

A study of adherence to antiretroviral therapy in a tertiary care hospital at Allahabad, India

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Abstract

Introduction: India has a large proportion of the global HIV-infected patients. Antiretroviral therapy (ART) is the cornerstone of HIV treatment. Antiretroviral drugs are highly toxic and lead to diverse adverse drug reactions (ADRs). Adherence to medications plays a prominent role in success of the therapy. This prospective study was done to study the adherence and analyze its associated factors. **Methodology:** The present study was conducted at ART Centre, Swarup Rani Hospital, Allahabad, Uttar Pradesh, India. Selection of the patients was done based on systematic random sampling method. Baseline enrollment was done over 2 months and follow-up was done monthly over 6 months. Information regarding sociodemographic profile, ART regimen, occurrence of ADRs, adherence to ART and factors affecting adherence was collected. Bivariate logistic regression was done to analyze the association of selected variables with adherence. **Results:** This study enrolled 163 participants among which 152 participants completed the study. During the study period, 94 participants reported the occurrence of at least one ADR. Nonadherence to ART therapy was seen in 31.6% of patients. The most common reason was forgetting to take the medicine (21.8%) followed by occurrence of ADRs (18.3%). No statistically significant association of nonadherence was found with the selected variables. **Conclusion:** Comprehensive research to assess nonadherence to ART therapy is the need of the hour. Policy formulations ought to be made to assess and promote effective adherence to enhance the longevity and quality of life of people living with HIV/AIDS. Concerted efforts by government and intersectoral collaboration are further needed to sustain promotive measures.

Key words: Adherence, adverse drug reaction, antiretroviral therapy, India

INTRODUCTION

HIV/AIDS caused by retrovirus has a significant global burden. The first reported case of HIV was by the United States's Centers for Disease Control and Prevention on June 5, 1981.^[1] Globally, 36.9 million people were living with HIV (PLHIV) by the end of 2014. Amongst them, nearly 2 million people were newly infected in 2014. Around 1.2 million people died due to HIV-related illness in the beginning

of 2015. By June 2015, 15.8 million PLHIV were accessing antiretroviral therapy (ART).^[2]

ART has drastically reduced the burden of mortality due to HIV/AIDS. Sustained virological remission can be attained through successful treatment. Adherence to ART is a major determinant of

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success in the treatment of HIV/AIDS. Adherence is defined as a patient's ability to follow the prescribed instructions.^[3] The WHO standards suggest that at least an adherence of 95% is recommended for success in the treatment of patients.^[4] Although the importance of ART adherence is known, its practice still remains naive and challenging. Very high levels of adherence are particularly recommended where non-nucleoside reverse transcriptase inhibitors (NNRTI) are given due to their varied side effect profiles.^[5] A combination therapy of nucleoside reverse transcriptase inhibitors (NRTI) and NNRTI are usually used as first-line regimens in India in accordance to the WHO guidelines.^[6] Monitoring for adherence is essential to enhance the drug effectiveness and successful viral suppression. It has also been shown that nonadherence to ART is a major cause of HIV drug resistance.^[7,8]

Evaluation of the factors affecting adherence is needed to strengthen the treatment and improve the outcome of patients on ART. In resource-constrained settings, assessment of adherence was done by self-reported recall due to its feasibility. However, use of more than one measure is recommended for more valid adherence assessment.^[9] The objective of the present study was to assess the adherence and factors affecting the adherence to ART regimen among patients attending ART center at Swarup Rani Nehru Hospital, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, India.

METHODOLOGY

The study was conducted in the ART center in Swarup Rani Nehru Hospital at Allahabad, Uttar Pradesh. Ethical clearance was obtained from the Institutional Ethics Committee before the start of the study. The study period was of 8 months which included 2 months of enrolment period and subsequent follow-up of 6 months. The selection of patients was done following systematic random sampling method. Every third patient visiting the ART center on Monday and Thursday (from 9 am to 1 pm) was considered for inclusion. Patients registered (both new and old patients) in the ART center taking ART, who were willing to participate and gave consent were considered for inclusion in the study. Participants who were seriously ill, suffering from psychiatric disorders and who could not comprehend interview questions were excluded from the study. A written informed consent was taken from the patient and an attendant in a local language (Hindi) and assent was taken from parents/caregivers in participants who were below 18 years.

After initial enrolment into the study, each patient was interviewed for 30–40 minutes in pretested semi-structured interview schedule (based on Morisky Scale and Simplified Adherence Questionnaire). Each study participant was then given an identification card containing a unique identification code, date of follow-up visit, and the investigator's contact number to contact if there is any emergency during or after the study period. Norms of confidentiality were strictly maintained and followed.

During the follow-up period, every patient was inquired about any adverse drug reaction (ADRs) and use of any concomitant medications. At the end of 6 months of follow-up period, information was obtained regarding adherence to ART. Patients who missed at least one or more doses in the past week were considered to be non-adherent. Data was entered using Epi Info 7.1 (Epi Info [computer program]. Version 6. Atlanta (GA): Centers for Disease Control and Prevention; 1994) and statistical analysis was done using STATA 14 (StataCorp. 2015. *Stata Statistical Software: Release 14*. College Station, TX: StataCorp LP) and SPSS 22 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

RESULTS

A total of 170 patients were approached and baseline interview schedule was administered among 163 (7 were excluded) patients. During the course of the study, 11 patients were lost to follow-up. Hence, the present prospective study was conducted among 152 patients. There were 86 males and 66 females in the study. Details of the sociodemographic characteristics of the study participants are summarized in Table 1. Majority of the participants (75.4%) had a history of contact with a retrovirus-infected individual. Among the study participants, there was a median delay of 5.5 days from the detection of HIV status to initiation of ART. Almost half of the participants (49.3%) had a CD4 count >250 μ L at the time of initiation of ART. Majority of the participants (66.4%) were on tenofovir+lamivudine+efavirenz (TLE) regimen. At least one ADR was reported in 62% (94 participants) with TLE constituting the maximum ADRs (66.9%).

Adherence to ART medications was assessed at the end of 6 months of follow-up. It was found that 76.3% participants never forgot to take medicines, 95.4% were careful about taking medications, 31.6%

Table 1: Sociodemographic characteristics of the study participants

Characteristic	Male (n=86) n (%)	Female (n=66) n (%)	Total (n=152) n (%)
Age group (years)			
0-10	11 (12.8)	5 (7.6)	16 (10.5)
11-20	9 (10.5)	5 (7.6)	14 (9.2)
21-30	11 (12.8)	18 (27.2)	29 (19.1)
31-40	34 (39.5)	18 (27.2)	52 (34.2)
41-50	16 (18.6)	15 (22.8)	31 (20.4)
51-60	4 (4.7)	4 (6.1)	8 (5.3)
>60	1 (1.1)	1 (1.5)	2 (1.3)
Marital status			
Married	53 (61.7)	33 (50.0)	86 (56.6)
Unmarried	28 (32.5)	10 (15.1)	38 (25.0)
Divorced/separated	0	4 (6.1)	4 (2.6)
Widow/widower	5 (5.8)	19 (28.8)	24 (15.8)
Education			
Illiterate	20 (23.2)	34 (51.5)	54 (35.6)
Primary school completed	21 (24.4)	11 (16.6)	32 (21)
Middle school completed	24 (28)	14 (21.2)	38 (25)
High school completed	12 (14)	3 (4.6)	15 (9.8)
Intermediate or postschool diploma	2 (2.3)	1 (1.5)	3 (2)
Graduation or PG completed	7 (8.1)	3 (4.6)	10 (6.6)
Occupation			
Professional/semi-professional	2 (2.3)	0	2 (1.2)
Clerk, shopkeeper, farmer	18 (20.9)	1 (1.5)	19 (12.5)
Skilled worker	6 (7.0)	2 (3.0)	8 (5.3)
Semi-skilled worker	14 (16.3)	2 (3.0)	16 (10.6)
Un-skilled worker	20 (23.3)	19 (28.9)	39 (25.6)
Unemployed/student	26 (30.2)	13 (19.7)	39 (25.6)
Homemaker	0	29 (43.9)	29 (19.2)

missed at least one dose of drug in the last week and 30.9% missed at least one or more than one dose in the past 3 months.

The most common reason was forgetfulness to take the medicine (21.8%) followed by occurrence of ADRs (18.3%), worsening of symptoms (14%), lack of family support (13.7%), social stigma (12.6%) and difficulty in accessibility (8%). The remaining constituted small proportion as depicted in Table 2. It was observed that 31% of patients were nonadherent to the treatment at some point of time during their treatment course.

Various sociodemographic factors and selected variables were studied for association with nonadherence to ART. In the present study, 49 participants missed one or more doses during the last week and were categorized as non-adherent to ART. On bivariate analysis, participants who were of younger age, are married, living in nuclear family, were employed, had no delay in treatment and on TLE regimen were more adherent to treatment. However, there was no statistically significant association of these variables with adherence [Table 3].

DISCUSSION

The present study enumerates the adherence to ART among patients attending ART center at SRN Hospital, Allahabad. The median age of the study participants was 35 with a range of 21–40 years. This was similar as observed by Bhuvana *et al.*^[10] and Reddy *et al.*^[11] Majority of them (35.6%) were illiterate as observed in these two studies. A median delay of 5.5 days from the detection of HIV status to initiation of ART was seen among the participants. A study by Thuppal *et al.*^[12] showed a median delay of 36 days with tenofovir-based regimen and 116 days with zidovudine-based regimens. Less median delay for the initiation of ART in this study would be a positive measure towards health system efficiency in catering health-care services. It also reflects the increased awareness and accessibility of the patients in receiving health-care services.

It was seen that 32.2% patients missed at least one dose of drug in the past week. This study shows analogous result to other studies in India. A study done by Joshi *et al.* assessed adherence to be 75.5% among PLHIV.^[13] Another meta-analysis study assessed adherence to be 70%.^[14] The present

Table 2: Patient response related to adherence based on interview schedule

Characteristic	n (%)
Do you ever forget to take your medicine?	
Yes	36 (23.7)
No	116 (76.3)
Are you careless at times about taking your medicine?	
Yes	7 (4.6)
No	145 (95.4)
Sometimes if you feel worse, do you stop taking your medicines?	
Yes	4 (2.5)
No	148 (97.5)
Sometimes if you feel better, do you stop taking your medicines?	
Yes	1 (0.7)
No	151 (99.3)
Thinking about the last week. How often have you not taken your medicine?	
Never	104 (67.8)
1±2 times or more	49 (32.2)
Did you not take any of your medicine over the past weekend?	
Yes	6 (3.9)
No	146 (96.1)
Over the past 3 months, how many days have you not taken any medicine at all?	
≤2	105 (69.1)
>2	47 (30.9)
Have you ever decided to stop taking ART altogether?	
Yes	4 (2.6)
No	148 (97.4)
If nonadherent, what are the reasons (multiple responses possible)	
Difficulty in accessibility	7
Difficulty in timings	2
Social stigma	11
Frequent visits	2
Lack of money	2
Adverse drug reactions	16
Improvement in symptoms	3
Worsening of symptoms	13
Lack of family support	12
Forget to take medication	19

ART=Antiretroviral therapy

study enumerated various reasons for nonadherence with forgetting to take the medicine (21.8%) followed by ADR occurrence (18.3%) as the most common. A global study demonstrates that the most frequently reported reasons for nonadherence were related to drug toxicity and side effects. The study also revealed that developing countries have further barriers due to the higher cost of treatment and frequent unavailability of medications.^[15] A systematic review in Asia showed that poor adherence was largely due to the financial burden for treatment and travel and diagnostic costs.^[16] Another study done in Nepal found that

Table 3: Association of various factors with adherence to antiretroviral therapy among study participants

Variable	Adherent	Nonadherent	Unadjusted OR (95% CI) P
Age (years)			
<19	22	8	1.4 (0.5-3.9)
>20	81	41	0.4
Sex			
Female	42	24	0.7 (0.3-1.5)
Male	61	25	0.3
Education			
Illiterate	33	21	0.6 (0.3-1.5)
Literate	70	28	0.2
Marital status			
Married	62	24	1.6 (0.7-3.3)
Unmarried/others	41	25	0.19
Occupation			
Employed	61	25	1.4 (0.6-2.9)
Unemployed	42	24	0.3
Family type			
Nuclear	86	38	1.5 (0.6-3.7)
Extended	17	11	0.37
Delay in treatment (days)			
<7	60	24	1.5 (0.7-3.0)
≥8	43	25	0.28
History of migration			
Yes	21	14	0.6 (0.3-1.5)
No	82	35	0.26
ADR			
Yes	39	19	0.96 (0.4-2.0)
No	64	30	0.9
Change in regimen			
Yes	32	18	0.8 (0.4-1.7)
No	71	31	0.48
ART regimen			
TLE	72	30	1.5 (0.7-3.2)
Others	31	19	0.28

ART=Antiretroviral therapy; ADR=Adverse drug reaction; TLE=Tenofovir+Lamivudine+Efavirenz

nondisclosure of HIV status, alcohol use and being female are major hindering factors for adherence.^[17] An Indian study showed that lack of social support and lack of reminders from family negatively influenced adherence.^[18]

With the increasing burden of HIV/AIDS, measures to provide effective management are needed. Since the major determinant of success of therapy lies in adherence to medication, enhanced counselling of the patient would be a dynamic tool. Programmed counselling of the patient regarding the continuum of therapy for HIV/AIDS is the need of the hour. "Patient-centered counselling" can be shifted to "family-centric counselling" intermittently during follow-up visits to ensure effective adherence. This study adds on to the existing knowledge by

identifying more intricate barriers in nonadherence to ART in Indian settings. As it is seen that most patients are nonadherent to dose because of forgetfulness, measures in the form of mobile message reminders could be effective. In the wake of development of “Digital India,” research can be done for testing the feasibility of mobile-based reminders. ADR monitoring and re-assurance of the patient are prime tools to increase the effectiveness of ART regimens. Further nation-wide research needs to be advocated in this arena to formulate reformatory measures.

The major strength of the study lies in the robust sampling method and assessing ADR along with adherence. The study was a prospective longitudinal study enhancing the patient-investigator relationship through multiple follow-up interactions. The major limitation of the study was assessment of adherence by only self-reported measures. Pill-counting method was not administered among the patients. The role of social desirability bias cannot be ruled out in this study. Since there was inclusion of old and newly enrolled patients on ART, baseline adherence could not be evaluated in all the patients and adherence was evaluated at the end of 6 months of follow-up.

CONCLUSION

PLHIV/AIDS need life-long therapy with ART. Role of nonadherence as a hindering factor for the success of therapy is well established. Advanced research methods to rationalize toxicity monitoring and promote adherence are the need of the hour. There is an immense need to study the favorable factors of nonadherence on a large scale and devise policy formulations to curb them. Measures to enhance the longevity and quality of life of PLHIV/AIDS needs to be focused upon. Sustainable modifications to promote adherence should be scaled up by concerted efforts of government and intersectoral collaboration.

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Conflicts of interest

There are no conflicts of interest.

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