Factors affecting antiretroviral treatment adherence among people living with human immunodeficiency virus/acquired immunodeficiency syndrome: A prospective study

Bharatesh D. Basti¹, Venkatesha Mahesh², Dattatreya D. Bant³, Geeta V. Bathija³

¹Department of Community Medicine, PESIMSR, Kuppam, Andhra Pradesh, ²Department of Community Medicine, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, ³Department of Community Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India

ABSTRACT

Context: Antiretroviral adherence is the second strongest predictor of progression to acquired immunodeficiency syndrome (AIDS) and death, after CD4 count. Adherence to antiretroviral therapy (ART) has been strongly correlated with human immunodeficiency virus (HIV) viral suppression, reduced rates of resistance, an increase in survival, and improved quality of life. Aims: To determine the adherence rates and factors affecting adherence to ART among people living with HIV/AIDS (PLWHA). Settings and Design: A Prospective study for 1 year was conducted among PLWHA, aged between 15 and 49 years, visiting ART center. Subjects and Methods: 242 PLWHA were included in the study. Structured questionnaire was used to obtain data on sociodemographic profile, factors affecting adherence. Adherence was assessed through self-reports, routine and random pill counts, and assessment of medical records. Statistical Analysis Used: Descriptive statistics, logistic regression, and Chi-square tests were computed using Epi Info 7 version CDC (Centers for Disease Control and Prevention) U.S. Department of Health and Human Services. Results: Adherence to ART was finally assessed on 242 PLWHA. Mean age of subjects was 35 ± 7.8 years. One hundred percent adherence rate (consistent adherers) for the whole 6 month period was seen only in 31.6% patients. Lower 6 month averages of 95–100%, 80–95%, and <80% were noted in 49.8%, 9.1%, and 9.5% patients, thus resulting in optimal adherence rate of >95% in 81.4%. Earning member (odds ratio [OR] =0.404) and weight difference (OR = 0.818) were most associated with the adherent individuals. Most common psychological reason was forgetfulness in 44.9%. Conclusions: Adherence rate was poor among PLWHA and economic factors play an important role in adherence.

Keywords: Adherence rate, determinants of adherence, people living with human immunodeficiency virus/acquired immunodeficiency syndrome

Introduction

Human Immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) has evolved as a major global public health problem with social and economic repercussions assuming pandemic proportions.[¹] Its estimated globally more than 71 million were infected with HIV as on December 2014, and nearly 36.9 million people were living with HIV/AIDS worldwide. Approximately, 4 million in the low- and middle-income countries were receiving antiretroviral therapy (ART).[²] There has been a notable 10-fold increase in these figures over the last 5 years.[³]

This is an open access article distributed under the terms of the Creative Commons Attribution NonCommercial ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Access this article online

Quick Response Code:
Website: www.jfmpc.com
DOI: 10.4103/2249-4863.222014

How to cite this article: Basti BD, Mahesh V, Bant DD, Bathija GV. Factors affecting antiretroviral treatment adherence among people living with human immunodeficiency virus/acquired immunodeficiency syndrome: A prospective study. J Family Med Prim Care 2017;6:482-6.
India carries the world’s third largest burden of HIV after South Africa and Nigeria with an estimated 2.27 million people between the ages of 15–49 years being affected constituting 88.7% of the total estimated number of people living with HIV/AIDS (PLWHA).\(^6\)\(^5\)

The goals of ART include prolongation of lifespan and improvement in quality of life, reduction of viral load and subsequent reduction of HIV transmission, and quantitative and qualitative immune reconstitution.\(^6\)\(^9\) To achieve desired outcomes, HIV/AIDS patients are required to have more than 95% adherence to ART. Antiretroviral adherence is the second strongest predictor of progression to AIDS and death, after CD4 count.\(^7\)\(^8\)

Failure to adhere could be due to multiple factors including late detection, stigma and discrimination, and difficulty in accessing health facilities, adverse effects of drugs, comorbidities, psychosocial factors, economic constraints, and availability of ART facilities.\(^9\) Adherence to ART being an important determinant of clinical and nonclinical outcomes, it is necessary to identify the factors that influence it both positively and negatively. This knowledge would help in planning and executing individualized management plans and community level interventions to ensure optimal results. Primary care physicians can utilize these factors related to adherence in the management of HIV. This can help them in improving the adherence rates among people infected with HIV/AIDS. This can help in managing the HIV/AIDS patients as any other chronic illness such as diabetes and hypertension.

This study was done to determine adherence rates and factors affecting adherence of ART among PLWHA.

**Subjects and Methods**

The study was carried out at ART centers in North Karnataka, India for a period of 1 year. People living with HIV/AIDS (PLWHA) aged between 15 and 49 years were recruited. Severely ill or HIV with complications (TB, hepatitis, etc.) were excluded from the study. Sample size of 242 was estimated using the adherence rates for ≥95% of doses at ART center as 83% from the study by Machtinger and Bangsberg.\(^7\)

Formula used for sample size was \(N = 4PQ/l^2\), 95% confidence limits and 6% permissible error and 5% attrition rate was presumed for sample size estimation.

PLWHA attending the ART center was sequentially approached on selected days during the study period. The first 242 patients who satisfied the inclusion criteria and consented to participate were included in the study. The study was approved by the Institutional Ethical Committee and written informed consent was obtained from all participants before the enrollment into the study. A structured questionnaire was used to obtain data on sociodemographic profile, factors affecting adherence, and laboratory investigations. Adherence was assessed through self-reports, routine and random pill counts, and assessment of medical records.

**Statistical analysis**

Data were analyzed using Epi Info Version 7 CDC (Centers for Disease Control and Prevention) U.S. Department of Health and Human Services. Descriptive statistics such as frequencies, proportions for qualitative data, and mean and standard deviation (SD) for quantitative data were computed. Chi-square test and \(t\)-test were the test of significance for qualitative and quantitative data, respectively. Multiple logistic regression was computed to identify the factors affecting adherence. \(P < 0.05\) was considered statistically significant.

Adherence rate was calculated according to the following formula.

\[
\text{Adherence rate} = \frac{\text{Number of pills expected to be taken} - \text{Number of pills missed}}{\text{Number of pills expected to be taken}} \times 100
\]

**Results**

Adherence on ART was finally assessed on 242 PLWHAs, mean age of subjects was 35 ± 7.8 years. Majority (59.5%) of them were in the age group 25–39 years, with female preponderance (55%). Higher education status was observed among males. Majority of the participants were Hindus (85.5%), residing in rural areas (62%) and were unskilled laborers (64.9%). Nearly half were from a poor socioeconomic background, and 35.1% were below poverty line. About 63.3% of males had multiple sexual partners (\(\chi^2 = 76.62, P < 0.0001\)). HIV-1 was predominant type in 94.6% and HIV-2 in 5.4%. Most common route of transmission was heterosexual (88.8%) and majority (53.7%) were initiated on ART within 6 months of diagnosis of HIV [Table 1].

Zidovudine (AZT) + lamivudine (3TC) + nevirapine (NVP) regimen (Regimen 1) was the most common regimen initiated in 54.1% patients followed by stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP) regimen (Regimen 2) in 43.8% patients. There was a significant preference for the stavudine (d4T) + lamivudine (3TC) + nevirapine (NVP) regimen in females, whereas zidovudine (AZT) + lamivudine (3TC) + nevirapine (NVP) regimen was preferred in males (\(\chi^2 = 37.833, P < 0.001\)).

Majority of the patients (66.1%) had CD4 counts <200 cells/mm\(^3\) at initiation of ART. At the end of 6 months of treatment, a significant improvement in CD4 counts was noted (\(t = 20.181, P < 0.001\)); 85% had CD4 counts >200 cells/mm\(^3\). Significant improvement in weight was also observed among subjects on ART (\(t = 9.636, P < 0.001\)).

**Treatment adherence**

One hundred percent adherence (no doses missed) was noted
A 100% adherence rate (consistent adherers) for the whole 6 month period was seen only in 31.6% patients. Lower 6 month averages of 95–100%, 80–95%, and <80% were noted in 49.8%, 9.1%, and 9.5% patients, thus providing an optimal adherence rate >95% in 81.4%.

The adherence rates in females were higher than in males but were not statistically significant ($\chi^2 = 3.429 \ P = 0.064$). There was no significant difference in adherence rates between the stavudine and zidovudine regimens or in the occurrence of adverse effects in adherent and nonadherent groups.

Univariate logistic model was followed by multivariable logistic model. $P < 0.1$ was considered statistically significant in the univariate model, and those significant variables were included in the multivariable model. Backward method was used, in which AIC and BIC values were used to compare the best-fitted model.

Earning member (odds ratio [OR] =0.404) and weight difference (OR = 0.818) were most associated with the adherent individuals. Economic factors and improvement in weight played an important role in adherence among HIV patients. No other factor significantly affected adherence rate [Table 3].

Missed doses

The mean number of doses missed over the period of 6 months was 21.7 (SD = 52.3). The total number of missed doses had negative correlations with improvements in CD4 counts ($P = 0.038*$) and weight ($P < 0.001$), i.e., with an increase in missed doses, there was a decrease in CD4 count and weight. One hundred and fifty-eight (68.4%) patients had missed at least 1 dose during the 6 months period. Multiple reasons that were cited for the same are shown in Table 4. Most common psychological reason was forgetfulness in 44.9%, socioeconomic reason was a loss of hours of job in 9% and adverse effect.

Discussion

In this study, it was observed that HIV was predominant in young, rural, economically, and educationally challenged subjects, indicating the need for awareness and improvement in social standards among this population. Higher prevalence of multiple sexual partners in males points toward the need for emphasizing safe sexual practices. Similar observations were made by other studies worldwide.

One hundred percent adherence rate (consistent adherers) for the whole 6 month period was seen only in 31.6% patients. One hundred percent adherence was noted in 81.8% patients at the end of 1 month, which dipped to 66.5% patients by the end of the 2nd month. However, a gradual increase was noted over the remaining 4 months: 70.8%, 72.2%, 76.9%, and 84% at the end of the 3rd, 4th, 5th, and 6th months, respectively [Table 2].

### Table 1: Distribution of people living with human immunodeficiency virus/acquired immunodeficiency syndrome according to different study characteristics

| Characteristic                  | n (%)   |
|---------------------------------|---------|
| Sex                             |         |
| Male                            | 109 (45)|
| Female                          | 133 (55)|
| Age (years)                     |         |
| 15-24                           | 16 (6.6)|
| 25-29                           | 54 (22.3)|
| 30-34                           | 44 (18.2)|
| 35-39                           | 46 (19)|
| 40-44                           | 39 (16.1)|
| 45-49                           | 43 (17.8)|
| Marital status                  |         |
| Married                         | 149 (61.5)|
| Unmarried                       | 12 (5)|
| Divorced                        | 20 (8.3)|
| Widow/widower                   | 61 (25.2)|
| Religion                        |         |
| Hindu                           | 207 (85.5)|
| Muslim                          | 30 (12.4)|
| Christian                       | 5 (2.1)|
| Locality                        |         |
| Rural                           | 150 (62.0)|
| Urban                           | 92 (38)|
| Literacy status                 |         |
| Illiterate                      | 71 (29.3)|
| Primary                         | 31 (12.8)|
| Middle                          | 31 (12.8)|
| Secondary                       | 75 (31.0)|
| Pneuniversity                   | 23 (9.5)|
| Degree                          | 11 (4.5)|
| Occupation                      |         |
| Unskilled                       | 157 (64.9)|
| Semiskilled                     | 1 (0.4)|
| Skilled                         | 68 (28.1)|
| Semi-professional               | 7 (2.9)|
| Others                          | 9 (3.7)|
| Socioeconomic status            |         |
| Upper                           | 1 (0.4)|
| Middle                          | 33 (13.7)|
| Poor                            | 123 (50.8)|
| BPL                             | 85 (35.1)|
| Type of HIV                     |         |
| HIV-1                           | 229 (94.6)|
| HIV-1 and HIV-2                 | 13 (5.4)|
| Mode of transmission            |         |
| Heterosexual                    | 215 (88.8)|
| Accidental                      | 4 (1.7)|
| Injections                      | 11 (4.5)|
| Unknown                         | 12 (5)|
| Patient is a earning member     |         |
| Yes                             | 80 (33.1)|
| No                              | 162 (66.9)|

BPL: Below poverty line; HIV: Human immunodeficiency virus

in 81.8% patients at the end of 1 month, which dipped to 66.5% patients by the end of the 2nd month. However, a gradual increase was noted over the remaining 4 months: 70.8%, 72.2%, 76.9%, and 84% at the end of the 3rd, 4th, 5th, and 6th months, respectively.
Table 2: Distribution of patients according to adherence percentages at the end of each month and 6 months average

| Adherence (%) | At 1st month | At 2nd month | At 3rd month | At 4th month | At 5th month | At 6th month | Average for 6 months |
|---------------|--------------|--------------|--------------|--------------|--------------|--------------|----------------------|
| 100           | 198 (81.8)   | 161 (66.5)   | 170 (70.8)   | 169 (72.2)   | 186 (76.9)   | 194 (84)     | 73 (31.6)           |
| 95-99         | 27 (11.2)    | 45 (18.6)    | 26 (10.8)    | 27 (11.5)    | 19 (8.2)     | 12 (5.2)     | 115 (49.8)          |
| 80-85         | 5 (2.1)      | 13 (5.4)     | 15 (6.3)     | 16 (6.8)     | 9 (3.9)      | 10 (4.3)     | 21 (9.1)            |
| <80           | 12 (5)       | 23 (9.5)     | 29 (12)      | 22 (9.4)     | 19 (8.2)     | 15 (6.5)     | 22 (9.5)            |
| Total         | 242          | 242          | 240          | 234          | 233          | 231          | 231                 |
| Missing*      | 0            | 0            | 2            | 8            | 9            | 11           | 11                  |

*These are number of missing patients excluded for calculation of adherence percentages due to their deaths in the previous months.

Table 3: Multiple logistic regression to find out the factors playing a role in adherence

|          | B      | P      | AOR   | 95% CI for Exp (B) |
|----------|--------|--------|-------|--------------------|
| Gender   | 0.596  | 0.252  | 1.815 | 0.654              |
| Alcohol intake | 0.155  | 0.679  | 1.168 | 0.559              |
| Earning member of the family | -0.906 | 0.038* | 0.404 | 0.172              |
| Depression | -0.618 | 0.147  | 0.539 | 0.234              |
| Weight improvement | -0.201 | 0.801* | 0.818 | 0.725              |

|          | n (%)  |
|----------|--------|
| Psychological reasons |
| Forgetfulness* | 71 (44.9) |
| Depression*    | 36 (22.8) |
| Fear of disclosure | 34 (21.5) |
| Loss of interest in treatment | 19 (12) |
| Irritated due to repeated illness | 9 (5.7) |
| Feels better so does not take treatment | 4 (2.5) |
| Ran out of pills | 3 (1.9) |
| Anxiety/stress | 2 (1.2) |
| Socioeconomic reasons |
| Loss of hours of job/household work* | 14 (8.9) |
| Myths and misconceptions about ART/ HIV* | 13 (8.2) |
| No source of income | 12 (7.6) |
| Highly unstable situation | 12 (7.6) |
| Low level of literacy | 5 (3.2) |
| Discrimination | 5 (3.2) |
| No support from family/friends | 4 (2.7) |
| Migration | 3 (1.9) |
| False address | 3 (1.9) |
| Increase in hospital expenses | 2 (1.2) |
| Adverse effects/health system reasons |
| Due to adverse effects/complications* | 27 (17.1) |
| Due to comorbidities* | 16 (10.1) |
| Due to opportunistic infections | 13 (8.2) |
| Lack of information/motivation | 7 (4.4) |
| ART too far from residence | 7 (4.4) |
| Taking private Rx | 3 (1.9) |
| Reminders not sufficient | 2 (1.2) |

*Some had multiple reasons. HIV: Human immunodeficiency virus; ART: Adherence to antiretroviral therapy.

About 94.3% adherence at baseline and 91.3% adherence at 3 months were observed in the study by Amberbir et al., the principal reasons reported for skipping doses in this study were simply forgetting, feeling sick or ill, being busy, and running out of medication in more than 75% of the cases similar to the present study.[14] In the study by Safren et al. in Chennai observed 74.3% adherence at 6 months, and in the study by Shah et al. in Mumbai observed 73% adherence.[11,13] The self-reported adherence rate of the patient on ART was 81.1% in the study by Belayihun and Negus.[18]

Forgetfulness, depression, and fear of disclosure were the most common psychological reasons for missed doses among subjects, constituting about 90% of reasons in the present study. According to the study by Wanchu et al., the major reasons for nonadherence were financial constraints, forgetting to take the medication, drug toxicity, and lack of access to the drug, fear of getting immune to the benefit of the drug, and to avoid adverse effects.[18] This is in accordance with the present study except for the financial constraints in the present study as the ART drugs are supplied free. In CARES study, the most frequently reported reasons for missing doses were forgetfulness, being busy, and antiretroviral side effects similar to the present study.[15] In the Vancouver Injection Drug Users Study (VIDUS) by Kerr et al., forgetting was the most frequently cited reason (27%) for missing doses of HAART in accordance with the present study.[16]

In the present study, earning member (OR = 0.404) and weight difference (OR = 0.818) were most associated with the adherent individuals. No other factor significantly affected the adherence rate among PLWHA.

Byakika-Tusiime et al., in their study in Kampala, Uganda, found that factors associated with nonadherence were marital status (OR = 2.93, 95% confidence interval [CI]: 1.32–6.50) and low monthly income <50 US dollar; (OR = 2.77, 95% CI: 1.64–4.67).[15] In the study by Amberbir et al., patients who were not depressed were two times more likely to be adherent than those who were depressed (OR: 2.13, 95% CI: 1.18, 3.81). However, at the follow-up visit, social support (OR: 2.42, 95% CI: 1.29, 4.55) and the use of memory aids (OR: 3.29, 95% CI: 1.44, 7.51) were found to be independent predictors of adherence.[13] In a study by Holzemer et al., HIV-positive clients with higher symptom scores, particularly depression, were more likely to be nonadherent to medication.[18] Travel distance and economic factors were the main challenges associated with ART adherence in the study by Chinedzai et al.[19]

Low adherence rates and suboptimal adherence rates observed may be due to time taken by the patients to get adjusted with treatment schedule, initial side effects, comorbidities, and delay.
Adherence rate was poor among PLWHA, and hence factors affecting adherence has to be addressed to ensure optimal adherence for ART. Economic factors affected adherence, than other factors in this study. Hence, decentralizing the ART center facilities to PHC level and use of alternative strategies such as ART drugs supply similar to the DOTS strategy used in RNTCP is needed. Strengthening IEC activities particularly in the rural areas, with a focus on eliminating the stigma and discrimination, travel concessions in railways and buses for seeking medical care to HIV/AIDS cases is the need of the hour. Provision of social assistance in terms of employment support, monetary or food grains, and moral support is required. Strengthen positive network of people living with HIV/AIDS (PLWHA). Regular ART adherence education and counseling, improved training on medication self-management skills, reminders, improved adherence monitoring, and health-care services should be priority strategies for improving adherence to ART among HIV/AIDS patients.

Acknowledgment
1. ART Centre Medical Officer, ART Centre KIMS, Hubli
2. Patients who cooperated to participate in the study.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References
1. Simon V, Ho DD, Abdool Karim Q. HIV/AIDS epidemiology, pathogenesis, prevention, and treatment. Lancet 2006;368:489-504.
2. World Health Organization. Global Update on the Health Sector Response to HIV, 2014. Geneva, Switzerland: World Health Organization; 2014.
3. World Health Organization, UNAIDS. 09 Epidemic Update. London: World Health Organization; 2009.
4. NACO. India Country progress Report. UNGASS; March, 2010.
5. NACO. A Technical Brief. GOI. Delhi: HIV Sentinel Surveillance and HIV Estimation; 2008.
6. NACO. Department of AIDS Control. Ministry of Health and Family Welfare Government of India. Antiretroviral Therapy Guidelines for HIV-Infected Adults and Adolescents Including Post-Exposure Prophylaxis; May, 2007.
7. Machtinger EL, Bangsberg DR. Adherence to HIV Antiretroviral Therapy. HIV in Site Knowledge Base Chapter; May, 2005; Content Reviewed; January, 2006. http://hivinsite.ucsf.edu/InSite?page=kb-03-02-09 [Last accessed on 2016 Mar 26].
8. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. November 3, 2008. p. 1-39. Available from: https://aidsinfo.nih.gov/contentfiles/adultandadolescentgl002111.pdf [Last accessed on 2016 Mar 28].
9. Mills EJ, Nachega JB, Buchan I, Orbinski J, Attaran A, Singh S, et al. Adherence to ART in Sub-Saharan Africa and NA, a meta Analysis. J Am Med Assoc 2006;296:670-90.
10. Amberbir A, Woldemichael K, Getachew S, Girma B, Deribe K. Predictors of adherence to antiretroviral therapy among HIV-infected persons: A prospective study in Southwest Ethiopia. BMC Public Health 2008;8:265.
11. Safren SA, Kumaraamy N, James R, Raminani S, Solomon S, Mayer KH. ART adherence, demographic variables and CD4 outcome among HIV-positive patients on antiretroviral therapy in Chennai, India. AIDS Care 2005;17:853-62.
12. Shah B, Walshe L, Saple DG, Mehta SH, Ramnani JP, Kharkar RD, et al. Adherence to antiretroviral therapy and virologic suppression among HIV-infected persons receiving care in private clinics in Mumbai, India. Clin Infect Dis 2007;44:1235-44.
13. Bekele Belayhun and Rahma Negus, “Antiretroviral Treatment Adherence Rate and Associated Factors among People Living with HIV in Dubti Hospital, Afar Regional State, East Ethiopia,” International Scholarly Research Notices, 2015 ;2015:5. doi:10.1155/2015/187360.
14. Wanchu A, Kaur R, Bambery P, Singh S. Adherence to generic reverse transcriptase inhibitor-based antiretroviral medication at a Tertiary Center in North India. AIDS Behav 2007;11:99-102.
15. Wang X, Wu Z. Factors associated with adherence to antiretroviral therapy among HIV/AIDS patients in rural China. AIDS 2007;21 Suppl 8:S149-55.
16. Kerr T, Palepu A, Barmess G, Walsh J, Hogg R, Montaner J, et al. Psychosocial determinants of adherence to highly active antiretroviral therapy among injection drug users in Vancouver. Antivir Ther 2004;9:407-14.
17. Byakika-Tusime J, Ouygi JH, Tumwirikize WA, Katabira ET, Mugyeniy PN, Bangsberg DR. Adherence to HIV antiretroviral therapy in HIV+ Ugandan patients purchasing therapy. Int J STD AIDS 2005;16:38-41.
18. Holzemer WL, Corless IB, Nokes KM, Turner JG, Brown MA, Powell-Cope GM, et al. Predictors of self-reported adherence in persons living with HIV disease. AIDS Patient Care STDS 1999;13:185-97.
19. Chinedza M, Mutseyekwa F, Chideke-Munodawafa A. Perceived barriers to accessing and achieving adherence in antiretroviral therapy among HIV patients at a rural mission hospital in Zimbabwe. Eur Sci J 2011;9:277-87.
20. Sasaki Y, Kakimoto K, Dube C, Sikazwe I, Moyo C, Syakantu G, et al. Adherence to antiretroviral therapy (ART) during the early months of treatment in rural Zambia: Influence of demographic characteristics and social surroundings of patients. Ann Clin Microbiol Antimicrob 2012;11:34.