purchase their drugs over the counter from different private pharmacies. Due to cost implications, these ARVs may often be dispensed with different therapy combinations or suboptimal doses.[17–19] This underscores the need for intervention, as it may contribute to emergence of drug resistance. However, there are only a few published reports on barriers to adherence in Tanzania. To appreciate the benefits of ART in improving the quality of life of HIV-infected patients, it is imperative to monitor and understand the factors underlying nonadherence.

The objective of this study was to assess the usefulness of sociodemographic, anthropometric, and immunologic factors as predictors of different measurements of adherence among HIV patients on ART in a resource-limited setting.

Patients and methods

Study design

This study was part of a single-center prospective cohort, enrolling HIV-infected adult patients attending a Care and Treatment Center (CTC) that provides ART and HIV/AIDS-related services free of cost. The study was conducted at Amana District Hospital in Dar es Salaam, Tanzania, a CTC offering services to 4789 HIV-infected patients, about 200 patients every day. Two hundred fifty-four patients were recruited into the study during the months of May to July 2010. Selection criteria were either starting ART or being on ART for more than 3 months. The selection of patients was through convenient sampling. Each day, the nurse conveniently referred 10–15 new unselected patients to be recruited into the study.[20] A total of 220 patients were included in the final analysis, of whom 24 started ART at study entry and 196 were on ART for more than 3 months.

Ethics statement

Issues pertaining to patient confidentiality, benefits and risks to participating patients, justice, and rights and respect that the patients deserve were addressed by ethical clearance and informed consent. The study was approved by the Muhimbili University of Health and Allied Sciences (MUHAS) Research Ethics Committee. We only recruited patients who were willing to participate in the study and who signed an informed consent prior to inclusion. Patient codes were used to delink the patient data in databases. There were no incentives offered for participating in the study.

Baseline data collection

We designed a structured questionnaire adapted from AIDS clinical trials[21] to collect data at study recruitment. The questionnaire was set up in English, and then translated to Swahili, using the Brislin translation model[22] in which questions were back-translated between English–Swahili–English in order to ensure valid translation. The questionnaire captured baseline information investigating sociodemographic factors (such as age, education, employment, distance from the hospital, and income), knowledge with respect to current ART (such as drugs and their dose), perceived health status, reasons for nonadherence, and social support network (such as number of other people aware of their HIV status, persons helping to remind regarding appointment, and taking pills). Adherence data were collected at the recruitment, and at the end of first, second, and 12th months of follow-up. Information about readiness, treatment support, and perceived health improvement for patients who were on treatment at study entry was collected at the recruitment. However, for those who started ART at study entry, this information was collected at the end of month 1 interview. Weight and height were derived from clinical records and used to calculate body mass index (BMI).

Adherence data collection

Adherence was measured using pharmacy refill, self-report, and appointment keeping methods, as described for each method. Adherence measurements by the visual analog scale

(VAS), Swiss HIV Cohort Study Adherence Questionnaire (SHCS-AQ), appointment, and clinical records were taken at four time points during a 1-year follow-up, including at recruitment (zero), 1, 2, and 12 months after recruitment.

For each method and time point, the adherence was defined as achieving adherence percentage above a predetermined cutoff. For each method, the overall adherence was defined as achieving the mean adherence above the cutoff for each method over the year of follow-up. The nonadherence cutoff was obtained by validating each adherence method against virologic outcome after 1 year of follow-up.[20] These optimal cutoffs significantly predictive of virologic failure were 95%, 80%, and 95% for VAS, appointment keeping, and pharmacy refill, respectively.[20] Numerical adherence values were dichotomized based on a validated cutoff, because the values are skewed toward 100.

Assessment by self-report

During the 1-year follow-up, self-report was measured using a validated questionnaire,[23] which was administered to assess patients who missed dosages over the previous 1 month at each of the four time points described previously.[20] The validated study tool consists of two major sections: 1) VAS, which probed the percentage of doses taken in the previous month; and 2) two questions from the SHCS-AQ regarding frequency of missed doses and whether a patient ever missed two consecutive doses (drug holiday) in the previous month. By definition, reporting missing of at least one ARV dose in the month preceding the interview was scored as nonadherent.[23]

Appointment keeping measurement

Appointment keeping was deduced from the electronic health records and database as previously described, where a cutoff <80% was used to define nonadherence as established by the validation of this adherence method using viral load measurement as a standard.[20]

Pharmacy refill adherence

Each refill period was identified as the interval between last visit date and the scheduled new date. Pharmacy refill adherence was calculated from the electronic pharmacy records as previously described, where <95% cutoff[20] was used to define nonadherence. All pharmacy records were retrieved from the same hospital where patients were scheduled to visit every month.

Clinic self-reported adherence

At each visit, nurse councilors interviewed patients about missing doses in the preceding visit interval. Nonadherence was noted in patient records if patients claim to consume less than 95% of the dispensed ARV pills. These records were retrieved for comparison with the above adherence measures.

Laboratory testing

CD4 T-cell count measurements

CD4 T-cell counts of study participants were obtained from the electronic health records. CD4 T-cell counts were determined using the FACSCalibur system (Becton Dickinson, San Jose, CA, USA). Testing was performed at intervals of 6 months at Amana District Hospital Laboratory and the measurement closest to the adherence measurement visit was included in the analysis.

Viral load testing

Viral load measurements are not routinely collected at the hospital. Therefore, at recruitment, blood samples were collected from each study participant. The whole blood sample was centrifuged at 1,500 rpm for 30 minutes; the plasma was aliquoted into triplet cryovials and frozen at –80°C until the time of the assay. Plasma HIV-1 RNA levels were determined using Cobas Amplicor HIV-1 monitor assay version 1.5 (Roche Molecular Systems, Branchburg, NJ, USA). The assay had a detection limit of 400–750,000 copies/mL using a standard protocol testing. Batch testing was performed at the Department of Microbiology and Immunology, MUHAS. Viral suppression or undetectable viral load refers to the presence of viral RNA below the detection limit of 400 copies/mL.

Data storage and statistical analysis

Data were recorded in a Microsoft Access database and analyzed using R-statistical package version 2.15.1.[24] Patients who had at least one adherence measurement were included in the analysis. Descriptive analyses including median interquartile range (IQR) for numerical variables, frequencies, and proportions for categorical variables were performed and tested for association using Fisher's and chi-square tests for categorical variables and Wilcoxon signed rank test for continuous values. A P-value of <0.05 was regarded as statistically significant. A logistic regression model was used to determine the association between the independent sociodemographic, anthropometric, immunologic, and virologic characteristics to the dependent dichotomized adherence outcome. Variables that were significant in univariate analysis were subjected to multivariate analysis. Results are presented as odds ratio (OR) and 95% CI.

Results

Of the 254 patients recruited into the study, 34 were excluded from analysis for various reasons. Four withdrew their consent to participate, one was under 18, two were pregnant, two did not provide self-reported adherence at any time point, 24 did not provide a baseline blood sample, and one was transferred to a new center before further interview. The remaining 220 patients were followed for a median (IQR) period of 12 (12–14) months, depending on the time of recruitment. Baseline characteristics of these 220 patients are represented in Table 1. Sociodemographic characteristics for all patients were collected at study entry. The respondents were predominantly female (63.6%), had median age of 39, and the majority (75.6%) had grade 7 education or less. Most respondents (81.9%) had no income or earned less than 50 euros per month. Only 42.2% of the respondents worked on salaried jobs as civil servants or in private companies. Fifty-six patients (25.6%) had a CD4 T-cell count less than 200 cells/μL.

Twenty-four patients (10.9%) started ART at study entry. The remaining had a median (IQR) duration of ART of 25(18–38) months. Of the respondents who were on ART at study entry, 170 (87%) had undetectable viral load

Table 1 Sociodemographic and treatment characteristics of study participants at Amana District Hospital, in Dar es Salaam, Tanzania (N=220)

Characteristics	Median (interquartile range)	N (%)
Age (years)	39 (34–47)	
Female gender		140 (63.6)
Weight (kg)	59 (51–69)	
Men	61 (54–68)	
Women	57 (50–70)	
Body mass index (kg/m^2)	23.2 (20.5–27.8)	
Marital status		
Married		100 (47.6)
Single/divorced/separated/widow		110 (51.4)
Religion		
Christian		99 (49.3)
Muslim		101 (50.2)
Education		
Up to grade 7		161 (75.6)
>Grade 7		52 (24.4)
Employment status		
Not mentioned		49 (22.3)
Never employed		34 (15.5)
Small-scale business		44 (20.0)
Civil servant		10 (4.5)
Private servant		83 (37.7)
Income (€ per month)		
None		75 (34.7)
<50		102 (47.2)
50–250		38 (17.6)
250–500		2 (0.9)
Currently consuming alcohol		107 (51.0)
Distance to CTC (km)	7 (3–8)	
Time since HIV diagnosis (months)	27 (18–43)	
WHO HIV disease staging		
1		12 (5.5)
2		39 (17.7)
3		148 (67.3)
4		21 (9.5)
CD4 T-cell count (cells/μL)	288 (198.5–465.5)	
CD4 T-cell count category		
<200		56 (25.6)
200–350		77 (35.2)
351–500		44 (20.1)
≥500		42 (19.2)
Viral load (log)	4.7 (4.1–5.2)	
Viral load category (copies/mL)		
>100,000		18 (8.2)
10000–100,000		19 (8.6)
2000–10,000		3 (1.4)
401–2,000		8 (3.6)
<400		172 (78.2)
Duration of ART (months)	23.5 (15.5–36)	
Has disclosed status to more than two relatives[a]		86 (41.7)
Discuss about medicines with family member[a]		92 (43.6)
Family member reminds to take pills[a]		89 (42.2)
Satisfaction with clinic services[a]		
Full		114 (54.3)
Half		33 (15.7)
Moderate		51 (24.3)
Less		12 (5.7)
Offer to share pills[a]		8 (3.8)
Use traditional medicine[a]		10 (4.7)
Reminder device used[a]		
Watch		93 (50.3)
Phone watch or alarm		63 (34.0)
Radio		10 (5.4)
Mosque "adhan"		3 (1.6)
TV		4 (2.2)
Combined		12 (6.4)
Agree that ART protects health[a]		208 (98.6)
Health condition after ART[a]		
Improved		140 (66.4)
Worsened/not changed		71 (33.6)

Notes: [a]Information about readiness, treatment support, and perceived health improvement for patients who were on treatment at study entry were collected at the first interview, for those who started therapy at study entry this information was collected at the second interview. All sociodemographic characteristics for all patients were collected at the first interview.

Abbreviations: ART, antiretroviral therapy; CTC, Care and Treatment Center; WHO, World Health Organization.

measurement. The mean VL for patients initiating ART was 252,900 copies/mL. A fixed combination of twice-a-day dose of Triomune-30, a coformulation of stavudine (d4T), lamivudine (3TC), and nevirapine (NVP), was the commonly dispensed therapy to 101 (45.9%) respondents. One patient received d4T + 3TC + efavirenz (EFV), and 97 patients (44.1%) were on combivir (zidovudine [AZT] + 3TC)-based therapy in combination with EFV, NVP, or abacavir (ABC) in 54, 42, and one patient(s), respectively. A combination of tenofovir–emtricitabine (TDF-FTC) was dispensed to 21 (9.5%) patients in combination with EFV or NPV. Patients who initiated ART at study entry did not change regimens in the course of their first year of treatment, while for those already on ART, the number of therapy changes since start of their therapy up to end of this study increased with therapy duration.

We could not interview all 220 patients at all four periods because of the logistics involved in tracking them monthly. A total of 62 patients could give responses at all interviews of these, and 36(58.1%), 24(32.3%), and 2(3.2%) were always adherent, sometimes adherent, and never adherent, respectively, according to VAS. In case of SHCS-AQ results, 40(64.5%), 21(33.9%), and 1(1.6%) patients were always adherent, sometimes adherent, and never adherent, respectively. However, on individual follow-up months, self-reported adherence ranged from 75.7% to 88.4% and 81.1% to 92.6% by VAS and SHCS-AQ methods, respectively (Table 2). Adherence measurements by appointment, pharmacy refill, clinical records, and overall adherence are shown in Table 2.

Of all 660 responses collected during the four interviews conducted during the study, 29(4.5%) reported to have taken drug holidays. The major reasons for nonadherence as reported by these patients were simply forgetting (52.1%) or traveling without medication (26.5%). Most nonadherent patients (64.1%) reported missing drugs only once in a month preceding the interview. Of the remaining, 10 (8.5%), 15 (12.8%), 16 (13.7%), and 1 (0.9%) missed doses once in 2 weeks, once in a week, more than once in a week, and every day, respectively.

Linear regression analysis showed that the two self-reported adherence measures (VAS and SHCS-AQ) correlate well with each other, while appointment keeping adherence and pharmacy refill adherence significantly correlated with each other ($P<0.05$). We could not correlate the clinic self-reported adherence, because all patients reported good adherence in all 4 months except one patient who reported nonadherence in the last interview, and therefore did not find this variable reliable enough to take it along in our further analysis. An interesting finding was that baseline virologic suppression of HIV-infected patients who were on ART at study entry (all >3 months) was significantly associated with good adherence measured by pharmacy refill adherence (Table 3).

There was no significant difference in any adherence measurement according to treatment regimen. In regard to sociodemographic factors, several were associated with likelihood of predicting overall good adherence by self-report, appointment, and pharmacy refill adherence (Table 4A). Although the significance of these factors differs based on the method used to measure adherence, in general, univariate analysis identified older age, less consumption of alcohol, more advanced World Health Organization staging, having education less than or equal to grade 7, perceiving ART benefits, and lower weight or BMI at recruitment as significant predictors of good adherence (Table 4A). Older

Table 2 Adherence scored according to self-report (VAS and SHCS-AQ), appointment, pharmacy refill, and clinical records

Time (months)	VAS[a]	SHCS-AQ[b]	Appointment[c]	Refill[d]	Clinical records[e]
	N (%)[f]	N (%)	N (%)	N (%)	N (%)
0[g]	140 (75.7)	150 (81.1)	163 (85.5)		185 (100)
1	142 (84)	148 (87.6)	144 (90.6)		113 (100)
2	107 (88.4)	112 (92.6)	104 (88.9)		116 (100)
12	137 (81.5)	145 (86.3)	142 (87.1)		155 (99.4)
Overall[h]	190 (86.4)	152 (69.0)	174 (79.8)	114 (51.8)	–

Notes: [a]VAS: nonadherent if self-reporting taking <95% adherence on the VAS in the month preceding the interview. [b]SHCS-AQ: scored nonadherent if forgot two consecutive doses or missing one or more doses in the last one month. [c]Appointment: nonadherent if delayed for >20% of scheduled days to appointment. [d]Refill: nonadherent if <95% of refills were made in the year of study. [e]Clinical records: nonadherent if reported taking <95% of their supply. [f]N: number of patients, % is expressed with respect to the number of records available, which may differ for each time point and measurement. For VAS, out of a total of 220 patients, 185, 169, 121, and 168 records were available at 0, 1, 2, and 12 months, respectively. [g]Month 0: no adherence parameters were recorded from patients who were starting therapy. [h]Overall adherence: scores average adherence parameter per patient according to criteria in columns c, e, and f. Overall SHCS-AQ adherence was calculated by scoring a patient nonadherent if so reported in any month.

Abbreviations: SHCS-AQ, Swiss HIV Cohort Study Adherence Questionnaire; VAS, visual analog scale.

Table 3 Association between adherence during the study and virologic suppression at study entry for patients already on treatment at study entry (all >3 months). Refer to Table 2 for definition of adherence measures a–h

Time (months)	VAS	SHCS-AQ	Appointment	Refill
	OR (CI) *P*-value	OR (CI) *P*-value	OR (CI) *P*-value	OR (CI) *P*-value
0	1.45 (0.53–3.69) 0.44	0.91 (0.25–2.64) 0.88	2.93 (0.95–8.26) 0.05	
1	1.84 (0.48–5.88) 0.33	0.41 (0.02–2.23) 0.41	2.72 (0.56–10.32) 0.16	
2	nd	nd	nd	
12	0.77 (0.17–2.54) 0.7	1.12 (0.25–3.79) 0.86	0.42 (0.02–2.27) 0.41	
Overall	2.25 (0.75–6.03) 0.12	0.77 (0.29–1.87) 0.58	1.52 (0.52–3.97) 0.41	2.34 (1.01–5.76) **0.05**

Notes: Significant association is shown in bold.
Abbreviations: nd, not defined (no patient was nonadherent and having detectable viral load); OR, odds ratio; SHCS-AQ, Swiss HIV Cohort Study Adherence Questionnaire; VAS, visual analog scale.

age and perceiving health improvement after ART significantly associated to undetectable viral load at study entry, considering only those already on ART. On contrary, the number of therapy changes and distance traveled by patients to the CTC were not identified as predictors of adherence. Similar results were obtained for individual months and methods.

In multivariate analysis (Table 4B), older age, less consumption of alcohol, more advanced WHO staging at start of ART, and low BMI at recruitment remained significant predictors of good adherence for at least one of the measurements.

Discussion

To our knowledge, this is the first longitudinal study examining different adherence measurement techniques and determining the predictors of nonadherence from an array of sociodemographic and anthropometric factors and biomarkers in a large cohort of patients on ART in Tanzania. The study population comprised of people with low income, low employment, and low education levels (only 24.4% had education above grade seven). Women constituted more than two thirds of the respondents, which is consistent with previous studies in sub-Saharan Africa.[14,25,26]

The proportion of respondents who reported consistently taking their medication during the study period is in agreement with other previous reports. Overall adherence was 86.4% and 69% of patients who had responded to VAS and SHCS-AQ, respectively. Studies that utilized self-reported adherence at a single time point in Tanzania indicated a prevalence of 70%–94%.[17,27–30] Multiple measurements were taken in one study in North Tanzania that tested the acceptability of medication event monitoring system (MEMS) bottles. That study indicated that the proportion of doses taken in 9–15 hours within specified time was 74%, 63%, and 62%, in three respective follow-up months.[31]

At the enrollment period, high levels of baseline virologic suppression were observed in 87% of HIV-infected patients who were already on ART for more than 3 months. This baseline virologic suppression (Table 3) is an indicator of good adherence in the future among patients on ART. It suggests that for patients who were already on treatment, having reached an undetectable viral load at study entry is significantly associated with pharmacy refill adherence during the study.

Moreover, these patients had a good immunologic profile with only a quarter of patients having CD4 T-cell count of less than 200 cells/μL.

The most cited reasons for nonadherence were forgetfulness and being away from home as documented also in other studies.[14,21,32,33] In other studies, forgetfulness has being linked to HIV-associated neurocognitive disorders and consequently to nonadherence to ART.[34] It is possible that, due to fear of stigmatization, patients would choose to skip their medication when in public and away from home.

Noteworthy, the clinic self-reports of adherence were much higher than self-reports determined using our questionnaire at coinciding time intervals. Most patients, who reported nonadherence by VAS or SHCS-AQ methods, registered an opposite response about adherence to the health care workers. This discrepancy may be due to fear that disclosure of nonadherence would subject them to negative reactions from the health personnel and get them deprived of treatment benefits.

The levels of self-reported adherence in this study are comparable to those in other resource-limited countries with adherence proportions at 96%, 82%, and 78% in Ethiopia, Kenya, and Cote d'Ivoire, respectively[14–16] and some high-income countries.[13,32] High levels of adherence in sub-Saharan Africa have been explained by a desire to stay healthy and preserving this wellness as a social capital to continue social and financial support from helpers, which include

Table 4 Univariate (A) and multivariate (B) association of significant sociodemographic and anthropometric factors by overall self-reported, appointment, and pharmacy refill adherence during the study and undetectable viral load at study entry

Characteristics	VAS		SHCS-AQ		Appointment		Refill		Undetectable viral load (at study entry)	
(A)										
	OR (CI)	***P*-value**	**OR (CI)**	***P*-value**	**OR (CI)**	***P*-value**	**OR (CI)**	***P*-value**	**OR (CI)**	***P*-value**
Age (per 10 years older)	2.38 (1.42–4.3)	<0.01	1.4 (1.01–1.98)	**0.05**	1.35 (0.92–2.02)	0.13	1.14 (0.85–1.54)	0.37	3.36 (1.82–6.84)	<**0.01**
Currently consuming alcohol	0.24 (0.09–0.66)	<0.01	0.23 (0.09–0.53)	<**0.01**	1.4 (0.5–5.02)	0.55	0.64 (0.27–1.47)	0.3	0.78 (0.27–2.86)	0.68
WHO staging at start of therapy (per one stage more advanced)	1.76 (1.01–3.04)	**0.04**	0.53 (0.29–0.94)	**0.03**	0.82 (0.48–1.34)	0.44	1.34 (0.91–2)	0.15	0.94 (0.5–1.68)	0.84
Having up to grade 7 education	2.54 (1.1–5.73)	**0.03**	1.56 (0.8–3)	0.18	0.33 (0.11–0.81)	**0.03**	1.21 (0.65–2.27)	0.55	1.32 (0.51–3.18)	0.55
Perceiving health improvement during ART	2.4 (1.06–5.49)	**0.04**	0.83 (0.44–1.54)	0.55	0.68 (0.31–1.41)	0.32	0.97 (0.55–1.72)	0.93	2.51 (1.09–5.87)	**0.03**
Body mass index at recruitment (per unit increase)	0.97 (0.92–1.03)	0.32	1.01 (0.96–1.06)	0.74	0.94 (0.89–0.99)	**0.02**	0.98 (0.93–1.02)	0.28	1.04 (0.97–1.14)	0.34
Weight at recruitment (per unit increase in kg)	0.96 (0.93–0.99)	**0.02**	1 (0.98–1.03)	0.85	0.99 (0.96–1.01)	0.36	0.99 (0.97–1.01)	0.26	1.01 (0.98–1.05)	0.45
(B)										
	AOR (CI)	***P*-value**	**AOR (CI)**	***P*-value**	**AOR (CI)**	***P*-value**	**AOR (CI)**	***P*-value**	**AOR (CI)**	***P*-value**
Age (per 10 years older)	3.11 (1.55–6.93)	<0.01	1.44 (0.97–2.18)	0.08	1.49 (0.95–2.41)	0.09	1.3 (0.93–1.85)	0.13	3.08 (1.59–6.64)	<0.01
Currently consuming alcohol	0.44 (0.14–1.50)	0.17	0.24 (0.09–0.62)	<0.01	1.42 (0.41–6.64)	0.61	0.64 (0.25–1.58)	0.34	1.63 (0.45–7.97)	0.49
WHO staging at start of therapy (per one stage more advanced)	1.71 (0.92–3.21)	0.09	1.78 (1.14–2.84)	**0.01**	0.81 (0.45–1.42)	0.48	1.32 (0.88–2)	0.18	0.82 (0.43–1.5)	0.54
Having up to grade 7 education	2.37 (0.85–6.47)	0.09	1.51 (0.72–3.13)	0.27	0.35 (0.11–0.93)	**0.05**	1.15 (0.58–2.27)	0.69	1.28 (0.43–3.5)	0.64
Perceiving health improvement during ART	1.48 (0.52–4.07)	0.45	0.66 (0.31–1.33)	0.25	0.7 (0.29–1.58)	0.4	0.9 (0.48–1.68)	0.74	2.15 (0.8–5.83)	0.13
Body mass index at recruitment (per unit increase)	0.94 (0.88–1.01)	0.09	1 (0.95–1.06)	0.99	0.93 (0.88–0.98)	**0.01**	0.97 (0.92–1.02)	0.23	1.06 (0.97–1.19)	0.28

Notes: Overall adherence used in this analysis was calculated as mean adherence of the four time points during 1-year follow-up. All baseline characteristics in Table 1 were subjected to univariate analysis using logistic regression. Any variable that was significant (*P*-value <0.05) in the univariate analysis was included in the multivariate analysis. The association of factors with undetectable viral load was only for those on treatment at study entry (all >3 months). WHO staging at the start of treatment was collected retrospectively for those who were already on treatment at study entry. Definitions of nonadherence and overall adherence are listed in Table 2. Significant *P*-values are shown in bold.
Abbreviations: AOR, adjusted odds ratio; ART, antiretroviral therapy; OR, odds ratio; SHCS-AQ, Swiss HIV Cohort Study Adherence Questionnaire; VAS, visual analog scale; WHO, World Health Organization.

family, friends, and health care workers.[26] Moreover, good adherence is also a result of free ART programs, maintained effort to continuous ARV supply chain and due to adherence counseling offered to patients before the start of ART and at each refill visit afterward. The provision of medications free of charge to the patients was associated with a higher probability of having undetectable viral loads at months 6 and 12 than with patients who pay part or all of the cost of ART.[35] In a study by Ramadhani et al,[30] it was shown that the proportion of months that patients paid for their ART was associated with incomplete adherence.

Using univariate and multivariate analyses, older age was found as a significant predictor of adherence to ART regimens. Age has been shown as an important predictor for adherence in other studies.[14,36–39] This can be explained by the fact that elderly patient may have survived earlier adherence barriers, and knowing the benefits of the survival, they choose to overcome nonadherence behavior. Due to peer pressure young people are faced with situations that lead them to nonadherence. Alcohol consumption was another barrier found to influence nonadherent behavior. The use of alcohol and drug abuse has been cited as barriers to good adherence in several settings.[40] Patients may skip medications after alcohol consumption out of fear of toxic interactions between the two. Not perceiving good health after starting ART, having more weight or body mass index at study entry, and having less advanced WHO clinical staging are factors related to health improvement but were negatively associated to adherence in this study. This suggests that patients who are asymptomatic are more likely to be nonadherent, contrary to symptomatic patients or those with low weight and CD4 T-cell counts. This suggests that disease severity plays a role in moderating adherence behavior. The sicker the persons the more serious they take their adherence. Thus, weight being taken by this setting is seen as the state of well-being. Such behavior with respect to appointment adherence has been reported before.[37,41]

We found a negative association between education and adherence, contrary to most other studies in low- and middle-income countries[42,43] and higher-income countries[36,44] that show a positive association between education and adherence. Such association has been shown in other studies before.[16,45–48] A possible explanation is that patients with higher education belong to the employed class that is busy with professional activities.[48] These people spend long hours in public places where they would be unable to take medication for fear of stigma. These patients may also lack time for refilling drugs because of fear of losing their jobs. However, this association of employment and adherence could not be justified from our data in which most patients belonged to the basic education group and were not employed. Consequently, at least in our setting, factors, such as lack of education, being homelessness, substance abuse, and mental illness, health care workers should, therefore, not be used by health care workers to withhold ART from these patients for reasons of doubting adherence.[21] Emphasis should rather be given on basic adherence education and counseling patients can improve adherence in people from both higher and lower education category.

In the current study, distance to reach the CTC and income were not predictive of nonadherence as found in previous studies conducted in Tanzania.[30] For instance, most patients in this study came from the radius of 7 km within the city limits given the availability of many CTC centers that have been established by the government. In regard to income, lesser cost implication will hold true as long as ARV distribution remains free to patients.

Strengths and limitations

The strength of the study was the fact that we used adherence cutoffs that were validated against virologic outcome in the longitudinal cohort. Moreover, we used several measures of adherence to detect the predictors or barriers of nonadherence. The limitation of the study is that we assess predictors of different measures of adherence, but each of these adherence measures have different objectivity.[49] Self-reported measurement is more popular but is limited by recall bias and overestimation of adherence. Pharmacy refill adherence is also likely to overestimate adherence even though it is associated with virologic outcome. Electronic drug monitoring methods have been closely associated with virologic failure, and despite underestimating adherence, the gold standard of adherence measurement may be limited by storage, ingestion of medications outside of the device, and cost implication in resource-limited settings. Another limitation is that, this is a single-center study in which a few patients had a number of missed follow-ups and missing data points and, therefore, another limitation of our findings is that it may not be generalizable to all settings.

Given the current adherence barriers, the government should educate health care workers to improve their patient relationships and confidence to patients and emphasize adherence counseling. If patients trust the health care personnel they can easily disclose their adherence behavior and allow appropriate intervention to be administered. Furthermore, adherence could be improved by introducing persistent counseling or modified directly observed therapy emulating similar successful programs in Haiti,[26,29,50] which ensures efficient use of ARVs with emphasis on young patients.

While adherence still remains good, sub-Saharan Africa will need to continue more emphasis on intervention and ART coverage and less in individualized clinical measurements like viral loads and CD4 T-cell count.[51] Use of adherence measure and knowledge of barriers to adherence can serve as indicator but not predictor of rising HIVDR levels without using expensive clinical measurements or genotyping. Costs saved by preventing HIVDR can continue to be directed into design of ART scale-up programs, patient retention, and adherence support.[38,52]

Conclusion

Patients in this setting have relatively good adherence, but adherence is influenced by factors such as young age and perception of well-being. Policy makers need to take these points into consideration in order to improve adherence counseling strategies to specific groups of patients receiving ART.

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