Patient factors impacting antiretroviral drug adherence in a Nigerian tertiary hospital

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ABSTRACT

Objective: To study the adherence levels and explore factors impacting them in out-patients on antiretroviral therapy (ART) at the AIDS Prevention Initiative in Nigeria antiretroviral clinic of the Jos University Teaching Hospital. **Materials and Methods:** We administered a structured questionnaire to 461 patients presenting to the clinic. Adherence was measured using the patient self-report. The association between independent variables and adherence to ART was measured through odd ratios (OR) in the univariate analysis. The best predictors of adherence were determined through multiple logistic regression models with backward elimination. **Results:** The adherence level was found to be 87.9%. The following factors were found to have strong impact on adherence in the univariate analysis: age (OR 1.04), sex (OR 1.14), employment (OR 1.29), knowledge of HIV (OR 1.11), thrice daily frequency of drug intake (OR 1.68), twice daily frequency (OR 2.18), alcohol nonintake (OR 0.29), knowledge of ARVs (OR 1.23), pill burden (OR 1.20), and HIV status disclosure (OR 1.08). In the multivariate analysis, only age, alcohol nonintake and twice daily, frequency of drug intake affected adherence (*P* < 0.05). **Conclusions:** To increase adherence and the effectiveness of ART, there is need to continuously emphasize the use of adherence devices and reminders. Counseling and adherence education should also be emphasized especially for younger patients and those with low educational levels.

Key words: Adherence, antiretroviral, HIV/AIDS, patients

INTRODUCTION

Human immunodeficiency virus infection (HIV) remains a worldwide health crisis. Nearly 40 million people infected, 95% of them in developing countries.[1] With a widespread use of antiretroviral (ARV) drugs, the once fatal disease is now a manageable chronic illness.[2] The drugs improve immune status, reduce viral load,[3] and incidence of hospitalization and mortality.[4] Patients also take medications for managing opportunistic infections with these drugs. These can add up to 16–20 pills daily, some requiring specific food or fluid restrictions. Furthermore, ARV drugs have side effects that may be temporary—nausea, vomiting, diarrhea or longer lasting—neuropathy, lipodystrophy.

All these increase adherence challenges for patients and healthcare providers. For the goals of highly active antiretroviral therapy (HAART) to be achieved, high levels of adherence are required; an adherent patient being one who takes >95% of prescribed drug doses.[5] Missing even a few doses of ARV medication can lead to HIV drug resistance.[6]

Adherence is dynamic, changing over time with significant

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proportions of patients not reaching good/high levels of adherence. Average estimates of ARV nonadherence in the US range from 50% to 70%.[5] Meta-analysis of African studies on adherence to ART in Sub-Saharan Africa in 12,116 patients indicated a pooled estimate of 77% with good adherence.[7] Adherence has been found to be 49.2% in the Niger-Delta region of Nigeria.[8]

There have been many approaches to assess adherence, but these are imperfect and lack established standards.[4] Some include client self-report, electronic monitoring devices, pill counts, and pharmacy refill data. Other approaches involve provider estimation and measurement of plasma drug concentration.[5]

Although patient self-reports, one of the strategies to assess adherence has been touted as being an unreliable predictor of adherence, a patient's estimate of sub-optimal adherence is a strong predictor and should be taken seriously.[9] In resource-limited settings, the use of hi-tech strategies like biological markers may be impracticable or expensive. This study highlights the importance of client self-reports and an appreciation of patient factors impacting antiretroviral therapy (ART) adherence in helping us put in place strategies to improve adherence.

MATERIALS AND METHODS

Study area and study population
The study was a prospective investigation of patient factors impacting adherence to ART carried out at the adult anti-retroviral clinic of the AIDS Prevention Initiative in Nigeria (APIN) Centre, in JUTH, Jos, Nigeria. Patients were receiving ARV drugs at the APIN centre from November 2009 to January 2010.

Sample size determination
The sample was calculated by setting the standard normal deviation at 1.96, with best guess of adherence at 50% and α level of 0.05. The calculation yielded 384 patients and allowing for 20% attrition rate, we have a total sample size of 461 patients.

Sampling
Ten patients were selected daily from the sampling frame (which was a daily list of 200–230 patients booked for appointment to the centre) by a simple random method using computer-generated random numbers.

Ethical considerations
Written informed consents were obtained from patients. The ethics committee of the APIN Centre and JUTH reviewed and approved the procedures through letter number JUTH/DCS/ADM/127/XXVI/1799.

Data collection
Questionnaire
A structured interviewer-administered questionnaire consisting of 24 questions was used. There were nine questions on socio-demographic data, four on patients' knowledge of HIV/AIDS, and three on patients' knowledge of ARV drugs, six on medication adherence, and two on drug side effects. Patients' medical records in the computer system were used to obtain information on drug regimen when the patient could not provide such information. A total of 461 patients from the study population were invited to complete a pretested questionnaire which recorded the personal data and variables in relation to adherence to prescribed medication after obtaining their consents. The questionnaire included 24 questions (There were nine questions on socio-demographic variables, four on knowledge and beliefs of HIV/AIDS, three on knowledge of the therapy, six on variables associated with medication adherence, and two on drugs side effects). The last part of the questionnaire recorded the patient's drug regimen. Adherence to treatment was assessed using patients' self-report. Good adherence to ART was defined as taking of greater than 95% of prescribed drug doses.

Inclusion criteria
All HIV-positive patients who have been on ART for at least 1 month and attending the clinic as well as all the patients on ART who consented to participate in the study.

Exclusion criteria
The following categories of patients were excluded from the study:
- All HIV-positive patients who were attending the clinic, but had not started ART.
- Patients who had been on ART for less than 1 month.
- All the patients who have not consented.

Statistical analysis
Data collected were analyzed using Epi-Info version 3.4.3, CDC, Atlanta, Georgia, USA. The magnitude of the association among the different variables in relation to adherence was measured through odds ratios (OR) and their 95% confidence intervals (CI). Determinants of good adherence were identified *via* a step-wise multivariate logistic regression model with backward elimination. All P < 0.05 were considered significant in all analysis.

RESULTS

A total of 461 respondents, males 160 (34.7%) and females 301 (65.3%) participated in the study. Of the respondents, 243 (52.7%) were married, 104 (22.6%) were single, 84 (18.2%) were widowed, 24 (5.2%) were divorced, and 6 (1.3%) are separated. Forty-six (10%) had no formal education, 94 (20.4%)

had primary education, 166 (36.10%) had secondary education, and 155 (33.5%) had tertiary education. A total of 154 (33.4%) were employed while 307 (66.6%) were unemployed at the time of interview. The level of knowledge about HIV infection and drug therapy were judged to be satisfactory 443 (96.1%) and 403 (87.4%) individuals respectively.

A total of 430 (93.3%) of the patients had disclosed their HIV status to friends or relations while 31 (6.7%) had not, though this was not associated with adherence to treatment. At the time of interview, 50 patients (10.8%) said they take alcohol, while the majority 411 (89.2%) do not. The majority, 346 (75.1%), did not belong to the social support group while 115 (24.9%) reported to belong to a social support group. Those who did not belong to a social support group had adherence ranging from 25 to 100% while respondents who belong to a support group had adherence ranging from 64 to 100%.

A total of 422 (91.5%) were on twice daily regimen, 32 (6.9%) on once daily regimen and 7 (1.5%) were on thrice daily regimen. As for pill burden, those taking two tablets a day were 178 (38.69%), three tablets a day 107 (23.2%), four tablets daily 68 (14.8%), five tablets daily 16 (3.5%), and eight tablets daily 4 (0.9%) patients.

A total of 156 (33.8%) respondents reported missed doses. The reasons for the missed doses are as reported in Table 1. A total of 120 (26.0%) respondents experienced side effects, with the commonest being skin rashes but this was not significantly associated with adherence.

Out of the 461 patients, 405 (87.9%) respondents had adherence >95% (95% CL 84.4–90.6%) while 56 (12.1%) had adherence <95% (95% CL 9.4–15.6%). Nonadherent patients were 56 (12.1%) with 95% CL being 9.4–15.6%. The 56 patients who were nonadherent were younger in age (mean age 33.7 years, standard deviation 6.640 with P value 0.0449). The adherent patients were older (mean age 36.4 years, standard deviation 9.5 with P value 0.0449).

Variables associated with adherence: Univariate analysis

Strong associations were observed between adherence and age, sex, employment, knowledge of HIV infection and knowledge of ARV drugs, pill burden, HIV status disclosure, twice daily regimen and alcohol non-intake were observed. Sex was associated with adherence but not statistically significant (OR 1.14, P-value 0.6673). Having a job was associated with good adherence but not statistically significant (OR 1.29; P-value 0.4141). The twice daily frequency of drug intake was associated with better adherence (OR 2.18, P-value 0.0859) than the thrice daily frequency (OR 1.68; P-value 0.6552). This was not statistically significant, but the trend was worth noting. Non-intake of alcohol protects against low adherence to ART and this was statistically significant. The age of a patient was statistically associated with adherence to therapy. Table 2 shows the crude OR for variables identified as predictors of adherence in the univariate analysis, the underlined P-values being significant.

Determinants of good adherence: Multivariate analysis

Multiple variables can affect a patient's adherence to ART at the same time. Therefore, all the statistically significant variables that were associated with adherence in the univariate analysis were included in a multivariate logistic regressions

Table 1: Reasons for missing doses (n = 156)

Reasons	N (%)
Forgot	65 (41.7)
Away from home	54 (34.6)
Too busy	12 (7.7)
Missing of clinic day	6 (3.8)
Unclear dosage instruction	6 (3.8)
Depression	3 (1.9)
Lack of transport fare	3 (1.9)
Religious fasting	3 (1.9)
Drug side effects	2 (1.3)
Hospitalization	1 (0.6)
Marital problems	1 (0.6)
Total	156 (100)

Table 2: Variables associated with adherence-univariate analysis

Variables	OR	95% Confidence limit	P-Value
Age	1.0351	1.0006 – 1.0707	0.0458
Sex	1.1398	0.6276 – 2.0703	0.6673
Employment	1.2921	0.6985 – 2.3902	0.4141
Knowledge of HIV Infection	1.1105	0.2485 – 4.9635	0.8908
Knowledge of ARVs	1.2276	0.5014 – 3.0056	0.6536
HIV Status Disclosure	1.0769	0.3626 – 3.1958	0.8939
Alcohol Non-Intake	0.2927	0.1461 – 0.5864	0.0005
Daily Frequency			
Twice	2.1817	0.8956 – 5.3145	0.0859
Thrice	1.6800	0.1724 – 16.5735	0.6552
Pill burden	1.1963	0.9772 – 1.4646	0.0825

OR: Odd ratios

Table 3: Variables associated with good adherence-multivariate analysis

Variables	OR	95% Confidence limit	P-value
Age	1.0504	1.0127–1.0895	0.0084
Twice daily frequency	2.7301	1.0480–7.1121	0.0398
Alcohol non-intake	0.2677	0.1305–0.5492	0.0003

OR: Odd ratios

model. The best determinants or predictors of good adherence were identified. This included only age, non-intake of alcohol, and twice daily frequency of drug intake (P -value for the interaction; 0.004, see Table 3).

DISCUSSION

This study showed an overall proportion of patients with good adherence to ART of 87.9%, which was significantly higher than that found in a similar study conducted in the Niger, Delta Region of Nigeria, in which the level of adherence to ART was determined to be 49.2%.[8] What accounted for the difference was the fact that the patients on ART in the APIN Centre get their ARV drugs and drugs for prevention and treatment of opportunistic infections free of charge, the patients in the Niger, Delta Region, had to pay for their drugs and most of them could not afford the costs. This resulted in the observed low adherence among other factors. However, the findings of this study agreed with the result of meta-analysis of African Studies on adherence to ART.[7] In addition, 33.8% of respondents reported missing doses in the previous month which was similar to the findings reported in a study in the USA.[5]

The commonest reasons for missing doses reported by the studied patients were forgetfulness, followed by traveling away from home, then being too busy, and unclear dosage instructions among others. This implies that the majority of nonadherent patients need medication adherence devices such as reminders, calendars, and strategies such as patient education and counseling. Other reasons for missing doses were depression, marital problems, drug side-effects, missing of clinic day due to lack of transport fare, hospitalization, and religious fasting.

This study also identified a number of variables which were associated with adherence in the univariate analysis such as age, sex, employment, knowledge of HIV infection and antiretroviral drugs, HIV status disclosure, alcohol intake, daily frequency of medication intake, and pill burden. It would be expected that increasing education which may increase knowledge of HIV and of antiretrovirals could increase adherence. Thus, persons with higher levels of education should be expected to have higher adherence. However, the best predictors as highlighted by multivariate analysis do not necessarily show this to be so. There were slightly two times more females in the study than males but even though the OR for sex was found to be 1.14, it is not statistically significant as the 95% CI (0.63–2.10) includes 1.0 with a P-value of 0.67. It was observed that the adherence

to medication was higher in older patients while low adherence correlate with the younger age.[10] This was demonstrated in this study. The adherence increased as the mean age increased. In the multivariate analysis, age was highly predictive of adherence with an OR of 1.05 and the 95% CI does not include 1.0 (95% CI 1.013–1.019). This was possibly due to the older patients' familiarity with correct medications usage and their increasing awareness of HIV infection as a disease that requires optimal medications adherence.[11] In addition, some studies have demonstrated that the male sex correlated with better adherence.[10] However, in this study, the female sex correlated with better adherence. This could be due to the fact that the majority of patients in this study were females. Social support helps the patients adhere better. However, in this study, belonging to a social support group was not associated with good adherence. This could be due to the fact that the majority of patients did not belong to the social support group.

Having an employment was associated with good adherence. This was because the employed patients have a source of income or money to transport them to clinic most of the time. HIV status disclosures were associated with good adherence. This could be due to the fact that the majority of patients had disclosed their HIV status to friends and relations and were taking their drugs openly and without fear of stigmatization. Alcohol intake was associated with low adherence while nonintake of alcohol was associated with good adherence, and this was statistically significant in this study. The majority of patients in this study did not take alcohol, and this protected against low adherence. Patients on ART who take alcohol have high tendency to forget to take their drugs. Frequency of drug intake was associated with adherence, and the twice daily frequency was more associated with adherence than the thrice frequency. This could be due to the fact that the majority of the studied populations (422 out of 461) were on the twice daily regimen. Older studies of medication adherence showed that once and twice dosing would give 95% medication adherence while the thrice dosing reduces it to 60%,[12] but the once dosing was surprisingly not associated with adherence in this study. This could be due to the fact that only few patients (7 out of 461) were on once daily dosing. Therefore, conclusions could not be made on the effects of frequency of drug intake on adherence to therapy in this study.

Generally, when patients take their drugs once or twice daily, they do not easily get fatigued. Finally, pill burden was associated with adherence though not statistically significant

($P > 0.05$). The smaller the pill burden, the better the adherence and *vice versa*. Difficulty in taking large number of pills can negatively affect adherence to therapy.[13]

CONCLUSION

The study shows that the antiretroviral drug adherence in out-patients on ART at the antiretroviral clinic in JUTH was low (adherence level was found to be 87.9%; 95% CL 84.4–90.6%). This is against the widely accepted standard of 95%.[5] It was also found that older patients (mean age 36.3) had better adherence compared to those that are younger (mean age 33.7). Frequencies of ARV drug intake and alcohol consumption were among other factors that affected level of adherence significantly. Given the demographic characteristics of the patients that attend this clinic the study directs attention to patient-specific factors for interventions that will improve adherence.

LIMITATIONS

The study was limited by the fact that adherence of patients who were just commenced on therapy could not be assessed as well as those lost to follow up. Another limitation was nonuse of virological and immunological laboratory investigations as well as the noninvestigation of the impact of the patient provider relationship on adherence.

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