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Patterns of adherence to scheduling and dietary instructions among patients on antiretroviral therapy in Pretoria, South Africa

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Background: Adherence in antiretroviral therapy (ART) is the extent to which the HIV-infected person's behavior corresponds to the prescribed medical advice in terms of using antiretroviral (ARV) drugs. Adherence includes acts such as following instructions regarding dietary or fluid restrictions and taking medications at the prescribed time. This study aimed to determine the extent to which persons on ART followed the scheduling and dietary instructions of their ARV drugs.

Methods: This was a cross-sectional descriptive study among 232 adult HIV-infected persons on ART using the AIDS Clinical Trials Group questionnaire.

Results: Based on self-reported adherence, 89.6% (208/232) of the participants reported complete adherence with regards to taking their prescribed medications. The specific dosing schedule of their ARV drugs was strictly followed by 47.4% (110/232) of the participants. Of the 146 patients with specific dietary instructions on how to take their ARVs, only 43.1% (63/146) followed them all of the time, 10.9% (16/146) never followed these instructions and 45.8% (67/146) partially followed these instructions. Participants who were unemployed were twice more likely to adhere to ART dosing schedules compared to others (OR=1.75; CI 1.03–2.96; p=0.05).

Conclusions: Participants in this study were adherent to taking prescribed medications only. They were found to be non-adherent to instructions regarding dietary or fluid restrictions and medication prescription time.

Keywords: Antiretroviral therapy, Dietary instructions, Dosing instructions, Medication adherence

Introduction

Adherence among patients on antiretroviral therapy (ART) in developing countries, including South Africa, continues to pose challenges to the healthcare delivery system. However, various studies in sub-Saharan Africa have shown that high levels of adherence, viral suppression and good clinical outcome are achievable in these resource-limited settings.[1-3] It is challenging to adhere to ART due to the complexity of the drug regimen, dosage timings and dietary restrictions,[2,3] thus strict adherence is not common.[4]

Several studies in sub-Saharan Africa reported low adherence among patients on ART.[5-9] In a sample of 109 patients on ART in Botswana only 54% of patients were adherent by self-report. This percentage increased marginally to 56% when provider assessment was used.[5] In another study among 400 patients on ART in Ethiopia, 24% were non-adherent when combined indicators of dose, time and dietary instructions were used. The authors further reported that the level of non-adherence increased to 27% after a 3-month reassessment.[6] A Nigerian study reported that 75% of the study participants (on a subsidized ART program) were non-adherent.[7] Patients in this study cited various reasons such as antiretrovirals (ARV) side-effects, non-availability of ARVs and forgetfulness for their non-adherence.[7] In a study in KwaZulu-Natal (South Africa) 30% of patients, among 735 HIV-infected patients, were found to be non-adherent to dose, schedule and dietary instructions.[8] While another South African study revealed that only about 50% of patients on ART reported taking at least 95% of their prescribed ARVs.[9] The minimum acceptable required level of adherence is 95%,[10] thus the observed reported cases are considered inadequate. Adherence of 95% is necessary to minimize the development of viral resistance and to achieve the optimum benefit of ART.[10]

In general, most of the common ARVs have no dietary restrictions but they have to be taken at certain intervals for them to reach optimal levels in the body that can act against the virus.[10,11] The reason for dietary restrictions in ART emanated from the fact that some ARVs (e.g., didanosine and indinavir) are known to interact with food causing delay in the absorption of the drugs in the stomach, which often results in adverse

reactions.[11] Other drugs such as saquinavir and nelfinavir actually require food to be present in the stomach to enhance their absorption. Therefore, the food-drug interactions of a chosen ART regimen have to be fully explained to the individual to minimize potential adverse reactions that could arise from such interactions. This is very important to enable the person to adhere to such ARVs.[10,11]

Non-adherence to medication in ART is not limited to missing medication intake but also includes other acts like not following instructions regarding dietary or fluid restrictions and not taking ARVs at the prescribed time. This study was designed to assess adherence to dosing schedule and dietary instructions among patients on ART. The aim was to determine the extent to which patients on ART followed dosing and dietary instructions of their prescribed medications.

Methods

Study design

This was a cross-sectional descriptive study conducted between January and June 2011 at the Hope for Life Centre Winterveldt, a non-governmental organization that provides comprehensive HIV/AIDS services to HIV-infected patients in a northern suburb of Pretoria, South Africa. Participants were informed that the research aimed to determine the patterns of adherence to anti-retroviral therapy.

Sample size

With the assumption that the prevalence of adherence varies between 60 and 70% based on the information available, an exact binomial test with a nominal 0.050 two-sided significance level will have 87% power to detect the difference between the null hypothesis proportion, p_0 of 0.600 and the alternative proportion, p_A, of 0.700 when the sample size is 232.[12] A total of 232 HIV-positive persons were enrolled in the study from a cohort of 2312 individuals.

Sampling

Participants were systematically sampled from a pool of eligible 2312 individuals using the inclusion criteria of 18 years and above, no cognitive impairment as determined by the mini-mental state examination and being on ART for at least 1 year. All 2312 eligible participants were serially numbered and every tenth person was chosen to participate in the study. Where a selected participant declined to participate the next person on the list was included. No one in the study declined participation. Strict confidentiality and anonymity was ensured throughout the study. The research findings presented in this article constitute an aspect of the research approved by the Higher Degrees' Ethics Committee of Department of Health Studies, University of South Africa.

Data collection tool

The study made use of two semi-structured questionnaires written in English. These questionnaires were administered by trained research assistants who were fluent in the home languages of the participants (Sesotho and Setswana). Administration of the questionnaires was conducted in private rooms and at convenient times for the selected participants. The estimated time for completing the questionnaires was approximately 60 minutes. The first questionnaire explored patients' demographic and disease-related characteristics such as age, gender, marital status, education, occupation and social habits. Other information included in the demographic data questionnaire were length of time since HIV diagnosis, disclosure of HIV status, possible way of being infected with HIV, length of time on ART, number of pills taken daily and available social support in terms of treatment buddy.

The second questionnaire was the AIDS Clinical Trials Group Adherence questionnaire, a 5-item tool that assesses adherence to doses, scheduling and dietary instructions. This tool also assesses patient's reasons for missing medication or not adhering to dietary requirements. The reasons for missing medication were not assessed in the current study. Medication adherence was defined as the percentage of prescribed ARV drugs taken in any form within the previous 4 days. Dosing instruction adherence was defined as the percentage of medications for which the correct dosage instructions were followed at each prescribed dose. Dietary instructions adherence was defined as the percentage of medications for which the correct dietary instructions were followed at each prescribed dose.

The proportion of doses missed in the last 4 days was calculated for each participant, together with the extent to which they adhered to the prescribed dosing schedule of ART and to any special dietary instructions. Participants were asked about the number of ARV drug doses missed of a medication during each of the 4 days before a clinic visit. In addition, other aspects of adherence behavior were assessed with four questions regarding adherence to the daily schedule as follows: 'Most ARV medications need to be taken on a schedule, such as 2 times a day or 3 times a day or every 8 hours. How closely did you follow your specific schedules over the last 4 days?' and 'Do any of your medications have special instructions such as take with food or on an empty stomach or with plenty of fluids? If so, how often did you follow those instructions over the last 4 days?'. The ARV drugs used by the participants, their dosing schedules and dietary instructions are shown in Table 1.

Data analysis

The data was analyzed using Stata 12 (StataCorp, College Station, TX, USA). Descriptive statistics were presented first, followed by summary statistics of the variables (means were used for continuous variables and frequencies for categorical characteristics). In addition, χ^2 tests were undertaken to evaluate the association between adherence measures and the demographic characteristics. Logistics regression analysis was used to assess individual factors (odd ratios) that influence the adherence and non-adherence level. Finally, multivariable logistic regression was undertaken to assess the factors together to identify those factors that influence the adherence by looking at the adjusted odd ratios. Confounders and problem of multiplicity were controlled for and a p-value of <0.05 was considered to be statistically significant.

Results

The mean age of the study participants was 40 years (SD 15.6). The majority were female 70.2% (163/232), with 75.8% (176/232) 35 years and older, 60.7% (141/232) never married, 29.7%

Table 1. The antiretroviral (ARV) drugs used by the participants, their dosing schedules and dietary instructions in a study in Pretoria, South Africa

Antiretroviral drugs	Dosing schedule	Dietary instructions
Nucleoside reverse transcriptase inhibitors (NRTIs)		
Stavudine	Every 12 hrs	No dietary restrictions
Abacavir	Every 12 hrs	Avoid taking with alcohol
Lamivudine	Every 12 hrs	No dietary restrictions
Didanosine	Once daily	Dissolve tablet in water, take on empty stomach, or take 1 hr before or 2 hr after food
Zidovudine	Every 12 hrs	No dietary restrictions
Zalcitabine	Every 8 hrs	No dietary restrictions
Tenofovir	Once daily	No dietary restrictions
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)		
Nevirapine	Once daily for the first 2 weeks, then every 12 hrs	No dietary restrictions
Efavirenz	Once daily	Take at night to decrease central nervous system adverse-effects. Do not take with high-fat meals.
Protease inhibitors (PIs)		
Kaletra	Every 12 hrs	Take with meal to increase absorption
Indinavir	Every 8 hrs	Take on empty stomach or low-fat meal
Saquinavir	Every 8 hrs	Take with meal to increase absorption
Nelfinavir	Every 8 hrs	Take with meal to increase absorption

(69/232) had at least primary level education and 56.5% (131/232) were unemployed. The habits and disease-related characteristics of the participants are shown in Table 2. Of the participants 62.5% (145/232) did not consume alcohol, 97.8% (227/232) had disclosed their HIV status and very few had suffered adverse effects that would of required them to stop taking their medications 13.3% (31/232). The majority of participants had been living with HIV/AIDS for more than 3 years (55.6%; 129/232). Sexual intercourse with an HIV-infected person was the highest modality of contracting HIV (62.9%; 146/232). In terms of social support a good number of the participants (93.5%; 217/232) had treatment buddies who assisted them in adhering to medications and in keeping their clinic appointments.

Most participants adhered to medication intake i.e., ingestion of the ARV drugs and 89.6% (208/232) did not miss any of their prescribed doses over the previous 4 days. Only 47.4% (110/232) strictly followed the specific dosage schedule, 24.5% (57/232) never followed the dosing schedule while the remaining 26.7% (65/232) partially followed schedule instructions. Out of the 146 patients with specific instructions on how to take their ARVs (e.g., take with food, on an empty stomach or with plenty of fluids), only 43.1% (63/146) followed them all of the time, 10.9% (16/146) never followed these instructions and the remaining 45.8% (67/146) partially followed the instructions. Table 3 shows the breakdown of the adherence to medication intake, dosing schedule and dietary instructions of the participants.

As shown in Table 4, adherence to dosing schedule was only associated with unemployment (OR=1.75; CI 1.03-2.96; p = 0.05). Table 5 shows that adherence to dietary instructions was also not associated with employment status (OR=1.53; CI 0.76-3.06;

p=0.295), having a treatment buddy (OR=1.69; CI 0.48-5.65; p=0.532) and attainment of secondary level education (OR=0.96; CI 0.48-1.95; p=1.00).

Table 6 shows the summary of logistics regression analysis to determine some explanatory demographic and disease-related characteristics for medication adherence. Keeping all the other factors fixed, married participants were twice more likely to adhere to medication compared with the unmarried participants (OR=1.93; CI 0.98-3.78; p=0.041). Those diagnosed with HIV for more than 36 months were three times more likely to adhere to their medication (OR=3.1; CI 1.36-6.94; p=0.007) compared with those who were recently diagnosed. On combining all the factors in a multivariable logistic regression, only being diagnosed with HIV for more than 36 months still had significant association with medication adherence. The adjusted odd ratio was 2.38 with a standard error of 0.851 and 95% CI of 1.18-4.80 (p=0.015).

Discussion

This study examined the patterns of adherence to ART-related dosage scheduling and dietary instructions among a group of adult HIV-infected patients on treatment. Based on medication, the level of adherence among the study participants was high: self-reported adherence over the preceding 4 days was 100% in 89.6% (208/232) of the study participants. This is higher than the self-reported adherence rate of 50-77% reported among patients on ART in earlier studies.[3,10] Though the participants in this study were highly adherent to their medications majority did not follow the necessary instructions that required them to

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Table 2. Patients' habits and disease-related characteristics (n=232)

Variable	n (%)
Alcohol consumption	
More than once daily	4 (1.7)
Once daily	2 (0.9)
A few times per week	10 (4.3)
About once a week	30 (12.9)
Seldom	41 (17.7)
Never	145 (62.5)
Daily cigarette smoking	
None	204 (87.9)
1–4 sticks	13 (5.6)
5–9 sticks	10 (4.4)
10–14 sticks	4 (1.7)
>15	1 (0.4)
The most likely way(s) of acquiring with HIV	
Sex with HIV+ person	146 (62.9)
Shared needles with HIV+ person	1 (0.4)
Mother-to-child transmission	1 (0.4)
Occupation exposure to blood/body fluid	3 (1.3)
Sexual assault	5 (2.2)
Blood transfusion or medical procedure	1 (0.4)
Do not know	75 (32.3)
Disclosure of HIV status to family members	
Yes	227 (97.8)
No	5 (2.1)
Duration of HIV diagnosis	
Between 12–23 months	44 (18.9)
Between 24–36 months	59 (25.4)
>36 months	129 (55.6)
Do you presently have a treatment buddy	
Yes	217 (93.5)
No	15 (6.4)
Extent of treatment buddy's help in medication adherence	
Not at all	17 (7.3)
A little	2 (0.8)
Sometimes	64 (27.5)
A lot	134 (57.7)
Duration of ART use	
Between 12–23 months	30 (12.9)
Between 24–36 months	74 (31.8)
>36 months	128 (55)
ART adverse reactions that required medications stop	
Yes	31 (13)
No	201 (87)

ART: antiretroviral therapy.

take medication at certain intervals. They were non-adherent to instructions regarding dietary or fluid restrictions and did not take medication at the prescribed time. Non-compliance with prescribed medicines in ART has been linked to recurrent opportunistic infections, frequent hospitalization and poor clinical outcomes among patients.[13,14]

The current study showed that there was a positive and statistically significant association between ART medication adherence and being married, as well as having been diagnosed with HIV for more than 36 months. There was also a marginal association between adherence to dosing schedule and being unemployed. This implies that married persons and those with long standing HIV disease were more likely to adhere to medication intake. The participants' level of education and alcohol consumption did not influence their adherence to medication as shown in Table 6. Although socio-demographic characteristics have not been consistently correlated with treatment adherence in several studies, research has shown that socio-demographic factors could be used to identify particular populations that would benefit more extensively from targeted interventions that address specific barriers to adherence.[15,16]

This study also failed to find any association between ART adherence and adverse reaction to ARVs and non-disclosure of HIV status. The numerous and potentially debilitating adverse effects of ARV drugs have been shown to contribute to irregular drug use and deliberately stopping of medication intake by some patients.[6,7,17] Furthermore, substance abuse, fear of disclosure of HIV status and family responsibility have been found to be barriers to adherence.[3,18,19] In this study, medication adherence was not influenced by the quantity of pills the participants had to take every day. ART has been described as a complex treatment due to the pill burden, dietary and fluid restrictions and timing of medication intake. The complexity of the drug regimen is one of the causes of non-adherence among patients on chronic medications.[18] Pill burden is also a major challenge since multiple drugs are used in ART that need to be taken in a day together with other requirements like timing of dosages and food requirements.[19]

Treatment buddies are people who volunteer to assist patients to keep clinic appointments and remind them to take their medications as prescribed. Various studies have shown the benefits of social support in enhancing adherence among persons infected with HIV.[3,6,8,] Our studies did not find any association between having treatment buddies and medication adherence, but showed a link between marriage and medication adherence. Research has shown that marital status can sometimes influence adherence to ART,[7,20,21] although adherence among married HIV-infected persons is often lower than those who were never married.[8] The fact that adherence to dietary instructions was not influenced by any of the participants' socio-demographic and disease-related characteristics in this study should be interpreted with caution. We admitted that this may be due to a lack of power to detect any differences since the sample size of 232 was required for the study to be powered to detect differences and only 146 individuals with dietary instructions were actually sampled. Further research is needed in this area as our finding is only based on a small cohort of patients.

The current study indicated that married patients and those with long-standing HIV disease were those who were more likely to adhere to medications. The only demographic characteristic associated with adherence to dosing schedule was employment status. In conclusion, this study shows that participants were adherent to taking prescribed medications which is commendable,

Table 3. Participants' selected characteristics relative to antiretroviral (ARV) adherence in a study in Pretoria, South Africa

Variable	Medication adherence n=232		Dosing schedule n=232		Dietary instructions n=146	
	Non-adherent n=24	Adherent n=208	Non-adherent n=122	Adherent n=110	Non-adherent n=83	Adherent n=63
Age group						
<34 years	4 (7%)	52 (93%)	29 (52%)	27 (48%)	18 (53%)	16 (47%)
34–44 years	12 (12.0%)	88 (88.0%)	56 (56%)	44 (44%)	37 (62%)	23 (38%)
>44 years	8 (10%)	68 (90%)	37 (49%)	39 (51%)	28 (54%)	24 (46%)
Sex						
Male	9 (13%)	60 (87%)	33 (48%)	36 (52%)	23 (58%)	17 (42%)
Female	15 (9.2%)	148 (90.8%)	89 (54.6%)	74 (45.5%)	60 (56.6%)	46 (43.4%)
Marital status						
Never married	11 (7.8%)	130 (92.2%)	75 (53.2%)	66 (46.8%)	50 (57%)	37 (43%)
Other	13 (14%)	78 (86%)	47 (52%)	44 (48%)	33 (56%)	26 (44%)
Education						
≤Primary education	11 (16%)	58 (84%)	36 (52%)	33 (48%)	27 (57%)	20 (43%)
≥Secondary education	13 (7.9%)	150 (92.1%)	86 (52.8%)	77 (47.2%)	56 (57%)	43 (43%)
Employment						
Employed	8 (7.9%)	93 (92.1%)	61 (60.4%)	40 (39.6%)	33 (63%)	19 (37%)
Unemployed	16 (12.2%)	115 (87.8%)	61 (46.6%)	70 (53.4%)	50 (53%)	44 (47%)
Alcohol consumption						
Sometimes	11 (13%)	76 (87%)	45 (52%)	42 (48%)	24 (53%)	21 (47%)
Never	13 (8.9%)	132 (91.1%)	77 (53.1%)	68 (46.9%)	41 (49%)	42 (51%)
Source of HIV infection						
Sex with HIV+ person	20 (13.7%)	126 (86.3%)	70 (47.9%)	76 (52.1%)	50 (56%)	40 (44%)
Other	4 (5%)	82 (95%)	52 (60%)	34 (40%)	33 (59%)	23 (41%)
Number of pills consumed daily						
2–5	18 (9.5%)	172 (90.5%)	99 (52.1%)	91 (47.9%)	71 (58.2%)	51 (41.8%)
6–10	6 (14%)	36 (86%)	23 (55%)	19 (45%)	12 (50%)	12 (50%)
Adverse reactions						
No	22 (10.9%)	179 (89.1%)	101 (50.2%)	100 (49.8%)	68 (54.8%)	56 (45.2%)
Yes	2 (6%)	29 (94%)	21 (68%)	10 (32%)	15 (68%)	7 (32%)
Treatment buddy						
No	2 (13%)	13 (87%)	7 (47%)	8 (53%)	5 (45%)	6 (55%)
Yes	22 (10.1%)	195 (89.9%)	115 (53.0%)	102 (47.0%)	78 (57.8%)	57 (42.2%)
ART use						
12–23 months	3 (10%)	27 (90%)	18 (60%)	12 (40%)	11 (55%)	9 (45%)
24–36 months	6 (8%)	68 (92%)	42 (57%)	32 (43%)	26 (60%)	17 (40%)
>36 months	15 (11.7%)	113 (88.3%)	62 (48.4%)	66 (51.6%)	46 (55%)	37 (45%)
HIV+ status disclosure						
No	1 (20%)	4 (80%)	2 (40%)	3 (60%)	1 (33%)	2 (67%)
Yes	23 (10.1%)	204 (89.9%)	120 (52.9%)	107 (47.1%)	82 (57.3%)	61 (42.7%)
HIV diagnosis						
12–23 months	9 (20%)	35 (80%)	21 (48%)	23 (52%)	13 (65%)	7 (35%)
24–36 months	6 (10%)	53 (90%)	37 (63%)	22 (37%)	22 (59%)	15 (41%)
>36 months	9 (6.9%)	120 (93.1%)	64 (49.6%)	65 (50.4%)	48 (54%)	41 (46%)

ART: antiretroviral therapy.

but they were non-adherent to the instructions regarding dietary or fluid restrictions, and did not take medication at the prescribed time. Instructions adherence needs to be emphasized during ART adherence counseling among patients. In addition, larger studies that focus on factors influencing adherence to dosing scheduling and dietary instructions among patients on ART is required.

Table 4. Associations between certain demographic characteristics and adherence to dosing schedule

Variables	OR	95% CI	p-value
Being unemployed	1.75	1.03-2.96	0.047
Alcohol consumption	0.95	0.56-1.61	0.892
Consuming 2-5 pills daily	0.89	0.46-1.76	0.865
No adverse reactions to ARVs	0.48	0.23-1.07	0.083
Disclosure of HIV status	1.68	0.28-10.26	0.670
Having treatment buddy	1.29	0.45-3.68	0.791
Secondary education	1.02	0.58-1.79	1.00

ARVs: antiretrovirals.

Table 5. Associations between certain demographic characteristics and adherence to dietary instructions

Variables	OR	95% CI	p-value
Being unemployed	1.53	0.76-3.06	0.295
Alcohol consumption	1.17	0.57-2.42	0.714
Consuming pills 2-5 pills daily	1.39	0.58-3.35	0.504
No adverse reactions to ARVs	0.57	0.22-1.49	0.350
Disclosure of HIV status	2.69	0.24-30.33	0.578
Having treatment buddy	1.69	0.48-5.65	0.532
Secondary education	0.96	0.48-1.95	1.00

ARVs: antiretrovirals.

Table 6. Adjusted odds ratios (AOR) of the association between selected characteristics and medication adherence

Variables	OR	SE	95% CI	p-value
Known HIV status between 24-36 months	2.036	0.947	0.82-5.07	0.126
Known HIV status >36 months	3.075	1.277	1.36-6.94	0.007
Consuming alcohol more than once daily	0.598	0.206	0.31-1.17	0.136
Taking 2-5 pills daily	1.093	0.479	0.46-2.58	0.839
No adverse reaction to ARVs	1.570	0.889	0.52-4.76	0.422
Non-disclosure of HIV status	3.110	2.896	0.50-19.26	0.221
Primary education	1.590	0.567	0.79-3.19	0.193
Marital status (married)	1.928	0.663	0.98-3.78	0.041
Being employed	0.919	0.315	0.47-1.79	0.806

ARVs: antiretrovirals; SE: Standard error.

Study limitations

The use of a cross-sectional design to investigate adherence to HIV medication at a point in time limits the degree to which causal inferences and generalizations can be made from the research findings. Furthermore, this study was conducted in a public health facility that provides free ART services and psycho-social support to patients on ART. This might have influenced the responses of the participants and the high level of medication adherence reported in this study. Another limitation is the self-report questionnaire that was used. Self-report could be affected by participants' motivation, poor recall and social desirability. Therefore, adherence to ART may be over-estimated by participants and non-adherence may be underreported.

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