

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.^[1] 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.^[2]

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.^[3] 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

Address for correspondence: Dr. Shruti Shastri, 412 VIP Paraspar Nagar, Indore, Madhya Pradesh - 452 012, India. E-mail: shruti.shastri@gmail.com

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illness averages 50% in developed countries.^[4] 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.^[5] In a recent study from India, the estimated prevalence of adherence to ART was around 81%.^[6]

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.^[7] The questionnaire was culturally adapted by consulting experts working in this field. Beck Depression Inventory (BDI-II) was used to assess current depression.^[8]

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.^[9] 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.

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). Table 1 shows the adherence level by self-reported and multi-method approach.

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

Table 2: Association of adherence with sociodemographic factors

Variables	Multi-Method Adherence			Total (%)	Chi-square (P)
	High (%)	Medium (%)	Low (%)		
Age (years)					
<30	44 (64.7)	13 (19.1)	11 (16.2)	68 (100.0)	0.013
31-45	168 (82.8)	14 (6.9)	21 (10.3)	203 (100.0)	
>45	39 (79.6)	3 (6.1)	7 (14.3)	49 (100.0)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100.0)	
Sex					
Male	160 (82.9)	12 (6.2)	21 (10.9)	193 (100.0)	0.109
Female	77 (70.6)	16 (14.7)	16 (14.7)	109 (100.0)	
TG	14 (77.8)	2 (11.1)	2 (11.1)	18 (100.0)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100.0)	
Religion					
Hindu	211 (78.7)	22 (8.2)	35 (13.1)	268 (100)	0.412
Muslim	26 (74.3)	6 (17.1)	3 (8.6)	35 (100)	
Other	14 (82.5)	2 (11.7)	1 (5.8)	17 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Marital status					
Married	170 (79.4)	20 (9.4)	24 (11.2)	214 (100)	0.961
Unmarried	34 (73.9)	5 (10.9)	7 (15.2)	46 (100)	
Widow	45 (77.5)	5 (8.7)	8 (13.8)	58 (100)	
Divorcee	2 (100.0)	0	0	2 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Education					
Illiterate	53 (70.7)	6 (8.0)	16 (21.3)	75 (100)	0.041
Primary	72 (73.5)	12 (12.2)	14 (14.3)	98 (100)	
Secondary & Higher Secondary	100 (85.5)	10 (8.5)	7 (6.0)	117 (100)	
Graduate	26 (86.6)	2 (6.7)	2 (6.7)	30 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Occupation					
Skilled	80 (83.3)	9 (9.4)	7 (7.3)	96 (100)	0.169
Semiskilled	83 (72.8)	14 (12.3)	17 (14.9)	114 (100)	
Unskilled	71 (79.8)	4 (4.5)	14 (15.7)	89 (100)	
Unemployed	17 (80.9)	3 (14.3)	1 (4.8)	21 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Type of family					
Nuclear	182 (79.5)	20 (8.7)	27 (11.8)	229 (100)	0.853
Joint	37 (74)	7 (14)	6 (12)	50 (100)	
Extended	18 (78.3)	1 (4.3)	4 (17.4)	23 (100)	
Singly (includes TG)	14 (77.8)	2 (11.1)	2 (11.1)	18 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Socioeconomic status (Modified BG Prasad)					
High	1 (25)	2 (50)	1 (25)	4 (100)	0.134
Upper middle	7 (87.5)	1 (12.5)	0	8 (100)	
Lower middle	42 (76.4)	6 (10.9)	7 (12.7)	55 (100)	
Poor	149 (77.6)	17 (8.8)	26 (13.5)	192 (100)	
Below poverty line	52 (85.2)	4 (6.6)	5 (8.2)	61 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	

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

Table 3: Association of adherence with risk factors

Variables	Multi-Method Adherence			Total (%)	Chi-square (P)
	High (%)	Medium (%)	Low (%)		
High risk factors					
Sex with Commercial sex workers	84 (83.2)	7 (6.9)	10 (9.9)	101 (100)	0.491
Multiple partners	27 (73.0)	6 (16.2)	4 (10.8)	37 (100)	
Spouse positive	74 (74.8)	12 (12.1)	13 (13.1)	99 (100)	
Homosexual	17 (77.3)	3 (13.6)	2 (9.1)	22 (100)	
Blood transfusion	25 (78.1)	1 (3.1)	6 (18.8)	32 (100)	
Other	24 (82.8)	1 (3.4)	4 (13.8)	29 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Depression					
Minimal	172 (98.3)	1 (0.6)	2 (1.1)	175 (100)	0.000
Mild	44 (72.1)	14 (23.0)	3 (4.9)	61 (100)	
Moderate	32 (55.2)	12 (20.7)	14 (24.1)	58 (100)	
Severe	3 (11.5)	3 (11.5)	20 (77.0)	26 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Tobacco use					
Yes	76 (82.6)	8 (8.7)	8 (8.7)	92 (100)	0.440
No	175 (76.7)	22 (9.7)	31 (13.6)	228 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	
Alcohol use					
Yes	24 (72.7)	6 (18.2)	3 (9.1)	33 (100)	0.175
No	227 (79.1)	24 (8.4)	36 (12.5)	287 (100)	
Total	251 (78.4)	30 (9.4)	39 (12.2)	320 (100)	

Table 4: Association of adherence with social and knowledge related factors

Variables	Multi-Method Adherence			Total (%)	Chi-square (P)
	High (%)	Medium (%)	Low (%)		
Staying with family					
Yes	231 (79.1)	26 (8.9)	35 (12)	292 (100)	0.579
No	20 (71.4)	4 (14.3)	4 (14.3)	28 (100)	
Disclosure to family					
Yes	223 (78.2)	28 (9.8)	34 (12)	285 (100)	0.699
No	28 (80)	2 (5.7)	5 (14.3)	35 (100)	
Perceived social support					
Yes	228 (78.3)	27 (9.3)	36 (12.4)	291 (100)	0.940
No	23 (79.4)	3 (10.3)	3 (10.3)	29 (100)	
Knowledge that HIV causes AIDS					
Yes	238 (77.8)	29 (9.5)	39 (12.7)	306 (100)	0.325
No	13 (92.9)	1 (7.1)	0	14 (100)	
Perception of HIV as serious problem					
Yes	233 (77.4)	29 (9.6)	39 (13)	301 (100)	0.173
No	18 (94.7)	1 (5.3)	0	19 (100)	
People Living with HIV/AIDS have to make big changes in lifestyle					
Yes	117 (79.6)	11 (7.5)	19 (12.9)	147 (100)	0.547
No	134 (77.5)	19 (11)	20 (11.5)	173 (100)	

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

Table 5: Association of adherence with disease-related factors

Variables	Multi-Method Adherence			Total (%)	Chi-square (P)
	High (%)	Medium (%)	Low (%)		
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/ μ L	70 (71.4)	8 (8.2)	20 (20.4)	98 (100)	0.046
101-200 cells/ μ L	138 (82.6)	15 (9.0)	14 (8.4)	167 (100)	
>200 cells/ μ L	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)	

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.^[14,19-21]

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

forgetfulness and high drug dosage as common reasons for non-adherence.^[13]

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.

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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Conflicts of interest

There are no conflicts of interest.

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