

# Adherence to ART in PLWHA at Yirgalem Hospital, South Ethiopia

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## Abstract

**Background:** Non-adherence to Antiretroviral Therapy is a major challenge to AIDS care, and the risks associated with it are extensive.

**Objective:** To assess factors associated with non-adherence among AIDS patients receiving Antiretroviral Therapy at Yirgalem Hospital, Southern Ethiopia.

**Method:** A comparative cross sectional survey was carried out at Yirgalem Hospital between July 10 and August 30, 2006. The two-proportion formula for unmatched case control study with 1:3 ratio was used to calculate the sample size. Systematic sampling was used to recruit patients. Using a structured and pre-tested questionnaire, data on drug adherence were collected through interview and pill count. Non-adherent patients were compared with adherent patients and associations with key risk factors were determined.

**Results:** Two hundred and ninety one AIDS patients were involved in the survey. Prevalence of adherence in the week before interview was 74.2%. Main reasons of non-adherence cited by the patients were; being busy or simply forgetting (51%), change in daily routine (9.4%), and being away from home (8.3%). Non-adherence was commoner among patients reporting symptoms in the past four weeks (Adj. OR=6.41, 95% CI: 2.41 to 17.08), who lived more than 47 km away (AOR= 2.48, 95%CI: 1.24 to 4.98), or who had dependents (Adj. OR=1.95, 95%CI: 1.06 to 3.57).

**Conclusions:** Efforts must be made to make the service accessible by commencement of ART service in more Health Centers; to improve patients' awareness of ARV adverse effects; and to provide social support to all People Living with HIV, particularly those who have dependents. [*Ethiop.J.Health Dev.* 2008;22 (2):174-179]

## Introduction

The number of People Living with HIV/AIDS (PLWHA) in Ethiopia is about 1 million, with prevalence in the urban and rural population 7.7% and 0.9% respectively (1, 2). Provision of Antiretroviral Therapy (ART) in Ethiopia started recently. ART shortens illness duration, improves quality of life and survival of PLWHA through reduction of viral load and increasing the level of CD<sub>4</sub> cells (3, 4, 5). Median survival time increased from 18 to 58 months in Brazil when ART was introduced (3). However, lack of adherence to ART is a major challenge to AIDS care. Adherence is taking the correct dose of medications, on schedule, and following dietary instructions (5). Poor adherence is linked to the development of drug resistance, higher mortality rates, lower rates of increase in CD<sub>4</sub> cell count, lower rates of undetectable viral load, lower therapeutic success and increased hospital days (3, 6).

Twenty percent of the participants missed at least one dose of ARV in a community setting study in Atlanta, Georgia (7). Greater than 90% adherence was recorded in 57.6% in Madrid, Spain (8). A study in North West Spain revealed adherence greater than or equal to 95% reported by 55.7% of patients (4). Adherence was poor in 28%, fair in 23%, and excellent in 50% of study subjects (9). Women were less adhering than men and adherence was related to depression among drug users (10). A study in Brazil showed the cumulative incidence of non-

adherence to be 36.9% (11). Adherence among patients in Soweto, South Africa was 88% (12). In Cape Town; 63% of patients maintained adherence levels of 90%. Two studies in Ethiopia reported 81.2% and 82.8% adherence to more than 95% of doses (13, 14).

Many factors have been cited as reasons for non-adherence in studies of Western countries (15, 16). In African settings, patients have achieved excellent rates of adherence with subsidized ART (17, 18). Reasons reported for non-adherence in African studies include forgetting, travel, fear of disclosure, shortage of pills, difficult schedules, cost, lack of access and privacy (19). In two studies in Addis Ababa, being too busy/forgetting, travels, depression, drug adverse effects, treatment fitting to daily routine, relationship with health care providers, patients' perceptions of their doctors' capacities, perceived access to support from their ART unit, and reliable pharmacies, keeping clinical appointments, using memory aids, and educational levels were associated with ART adherence (13, 14). Consistent factors for poor adherence include patient reported symptoms, stress, lack of social support, substance use, regimen complexity, self efficacy for medication taking and depression (20). Gender, race, age, ethnicity and literacy have showed inconsistent results in predicting adherence (20). The objective of this study was to assess factors associated with non-adherence among People Living with HIV receiving Antiretroviral Therapy at Yirgalem Hospital.

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## Methods

The study was conducted at Yirgalem Hospital, which is a referral hospital in SNNPR, whose population is about 15 million. Yirgalem town is found 317 Km South of Addis Ababa. In April 2003, ART delivery was started at Yirgalem Hospital with aid from the Norwegian Lutheran Mission (NLM).

A comparative cross sectional survey was conducted from July 10 to August 30, 2006 among PLWHA on ART follow up at Yirgalem Hospital. Outpatients receiving ART, who were at least 18 years old, able to give informed consent, and not seriously sick, were included in the study. Patients were recruited using systematic sampling. Adherence to ART was the outcome variable; socio-demographic variables and other patient-related factors were exposure variables. Using the two-proportion formula for an unmatched case control study, and assuming a ratio of non-adherent cases to adherent controls of 1:3, a type I error of 5%, and a non-response of 10%, a sample size of 74 non-adherent patients & 222 adherent patients was calculated to give 80% power to estimate an Odds Ratio of 2.4 for a given exposure. In the study done at Addis Ababa, OR of 2.4 and 95% CI of 1.5-5.4 was calculated for depression. Therefore, considering resources, availability of patients and power of the study, an odds ratio of 2.4 was used in the calculation of the sample size for this study. The prevalence of depression was assumed to be 20% among the adherent group and 37.5% among the non-adherent group. The sample size required for the above assumption was 277, but to get an adequate sample size for determining the level of adherence as a second objective of the study with a precision of 4%, the sample size was raised to 291 (we have added 14 subjects).

The questionnaire was adapted from that used in an earlier study in Addis Ababa (13). Interview, pill count, and record review were the methods used to collect data. Health professionals working in the ART unit were trained to collect data, and collected data were checked daily.

Data were entered using EPI-info version 2002, and before doing the analysis, the entire data was cross checked for reliability. A score of at least 14 in the Beck's Depression Inventory was considered to represent depression, while below 14 indicated no depression as used in previous study (13). The inventory consisted 21 set of questions; each question in a pair had four options that were graded as an integer value from 0 to 3. Knowledge related to adherence was classified as 'good' if the respondents answered all questions correctly. Medication adverse effect was defined as an unwanted effect caused by the administration of drugs. Distance was defined as the estimated distance of patient residency from Yirgalem Hospital measured in Km. Bivariate and multivariate logistic regression analysis were done with

SPSS statistical package. The strength of association was measured using Odds Ratios.

Ethical clearance was obtained from the Faculty of Medicine, AAU. A letter of permission was obtained from the concerned offices. After obtaining consent from each patient interview was done in a separate room in order to maintain privacy. Questionnaires were anonymous.

## Results

Two hundred and ninety one patients receiving ART participated; five patients were excluded because of sickness, deafness or refusal; thus the response rate was 98.3%. The mean (SD) age was 35.4 (8.5) years. About 52% of the participants were male, 43.3% were Amhara, and 57% were Orthodox. The proportion who were single was high (48.1%). More than half (54.6%) of the participants had attended high school and 12% had a diploma or higher level of education. The majorities (92.4%) were gainfully employed, though 54.3% reported earning less than 500 birr per month (Table 1).

Only 3.8% reported active substance use. Twenty-two percent claimed they had no social support and 88.3% had disclosed their sero-status; 18.6% fully and 69.8% partially. Only 5(1.7%) were found to be depressed. Thirty two percent knew the benefits of the regimen before starting ART and 94.1% thought that ART had benefited them by improving their quality of life or improving their symptoms. Initial and most recent mean CD<sub>4</sub> counts were 120.93 and 286.37 /mm<sup>3</sup> respectively. The average treatment duration was 10.2 months.

The commonest reported symptoms in the past month were lethargy, numbness, headache, abdominal pain, and fever or chills. Other symptoms were experienced by less than 10% of patients. However, if all reported symptoms are included, 73.2% of the respondents experienced at least one symptom in the past month. Thirteen percent had an adverse reaction to ART like skin rash, itching, nausea or vomiting, since starting ART.

The proportion of participants with good knowledge about adherence, ART benefits and ART eligibility was 68%, 28.2% and 57.7% respectively. More than half (52.2%) had no discomfort when taking their drugs in front of others. For 96.9% of the patients, the regimen was fitted to their daily routine. Almost all (98.6%) had a good relationship with and 82.1% felt they had open discussion with their doctors (Table 2). More than 99% were satisfied with the benefit they had obtained from ART, and with the ART unit appointment system, with 84.8% reporting regular follow up. At the time of the survey, 52.6% of patients had at least one child under their care, and of these, 11.1% were known to be sero-positive, 25.5% sero-negative, while 63.4% had not been tested.

Table 1: **Basic Socio-demographic and Psychosocial characteristics of PLWHA involved in the study, Yirgalem Hospital, South Ethiopia, 2006**

| Variables                           | Variable          | Number | Percent |
|-------------------------------------|-------------------|--------|---------|
| <b>Sex</b>                          | Male              | 152    | 52.2    |
|                                     | Female            | 139    | 47.8    |
| <b>Age</b>                          | 18-24             | 21     | 7.2     |
|                                     | 25-45             | 240    | 82.5    |
|                                     | >45               | 30     | 10.3    |
|                                     | Single            | 140    | 48.1    |
| <b>Marital status</b>               | Married           | 49     | 16.8    |
|                                     | Widowed           | 72     | 24.7    |
|                                     | Divorced          | 12     | 4.1     |
|                                     | Separated         | 18     | 6.2     |
|                                     | Illiterate        | 26     | 8.9     |
| <b>Education</b>                    | Read & write      | 6      | 2.1     |
|                                     | Elementary        | 65     | 22.3    |
|                                     | Secondary         | 159    | 54.6    |
|                                     | Diploma and above | 35     | 12.0    |
|                                     | ≤500              | 158    | 54.3    |
| <b>Income (Birr)</b>                | 501-999           | 33     | 11.3    |
|                                     | ≥1000             | 29     | 10.0    |
|                                     | Unstated (0)      | 71     | 24.4    |
|                                     | Work active/      | 269    | 92.4    |
| <b>Work/Employment</b>              | Employed          |        |         |
|                                     | Unemployed        | 22     | 7.6     |
|                                     | Yes               | 282    | 96.9    |
| <b>Belief on ARV Benefits</b>       | No                | 8      | 2.8     |
|                                     | Not sure          | 1      | 0.3     |
| <b>Perceived self Efficacy</b>      | Yes/ No           | 290    | 99.7    |
|                                     | Doubt             |        |         |
| <b>Substance use</b>                | No                | 1      | 0.3     |
|                                     | Yes               | 11     | 3.8     |
| <b>Type of substance use (n=11)</b> | No                | 280    | 96.2    |
|                                     | Alcohol           | 4      | 36.4    |
|                                     | Smoking           | 1      | 9.1     |
|                                     | Kcat              | 6      | 54.6    |

Adherence level in the week before assessment was 74.2% (no dose missed or delayed for greater than or equal to 90 minutes), while 26.1% did not follow treatment schedule and 5.5% did not follow instructions. The main reason for skipping or delaying doses was forgetting (51% of those non-adherents) (Fig 1).

Non-adherent patients and those who had been adherent were compared on key demographic, health, mental health, and social factors. Results of univariate logistic regression analyses showed that medication adverse effect (OR 6.85; 95% CI 2.65, 17.72), distance (OR 2.19; 95% CI 1.44, 5.25), adherence knowledge (OR 2.17; 95% CI 1.26, 3.77), satisfaction with social support (OR 1.87; 1.03, 3.40), and schedule fitting to daily routine (OR 3.94; 95% CI 1.03, 15.07) were more likely to be associated with adherence. Multivariate logistic regression, however, indicated that medication adverse effect, distance of ART clinic from residence and

presence of dependents had significant independent associations with treatment adherence (Table 4). Those with medication adverse effect were over 6 times more likely to be non-adherent than those with out medication adverse effect. Those who live in less than or equal to 47 Km were nearly 2.5 times more likely to adhere than those who live in greater than 47Km and those with dependents were 1.95 times more likely to be non-adherent than those with out dependents.

Table 2: **Treatment, clinical, and health service related variables of PLWHA involved in the study, Yirgalem Hospital, South Ethiopia, 2006**

| Variables  | Number | Percent |
|--|--------|---------|
| <b>Treatment duration (month)</b>                      |        |         |
| 1-6  | 103    | 35.4    |
| 7-12   | 103    | 35.4    |
| 13-24  | 71     | 24.4    |
| 26-36  | 14     | 4.8     |
| <b>ART benefit knowledge</b>                           |        |         |
| Good   | 82     | 26.8    |
| Unsatisfactory   | 209    | 73.2    |
| <b>ART eligibility knowledge</b>                       |        |         |
| Good   | 168    | 57.7    |
| Unsatisfactory   | 123    | 42.3    |
| <b>ART adherence knowledge</b>                         |        |         |
| Good   | 198    | 68.0    |
| Unsatisfactory   | 93     | 32.0    |
| <b>Perceived satisfaction in relationship with HCP</b> |        |         |
| No   | 287    | 98.6    |
| Yes  | 2      | 0.7     |
| Not sure   | 2      | 0.7     |
| <b>Perceived access to pharmacy</b>                    |        |         |
| Yes  | 284    | 97.6    |
| No   | 7      | 2.4     |
| <b>Number of minutes delayed</b>                       |        |         |
| <30  | 214    | 73.5    |
| 30-89  | 36     | 12.5    |
| ≥90  | 41     | 14.1    |

HCP=Health Care Provider

Table 3 **Patients who missed at least a dose by Self-report and Pill count, Yirgalem Hospital, South Ethiopia, 2006**

| Number of days         | Yes        | No         | Total Number (%) |
|------------------------|------------|------------|------------------|
|                        | Number (%) | Number (%) |                  |
| <b>Previous day</b>    | 4 (1.4)    | 287 (98.6) | 291 (100)        |
| <b>Past three days</b> | 6 (2.1)    | 285 (97.9) | 291 (100)        |
| <b>Past seven days</b> | 34 (11.7)  | 257 (88.3) | 291 (100)        |

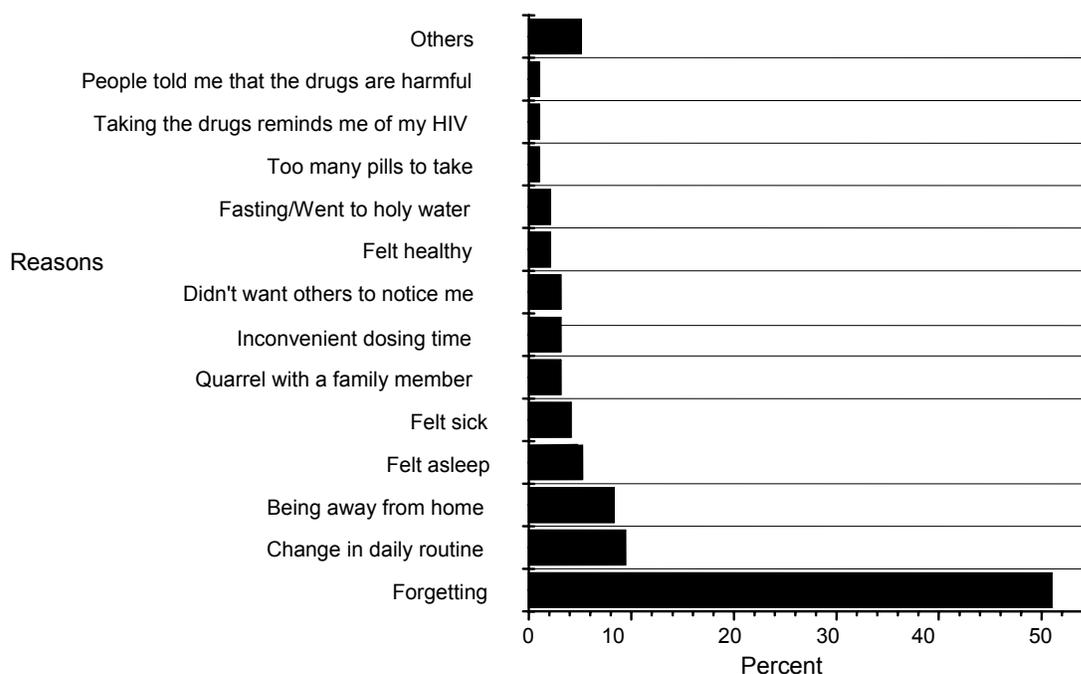


Figure 1: Reasons for non-adherence reported by patients, Yirgalem Hospital, South Ethiopia, 2006

Table 4: Association of variables with adherence among the study participants, Yirgalem Hospital, South Ethiopia, 2006

| Variables                                     | Non Adherent | Adherent | Crude OR, 95% CI   | Adjusted OR , 95% CI |
|---|--------------|----------|--------------------|----------------------|
| <b>Medication adverse effect/HIV symptoms</b> |              |          |                    |                      |
| No  | 68           | 145      | 6.85 (2.65, 17.72) | 6.41 (2.42, 17.18)** |
| Yes   | 5            | 73       | 1.00               | 1.00                 |
| <b>Address (Distance to health facility)</b>  |              |          |                    |                      |
| >47 km  | 34           | 62       | 1.00               | 1.00                 |
| ≤47 km  | 39           | 156      | 2.19 (1.44, 5.25)  | 2.48 (1.24, 4.98)*   |
| <b>Caring for children</b>                    |              |          |                    |                      |
| No  | 42           | 111      | 1.00               | 1.00                 |
| Yes   | 31           | 107      | 1.31 (0.77, 2.23)  | 1.95 (1.06, 3.57)*   |
| <b>Depression</b>                             |              |          |                    |                      |
| No  | 1            | 4        | 1.00               | 1.00                 |
| Yes   | 72           | 214      | 0.74 (0.15, 12.23) | 3.51 (0.01, 920.87)  |
| <b>Knowledge on ART benefit</b>               |              |          |                    |                      |
| Unsatisfactory                                | 53           | 156      | 1.00               | 1.00                 |
| Good  | 20           | 62       | 1.05 (0.58, 1.91)  | 2.05 (0.85, 2.76)    |
| <b>Knowledge on ART eligibility</b>           |              |          |                    |                      |
| Unsatisfactory                                | 38           | 85       | 1.00               | 1.00                 |
| Good  | 35           | 133      | 1.70 (0.996, 2.90) | 2.46 (0.92, 6.57)    |
| <b>Knowledge on Adherence</b>                 |              |          |                    |                      |
| Unsatisfactory                                | 33           | 60       | 1.00               | 1.00                 |
| Good  | 40           | 158      | 2.17 (1.26, 3.76)  | 1.77 (0.85, 2.76)    |
| <b>Satisfaction with social Support</b>       |              |          |                    |                      |
| No  | 23           | 43       | 1.00               | 1.00                 |
| Yes   | 50           | 175      | 1.87 (1.03, 3.40)  | 0.39 (0.24, 40.99)   |
| <b>Schedule fitting daily routine</b>         |              |          |                    |                      |
| No  | 5            | 4        | 1.00               | 1.00                 |
| Yes   | 65           | 214      | 3.94 (1.03, 15.07) | 0.39 (0.24-40.99)    |

## Discussion

Adherence in this study was found to be higher than in most developed countries, where rates ranged from 50% to 70% (8, 9). It was lower than that reported in Soweto, South Africa, but was higher than that reported in Cape Town. The level of adherence was comparable with those reported in Addis Ababa (81.2% and 82.8%) (13, 14). In the Addis Ababa studies, adherence level was determined for missing doses. The adherence level for patients who missed doses in our study was 88.7% which is slightly higher than the values reported in Addis Ababa. This may suggest that adherence in regional setting is better than central settings and that patients of low socio-economic status are able to achieve excellent rates of adherence with subsidized ART. Only one quarter of the Addis Ababa study population reported income of less than 500 birr per month (13) whereas more than half of our study population earned less than 500 birr per month.

We assessed adherence through self-report and pill count. Self-reporting may overestimate the rate of adherence to medication (5, 15). For the few patients who did not bring pills, self-estimation was done. Even though this type of approach is not as objective as counting of pills by the data collector, it provides useful additional information. Comparison of data collected using each method showed that the information gathered using the two approaches was consistent.

Presence of symptoms in the past month, distance of residence, and presence of dependents were all significantly associated with adherence in the multivariate analysis. Certain of these factors have been associated with adherence in other studies (20). The odds of adherence among those who came from a distance of less than or equal to 47 Km was about 2.5 times higher than that among those who came from greater than 47 Km. Distance may have an effect on the timing of appointments for patients. Patients from far away may not have frequent and regular follow up, probably due to transport and time costs. Lack of frequent follow up may lead to obtaining less information about adherence. This suggests that patients would benefit if ART services were available in more institutions located closer to beneficiaries' homes.

Social support may enhance adherence through encouragement, reassurance, reinforcement, systematic cues, bolstering of competence, and motivation, or by masking the effect of stress, anxiety, and depression (13). Social support was not significantly associated with adherence in the multivariate analysis. This may be due to the effect of confounders. Equally, depression was not associated with adherence, again, probably because only a very low proportion (1.7%) of patients scored above 14 on the Beck's Depression Inventory. In other studies, depression has been an important predictor of adherence (13, 20). Patients attending ART at Yirgalem Hospital appear to be a selected group of relatively healthy,

educated, affluent individuals, many of whom choose to attend from far away. More than 90% were actively at work, and 97% express high self-efficacy.

In agreement with studies in Brazil, Senegal and Addis Ababa, medication adverse effects were a significant predictor of adherence in this study (11, 13, 18). When asked a general question, only 13.7% patients reported experiencing medication adverse effect since the beginning of ART, but paradoxically, when asked closed questions about specific symptoms, 73.2% of respondents reported at least one symptom in the past month. Patients may not be aware that these symptoms are medication adverse effects; or patients may have been accepting adverse drug effects due to the physical, social, and emotional morbidity associated with AIDS patients. Adherence is usually increased by letting patients know at the outset which side effects are possible with a given regimen and monitoring for such effects, when they are most likely to be troublesome (15). Patient education on the adverse effects and adherence counseling are important.

The odds of adherence among those who did not have dependents was 1.95 times higher than among those who had dependents. PLWHA who had children may forget to take pills due to being busy or due to the stress of caring for their child. The leading reason of non-adherence reported by patients was being busy or simply forgetting. Social support and using reminders for these patients may reduce the problem. In contrary to the study done in Addis Ababa, convenience or perceived "fit" of medication regimens with daily routine was not significantly associated with improved adherence in our study. This may be due to very low numbers of patients who considered their medication regime not to be convenient in our study. Other variables like knowledge of ART benefit, knowledge on ART eligibility, and adherence knowledge which were significant predictors of non adherence in other studies did not show association with non adherence in our study. Confounding variables might have masked their real effect on non-adherence. The reasons patients cited for missing doses or delays in dosing time in our study were almost identical to those found in other studies (13, 19).

Based on the results we recommend that efforts be made to make the service accessible by commencement of ART service in more health centers to increase patients' awareness of the adverse effects of ARV and manage them, and to provide social support to all PLWHA and particularly to those caring for children.

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