Assessment of adherence and factors contributing to non-adherence among patients on anti-retroviral therapy in a tertiary care hospital: A cross sectional study

Rujuta S. Hadaye¹, Vyankat B. Jambhale², Shruti Shastri³

¹Department of Community Medicine, Seth. G.S. Medical College and KEM Hospital, Mumbai, Maharashtra, ²E.S.I.S. Hospital, Aurangabad, Maharashtra, ³Department of Community Medicine, R. D. Gardi Medical College, Ujjain, Madhya Pradesh, India

ABSTRACT

Background: For the successful treatment of human immunodeficiency virus (HIV), it is important that drugs should be taken regularly. Non-adherence not only increases chances of failure of treatment but also leads to the development of resistance to drugs and hence more focus has been given to adherence in the treatment protocol of HIV. Objectives: To determine the level of adherence, its determinants, and to ascertain reasons for non-adherence of antiretroviral therapy (ART) in patients with HIV/acquired immunodeficiency syndrome (AIDS). Methods: A cross-sectional study conducted at an adult ART clinic over a period of one year. The sample size was 320. A systematic random sampling technique was used. Semi-structured Adult AIDS Clinical Trials Group questionnaire was used. Beck Depression Inventory (BDI-II) for current depression and self-report of four days recall method and multi-method approach were used for adherence measurement. Results: The mean age of respondents was 37.26 ± 8.3 years. About 60.3% were males, 34.1% females, and 5.6% were transgenders (TGs). High adherence was found in 87.2% by self-report and 72.5% by multi-method approach. History of opportunistic infection and depression were found to be the best predictors of adherence. Reasons for short term non-adherence were found to be simply forgot to take medications, being away from home, busy with other things, and ran out of pills. Reasons for long-term non-adherence were financial difficulty, side-effects, and shift to alternate therapy. Conclusions: Significant non-adherence to ART necessitates addressing adherence issues in pre-ART counseling, the involvement of family and social support.

Keywords: Adherence, anti-retroviral therapy, HIV/AIDS

Introduction

To end human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) Epidemic, in 2014, 90–90–90 targets were launched i.e. by 2020, 90% of all people living with HIV (PLHA) will know their HIV status, 90% of all people with diagnosed HIV infection will receive antiretroviral therapy (ART) and 90% of all receiving ART will have viral suppression. This was estimated to result in 90% of PLHA diagnosis, 81% of all PLHA on ART, and 73% of all PLHA achieving viral suppression.[9] At the end of 2018, globally an estimated 79% of PLHA knew their status, 62% were receiving ART, and 53% had achieved suppression of the HIV virus with no risk of infecting others.[9]

Globally, around 36.7 million PLHA and 18.2 million have been accessing treatment. In India, about 2.1 million people were estimated to be living with HIV and 50% were on ART in 2015.[9] To achieve the third 90 target, i.e. 90% viral load suppression, a high level of adherence to ART will be required.

Adherence, unlike compliance, requires patient’s agreement to recommendations. Adherence to long-term therapies in chronic...
illness averages 50% in developed countries. In developing countries, rates are thought to be even lower. It is estimated that more than 10% of patients have reported missing one or more medication doses on any given day, and >33% report missing doses in the past four weeks. It is also found that 50% of prescriptions filled are not taken properly. In a recent study from India, the estimated prevalence of adherence to ART was around 81%.

Non-adherence has become a critical issue in population health from the perspective of quality of life and health economics. It not only increases the chances of failure of treatment, but also leads to the development of resistance to drugs and compromises the effectiveness of treatment, so more focus has been given to adherence in the treatment protocol of HIV. This study was conducted to determine the level of adherence, its determinants, and to ascertain reasons for non-adherence to ART in HIV/AIDS patients.

Materials and Methods

It was a cross-sectional study conducted at an adult ART clinic in a tertiary level hospital in an urban metropolis over a period of one year in 2008–2009. All HIV/AIDS patients with 18 years of age and above, who had completed at least three months of ART were included in the study. Estimated sample size with anticipated prevalence of adherence level as 70% was 320. At the time of study, 2712 patients were registered with ART center. Systematic random sampling technique was used to achieve sample size.

Institutional ethics committee approval was obtained and written informed consent was taken before data collection. A semi-structured questionnaire adapted from the Adult AIDS Clinical Trials Group (AACTG) was used. The questionnaire was culturally adapted by consulting experts working in this field. Beck Depression Inventory (BDI-II) was used to assess current depression.

Adherence was measured by self-report of four days recall method and multi-method approach including self-reporting, visual analogue scale, pill identification test, and pill count. Long-term adherence was assessed by including additional information regarding a total number of missed doses over the last seven days and thereafter as the patient remembered, last time the patient missed full days medication since the start of ART and number of times treatment stopped for >1 week since the start of ART.

Data were entered in Microsoft Excel and analysis was done using Statistical Package for the Social Sciences (SPSS) software.

Table 1: Adherence in respondents by self-reporting and multi-method approach

| Adherence   | n=320 | %Observed adherence | %Corrected adherence |
|-------------|-------|---------------------|----------------------|
| Self-reported adherence |       |                     |                      |
| High (>90%) | 302   | 94.4                | 87.2                 |
| Low (<90%)  | 18    | 5.6                 | 12.8                 |
| Total       | 320   | 100.0               | 100.0                |
| Multi-Method Adherence |       |                     |                      |
| High        | 251   | 78.4                | 72.50                |
| Medium      | 30    | 9.4                 | 8.75                 |
| Low         | 39    | 12.2                | 18.75                |
| Total       | 320   | 100.0               | 100.0                |

In research setting, the percentage of loss to follow-up individuals for the study period was 7.6%. Had these individuals been included in study, they would have been classified as having low adherence. Assuming that these 7.6% were equally distributed in observed adherence groups, a correction of 7.6% was applied to observed results.

Long-term adherence was also assessed where 18 (5.6%) respondents reported missing medication in past one week, 7 (2.2%) missed doses in last four weeks, 17 (5.3%) missed medications between one to three months ago, and number of respondents who missed medication >3 months back was 22 (6.9%). Around 35 (10.9%) of respondents had reported missing full day’s medication whereas only 8 (2.5%) patients had stopped treatment for more than one week.

Non-adherence was found to be statistically significant in younger age groups, with a low level of education and in individuals with severe depression [Tables 2 and 3]. Variables of social support and awareness of HIV show a similar level of adherence [Table 4].

Low adherence was found to be significantly associated with low baseline CD 4 count (<100), absence of opportunistic infection, patients who were taking ART over a longer period, and patients who had ever experienced side effects of ART [Table 5].

Multinomial logistic regression was applied to control for the effect of confounding factors. All variables which were significant on univariate analysis were selected for multinomial logistic regression. Adherence was a dependent factor and of which low adherence was taken as a reference category. Depression score was inversely associated with adherence and the presence of opportunistic infection shows high adherence.

More than one response was permitted from individuals who missed doses. Out of 107 respondents who missed doses, most common reasons cited for non-adherence were simply forgot (57, 53.3%) followed by away from home (38, 30.3%), ran out of pills (13, 14.9%), and busy with other things (12, 11.2%). Other
uncommon reasons included slept throughout the dose time, felt sick, change in daily routine, felt depressed, and did not want others to notice.

The most frequent reason cited by respondents who missed full day’s medication (n = 35) was that of being away from home for some duration (n = 15) and thus unable to get medications. All those who reported running out of pills (n = 6) as a reason for not taking medication for a full day, were taking medication from the private sector and hence unable to procure medications.

Those who stopped treatment for more than one week (n = 8), most common reasons cited for longer breaks in treatment were financial difficulty (n = 2) for those who first started treatment from private practitioners and later shifted to this center. Other
reasons were side effects (n = 5) and shift to other therapy (n = 1) like Ayurvedic medications.

**Discussion**

Non-adherence to ART is still a major cause of poor outcomes of HIV treatment with ART. High adherence over a long period of time helps to maintain negligible viral load, prevent transmission of disease, and reduces the possibility of contracting opportunistic infections. It improves the overall quality of life of patients. Studies suggested that >95% of adherence is required for optimal viral load suppression.[10]

ART is a chronic therapy and patients of lower socioeconomic status are dependent on treatment on municipal or government healthcare services. Affected males seem to access healthcare...
services more often than females. The adherence level by self-reporting was found to be more than the multi-method approach. Other studies also reported a similar level of adherence.\[11-13\]

Despite better availability of drugs, certain obstacles in treatment with ART affected its adherence. Older patients showed better adherence than younger patients as they showed responsible behavior towards disease and treatment. The education level of patients affected their adherence to treatment because of a better understanding of the disease and its complications. Other studies also supported these findings.\[12,14,15\]

HIV-associated stigma, long-term nature of therapy, and its side effects lead to physical, social, financial, and mental trouble to patients. The psychological status of patients affects their treatment behavior. Studies reported that experiencing depressive symptoms are associated positively with non-adherence. Depression had been shown to be an independent predictor of poor adherence in different studies.\[12,14,16,17\]

Association between the level of CD4 cell counts at the enrolment and adherence to therapy suggests that individuals with higher CD4 cell counts tend to have better adherence than those with lower levels of CD4 cell counts. This might be a reverse phenomenon that the better the adherence the higher the cell count.

Experience of illness incites the desire for health. History of opportunistic infection was found to be associated with higher adherence. After experiencing opportunistic infections related to HIV patients become more receptive to counseling and show better adherence to treatment. Another study reported that non-adherence was significantly associated with present opportunistic infection.\[18\]

ART is a chronic therapy and is associated with side effects too. Self-motivation, family support, and support from healthcare personnel are required for the uninterrupted intake of medicines. Otherwise, adherence wanes over the duration of treatment gradually. Low adherence was seen among subjects who were taking ART for >2 years and whoever experienced side effects of ART.\[19,20\]

Side effects of drugs and financial difficulty to buy them are two important reasons for non-adherence. But simply forgot to take medicine is still the most common reason cited for non-adherence. When medicines are available free of cost and counseling from healthcare workers is accessible, prioritizing health issues by individuals and families will only help in maintaining 100% adherence. Another study reported

| Variables                          | High (%) | Medium (%) | Low (%) | Total (%) | Chi-square (P) |
|-----------------------------------|----------|------------|---------|-----------|----------------|
| **Duration of diagnosis of HIV infection** |          |            |         |           |                |
| <12 months                        | 67 (79.8)| 6 (7.1)    | 11 (13.1)| 84 (100) | 0.244          |
| 13-24 months                      | 125 (82.2)| 12 (7.9) | 15 (9.9) | 152 (100) |                |
| >24 months                        | 59 (70.2)| 12 (14.3) | 13 (15.5) | 84 (100) |                |
| Total                             | 251 (78.4)| 30 (9.4) | 39 (12.2)| 320 (100) |                |
| **CD 4 count**                    |          |            |         |           |                |
| <100 cells/µL                     | 70 (71.4)| 8 (8.2)    | 20 (20.4)| 98 (100) | 0.046          |
| 101-200 cells/µL                  | 138 (82.6)| 15 (9.0) | 14 (8.4) | 167 (100) |                |
| >200 cells/µL                     | 43 (78.2)| 7 (12.7)  | 5 (9.1)  | 55 (100)  |                |
| Total                             | 251 (78.4)| 30 (9.4) | 39 (12.2)| 320 (100) |                |
| **Opportunistic infection**       |          |            |         |           |                |
| Present                           | 142 (85.0)| 13 (7.8) | 12 (7.2) | 167 (100) | 0.007          |
| Absent                            | 109 (71.2)| 17 (11.1)| 27 (17.7)| 153 (100) |                |
| Total                             | 251 (78.4)| 30 (9.4) | 39 (12.2)| 320 (100) |                |
| **Duration of treatment with ART** |          |            |         |           |                |
| <12 months                        | 119 (83.8)| 7 (4.9)  | 16 (11.3)| 142 (100) | 0.005          |
| 13-24 months                      | 87 (80.6)| 9 (8.3)   | 12 (11.1)| 108 (100) |                |
| >24 months                        | 45 (64.3)| 14 (20)   | 11 (15.7)| 70 (100)  |                |
| Total                             | 251 (78.4)| 30 (9.4) | 39 (12.2)| 320 (100) |                |
| **Side effects of ART**           |          |            |         |           |                |
| Yes                               | 155 (73.8)| 24 (11.4)| 31 (14.8)| 210 (100) | 0.021          |
| No                                | 96 (87.3)| 6 (5.4)   | 8 (7.3)  | 110 (100) |                |
| Total                             | 251 (78.4)| 30 (9.4) | 39 (12.2)| 320 (100) |                |
| **Satisfaction with provider**    |          |            |         |           |                |
| Yes                               | 237 (78.2)| 30 (9.9) | 36 (11.9)| 303 (100) | 0.340          |
| No                                | 14 (82.4)| 0         | 3 (17.6)| 17 (100)  |                |
| Total                             | 251 (78.4)| 30 (9.4) | 39 (12.2)| 320 (100) |                |
forgetfulness and high drug dosage as common reasons for non-adherence.\textsuperscript{13,18}

Primary care practitioners are first contact to the patients. HIV-related care from its prevention to diagnosis and successful treatment is based on the patient’s trust in the caregiver and patients trust their family physician more than anyone else. Hence, primary care physicians play an important role in the care of HIV-infected patients. Primary physicians can mentally prepare the patient and family about HIV treatment with ART. They can take the opportunity to talk and involve the family in HIV care and medication, which will help in increasing adherence. Also, they can provide moral support to patients and their families during the treatment with ART, which will boost the confidence to fight with side effects of ART and social stigma, help prevent depression and opportunistic infections, and improve adherence to medication.

\section*{Conclusions}

Adherence to HIV/AIDS treatment unlike other chronic diseases is affected by a range of factors. Hence, pre-ART counseling is an important component of adherence management in patients with HIV/AIDS. There has been a focus on the adherence issue at each session of counseling. Counselors need to discuss and find solutions about the social, mental, and financial problems faced by individuals as well. PLHA can be trained and utilized for counseling purpose and equal respect to such counselors should be given as that of a healthcare provider. PLHA associations, peer groups, and non-government organization’s (NGO) help in tracing lost to follow-up of ART patients.

Early detection, counseling, and treatment for depression and increased awareness of opportunistic infections and its effects among patients will help in improving adherence. Stress-relieving mechanisms like yoga and pranayama can help. Family involvement by increasing awareness among family members regarding treatment literacy and the need to constantly support PLHA socially and financially will help in enhancing adherence.

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There are no conflicts of interest.

\section*{References}

1. Bain LE, Nkoke C, Noubiap JJN. UNAIDS 90–90–90 targets to end the AIDS epidemic by 2020 are not realistic: Comment on “Can the UNAIDS 90–90–90 target be achieved? A systematic analysis of national HIV treatment cascades”. BMJ Global Health 2017;2:e000227.

2. World Health Organization, Factsheet Key facts HIV/AIDS 2019. Available from: https://www.who.int/news-room/fact-sheets/detail/hiv-aids. [Last accessed on 2019 Dec 12].

3. Park K. Textbook of Preventive and Social Medicine. 24th ed. Jabalpur: Bhanot Publication; 2017. p. 361-3.

4. WHO Report on Adherence to long term therapies—Evidence for action. 2003

5. Chesney MA. Factors affecting adherence to antiretroviral therapy. Clin Infect Dis 2000;30(Suppl 2):S171-6.

6. Alvi Y, Khalique N, Ahmad A, Khan HS, Faiz N. World Health Organization dimensions of adherence to antiretroviral therapy: A study at antiretroviral therapy centre, Aligarh. Indian J Community Med 2019;44:118-24.

7. AACTG baseline and follow up adherence questionnaires.

8. Beck AT. Beck Depression Inventory*-II Manual. The Psychological Corporation. Harcourt Brace and Company; 1996.

9. Steel G, Nwokike I, Joshi M. Development of a Multi-method Tool to Measure ART Adherence in Resource constrained settings: The South Africa Experience. USAID; 2007.

10. National AIDS Control Organization. National Technical Guidelines on Anti-Retroviral Treatment. National AIDS Control Programme. Ministry of Health, Govt. of India; 2018; p. 45.

11. Chesney MA. Factors affecting adherence to antiretroviral therapy. Clin Infect Dis 2000;30(Suppl 2):S171-6.

12. Sarna A, Pujari AK, Garg R, Gupta I, Van Dam J. Adherence to antiretroviral therapy and its determinants amongst HIV patients in India. Indian J Med Res 2008;127:28-36.

13. Morowatisharifabad MA, Movahed E, Farokhzadian J, Nikooie R, Hosseinzadeh M, Askarishahi M, et al. Antiretroviral therapy adherence and its determinant factors among people living with HIV/AIDS: A case study in Iran. BMC Res Notes 2019;12:1-5.

14. Gordillo V, Amo JD, Soriano V, Lahoz JG. Sociodemographic and psychological variables influencing adherence to antiretroviral therapy. AIDS 1999;13:1763-9.

15. Cauldbeck MB, O’Connor C, O’Connor MB, Saunders JA, Rao B, Mallesh VG, et al. Adherence to antiretroviral therapy among HIV patients in Bangalore, India. AIDS Res Ther 2009;6:7.

16. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squir C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med 2000;133:21-30.

17. Pokhrel KN, Pokhrel KG, Sharma VD, Poudel KC, Neupane SR, Mlunde LB, et al. Mental health disorders and substance use among people living with HIV in Nepal: Their influence on non-adherence to anti-retroviral therapy. AIDS Care 2019;31:923-31.

18. Gupta M, Das SC. Determinants contributing for poor adherence to antiretroviral therapy: A hospital record-based study in Balasore, Odisha. J Fam Med Prim Care 2019;8:1720-4.

19. Machtinger EL, Bangsberg DR. Adherence to HIV Antiretroviral Therapy: HIV in Site Knowledge Base Chapter; May. 2005. Content Reviewed; January 2006.

20. Andreo C, Bertholon DR, Bouhnik AD, Rossert H, Soletti J, Spire B, et al. Non adherence in HIV infected patients, supported by a community association. Sante Publique 2001;13:249-62.

21. Reisner SL, Mimiaga MJ, Skeer M, Perkovich B, Johnson CV, Safren SA. A review of HIV antiretroviral adherence and intervention studies among HIV infected youth. Top HIV Med 2008;17:14-25.