Factors Influencing Adherence to Anti-retroviral Therapy in HIV Patients Registered at ART Center Jhansi, Uttar Pradesh

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ABSTRACT

Context: After introducing 'Treat all policy' in the country and free ART (Anti-retroviral therapy) for all patients the biggest challenge is to optimize adherence to therapy and ensure viral suppression. The present study is aimed to determine the adherence pattern of HIV positive patients at ART center, Jhansi in Uttar Pradesh and to determine the factors influencing adherence.

Methods and Material: This cross-sectional study was conducted in an ART Centre of a teaching hospital. In this study 357 patients were interviewed using a modified version of ACTG questionnaire and adherence was calculated by pill count and recall method. Chi square test and logistic regression was done using SPSS.

Results: Nearly 72% patients had optimum adherence. On univariate analysis the factors found significant were sex of the patient, the education, the socioeconomic status, financial constraints, family support, WHO stage at diagnosis, alcohol addiction and tobacco addiction. On logistic regression four factors, having less than college education, WHO stage IV at diagnosis, alcohol intake and lack of family support were found to be predictors of non-adherence.

Conclusions: Family support, treatment of alcohol addiction improving education and job opportunities for these patients will improve adherence in HIV positive patients.

Key-words: Adherence, ART, PLHIV, ART Center, ACTG* Questionnaire, Uttar Pradesh

INTRODUCTION

India has the third largest epidemic of HIV disease in the world with an estimated 2.349 million PLHIV (People living with HIV).[1] With 548 ART centers and 1236 link ART centers and the 'Test and Treat' policy adapted in 2017, treatment is initiated for all HIV positive patients irrespective of CD4 count.[2] National technical guidelines by NACO(National AIDS Control Organization) say that an adherence of >95% is required to achieve best results.[3] Compliance to ART is the second strongest predictor of progression to AIDS(Acquired Immuno-Deficiency Syndrome) and death, after CD-4(cluster of differentiation-4) count. [4,5] Moreover, low adherence causes development of resistance to ART drugs which is not only a problem

for the patient but also a public health problem because that patients will transmit resistant strains to others. It is important to note that the act of prescribing is a shared decision between the patient and health care provider [6,7,8] Thus the biggest challenge is to achieve an optimal adherence to ART of ≥ 95%, and to minimize the missed and lost to follow up cases. 'Adherence' is a dynamic process. The factors affecting adherence and the order of their importance may vary in different regions of our country and even in the same region at different times. A continuous scrutiny of the factors affecting adherence are required as there is both temporal and geographic variation. Even after free drugs and a network of ART centers we are yet to reach the 90-90-90 target.

This study is the first to explore the factors affecting adherence to treatment of patients registered at ART center in Bundelkhand region of Uttar Pradesh.

The present study has been designed to determine the prevalence of optimal adherence to therapy at ART center, Jhansi. It will also determine the level of adherence to prophylaxis and treatment of opportunistic infections among them and will determine the factors associated with optimal adherence.

SUBJECTS AND METHODS

It is a hospital based cross sectional study conducted at ART center, MLB Medical College, Jhansi, Uttar Pradesh. Participants were selected from the HIV positive patients attending the OPD for their scheduled visits. All persons aged 18 years and above, of both sexes, diagnosed with HIV/AIDS and currently registered at ART center, Jhansi and receiving treatment for more than six months were requested to participate in the study. Pregnant women and those who were not willing to participate, those who were seriously ill and required hospitalization were excluded.

The study was conducted from Sept 2020- Dec 2020.

Sample size was calculated using prevalence of optimal compliance of 70% as mentioned in systematic review by Mhaskar R et al, [9] 95% confidence intervals and absolute precision of 5% (formula used: n = z^2pq/e^2; where n = sample size, z = value of standard normal deviate = 1.96 at 95% confidence interval [CI], p = prevalence of adherence, q=1–p, and e=absolute precision) the sample size came out to be 323 patients. Taking 10% extra for omissions or incomplete forms the total sample size comes out to be 355.

The regular OPD load at the ART center is between 30±10/day. The patients were selected by systematic random sampling. There were 1230 patients on treatment and the sample size was 355. So, the sampling interval was calculated as 3.5. So, every 3rd patient was selected for interview. If the patient did not meet the specified criteria the next person was chosen. On an average 8-10 patients were interviewed each day. Patients were interviewed twice a week.

The patients included in the study were asked about their bio-social determinants and complete clinical history using a pre-designed and pre-tested questionnaire designed in English. This was filled by the investigator and questions were asked in Hindi. The same investigator collected data from all patients by direct interview technique. Adherence was assessed by patient recall in which the patient was enquired about how many doses he/she has missed in the last one month and confirmed by pill count method. Optimum Adherence has been defined as patients with an adherence ≥ 95%. To determine the presence of family support, and reason for missing medicine section B and C of ACTG questionnaire[10]

were used respectively. Socio-economic assessment was done using modified B.G.Prasad scale.[11] The presence of depression was assessed by means of PHQ-9 scale.[12] The PHQ-9 score can range from 0 to 27, since each of the 9 items can be scored from 0 (not at all) to 3 (nearly every day). PHQ-9 scores of 5, 10, 15, and 20 represented mild, moderate, moderately severe, and severe depression, respectively. To assess the other factors, the patients were asked if the travel expenses were perceived as a financial burden to them as a simple yes/no question. We did not decide on a cut off for the expenses because the earning and paying capacity, the distance travelled and mode of travel varied widely from one patient to another. They were also asked about use of addictions like alcohol and tobacco as a yes/ no question. WHO staging[13] at diagnosis and present WHO stage was taken from their records. All patients were explained the purpose of the study and written informed consent was taken from them. The participants were assured about their privacy and confidentiality. Ethical clearance was taken from the institutional ethical committee.

RESULTS

Figure-1 shows that 257 patients (71.98%) had optimum adherence. Out of these 42.85% patients had 100% adherence and 29.13% had >95% to 100% adherence. In the present study 100 (28.02%) patients had suboptimal adherence. Out of 100 non adherent patients, 34 patients had adherence between 80-94% and 66 patients had <80% adherence which is termed 'poor adherence'. The most common reasons for missing treatment were running out of pills, busy with other things, were away from home, simply forgot, slept through the dose time, too sick to take medicine or felt good.
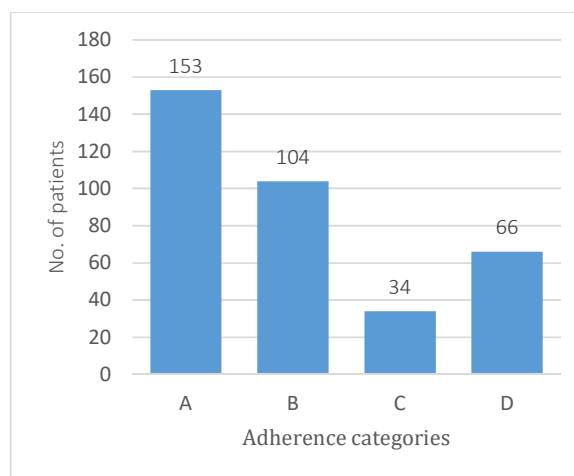
Category A is 100% adherence, Category b is >95 to <100% adherence, category C is <95% up to 80% adherence and Category D is <80% adherence.

Figure-1: Calculation of adherence to ART
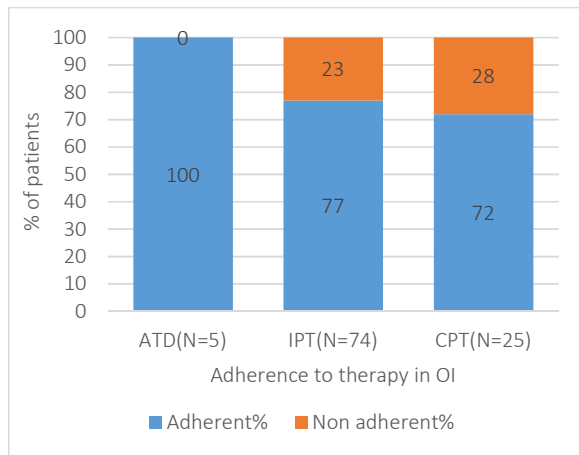
The number N in parenthesis indicate the total number of patients on Anti-tubercular drugs (ATD), INH prophylaxis therapy (IPT) and Co-trimoxazole prophylaxis therapy (CPT)

Figure-2: Prevalence of adherence to therapy and prophylaxis for opportunistic infection (OI) in percentages

Adherence was defined as not missing any dose given for prophylaxis and treatment of OIs in the last 1 month as there is no definition for Optimal adherence to IPT and CPT in the GOI guidelines)[3]

Figure-2 shows that there was a total of 5 patients on ATD at the time of interview. Out of these, all 5 were adherent to ATD but 4 out of 5 were adherent to ART. Among the study participants 74 patients were on IPT out of which 57 were adherent to IPT. Reason for being non adherent to IPT were given as side effects by 3 participants and fourteen patients did not wish to take an additional medicine. A total of 25 patients were on CPT out of which 18 were adherent. No other OI was seen in the participants interviewed in our study.

Table 1-4 show the various factors associated with adherence as per the five WHO domains namely the sociodemographic factors, patient related, therapy related, clinical condition related and health system related. The findings show that male sex, lower socio-economic classes and being illiterate were the socio demographic factors associated with non-adherence. Male sex has been found to have 1.71 times higher risk of being non adherent as compared to females, Odd's Ratio (OR) 1.71 (95% C.I 1.068-1.75). Being from socioeconomic class (SEC) IV and V had a 2.45 times higher risk of non-adherence, OR-2.455(95% CI 1.37-4.39).

Table-1: Association of social factors with adherence

Variable	Total number studied	Patients having Optimum adherence (%)	Chi square value	P value
Religion				
Hindu	327	233 (71.25)	1.04	0.31
Muslim	30	24 (80)		
Caste				
General	112	89 (79.46)	5.19	0.16
SC	84	56 (66.67)		
ST	19	12 (63.15)		
OBC	142	100 (70.42)		
Others	30	25 (83.33)		
Residence				
Rural	213	151 (70.89)	0.32	0.57
Urban	144	106 (73.61)		
Family support				
Yes	281	217 (77.22)	17.94	<0.01
No	76	40 (52.63)		
Education				
Illiterate	82	55 (67.07)	61.54	0.000
Primary	82	71 (86.58)		
Secondary	59	21 (35.59)		
Higher secondary	64	46 (71.88)		
College and above	70	64 (91.43)		
Employment status				
Employed	203	143 (70.44)		
Unemployed	154	114 (74.02)	0.56	0.46
Socioeconomic class				
I	46	43 (93.48)	16.06	<0.01
II	31	25 (80.65)		
III	26	18 (69.23)		
IV	94	59 (62.77)		
V	160	112 (70)		
Financial burden				
Yes	184	124 (67.39)	3.98	0.046
No	173	133 (76.88)		

Table-2: Association of demographic factors with adherence

Variable	Total number studied	Patients having optimum adherence (%)	Chi square value	P value
Age				
18-30	96	69 (71.87)	4.61	0.20
31-45	159	107 (67.29)		
45-60	85	67 (78.82)		
>60	17	14 (82.35)		
Gender				
Male	191	128 (67.02)	5.04	0.02
Female	166	129 (77.71)		
Marital status				
Married	243	177 (72.84)	0.98	0.87
Not married	114	80 (70.18)		
Type of family				
Nuclear	211	146 (69.19)	3.41	0.18
Joint	76	61 (80.26)		
Broken	70	50 (71.42)		

Table-3: Association of medical (patient and clinical condition related) factors with adherence

Variables	Total number studied	Patients having optimum adherence (%)	Chi square value	P value
Patient related factors				
Family history				
Spouse positive	185	133 (71.89)	0.001	0.98
Spouse negative	99*	71 (71.71)		
Route of transmission				
Heterosexual	271	193 (71.22)		
Blood related	22	15 (68.18)	1.39	0.85
Mother to child	14	11 (78.57)		
Unsafe injection	10	8 (80)		
Unknown	40	30 (75)		
Alcohol use				
Yes	55	27 (49.09)	16.91	<0.01
No	302	250 ()		
Tobacco use				
Yes	113	69 (61.06)	9.79	<0.01
No	244	188 (77.05)		
Perception to treatment				
Beneficial	298**	215 (72.15)	0.02	0.87
Non beneficial	11	5 (45.45)		
Clinical condition related				
WHO stage at diagnosis				
I	216	159 (73.61)	8.05	0.04
II	54	40 (74.07)		
III	57	42 (73.68)		
IV	30	16 (53.33)		
Presence of depression				
Yes	43	29 (67.44)	0.50	0.47
No	314	228 (72.61)		

*Out of 357 patients who were positive, only 284 had the HIV status of their spouses checked.

**48/357 patients replied 'not sure' to this question

Patients having college education had 5.19 times higher odds of being adherent to Anti-retroviral therapy, OR-5.19 (95%CI 2.17-12.43). Other socio-demographic variables mentioned in the table age, religion, caste and rural/urban residence were not found to be associated with adherence. Family support was found to be significantly associated to adherence OR-3.05, (95% CI 1.79-5.8) although marital status and type of family were not found to be statistically significant. The table also shows that the financial burden of travel was seen in 48.63% (124/257) of adherent individuals and 60% (60/100) of non-adherent individuals and is statistically significant (OR-1.61, CI 1.01-2.57). It is of importance that a very high percentage of individuals in both groups mentioned that travel cost was a burden.

transmission was heterosexual 75.91%, but the route of transmission was not found to affect adherence. Among the studied HIV infected patients, there were 184 patients (51.54%), whose spouse was also positive. For 73 (20.45%) patients the status of spouse was not known.

Table 4: Association of therapy and healthcare system related factors with adherence

Factors	Total number studied	Patients having optimum adherence (%)	Chi square value	P value
Therapy related factors				
Time since treatment				
<2yrs	80	59 (73.75)	1.76	0.41
2-5 yrs	110	74 (67.27)		
>5yrs	167	124 (74.25)		
Efavirenz based regimen				
With Efavirenz	333	238 (71.47)	0.49	0.49
Without Efavirenz	75	56 (74.67)		
Presence of side effects				
Yes	28	23 (84.21)	1.55	0.21
No	329	234 (71.12)		
Health care system related				
Satisfaction				
Satisfied	339	244 (71.98)	0.001	0.97
Dissatisfied	18	13 (72.22)		
Counseling				
Regular	189	134 (70.9)	0.26	0.62
Not regular	168	123 (73.21)		
ART availability				
Yes	334	239 (71.56)	0.48	0.49
No	23	18 (78.26)		

Few variables across the five dimensions were analyzed but not showed in final univariate analysis as they were not significantly associated with dependent variable

Table-5: Logistic regression of factors found significantly associated to predict non adherence

Variables	AOR*	95% CI **	p-value
Gender			
Male	1.14	0.64-2.02	0.659
Female	1		
Literacy			
<college education	3.48	1.38-8.78	0.008
College education	1		
Socio-economic status			
L,LM	2.02	0.98-4.16	0.58
U,UM,M	1		
WHO stage at diagnosis			
IV	2.56	1.10-5.93	0.03
I,II,III	1		
Family support			
No	2.38	1.34-4.22	0.003
Yes	1		
Alcohol intake			
Yes	2.45	1.18-5.08	0.02
no	1		
Tobacco intake			
Yes	1.39	0.79-2.46	0.25
No	1		
Financial burden			
Present	1.29	0.72-2.29	0.39
Absent	1		

*AOR- adjusted odds ratio, **CI- Confidence interval

Among the patient related factors, the main route of Family history was not found to be associated with adherence. Personal history of alcohol and tobacco use were found to be significantly associated with adherence OR-3.31 (95% CI: 1.83- 5.98) for alcohol and OR-1.816 (95% CI 1.13- 2.9) for tobacco consumption. Perception to treatment was not found to be significantly associated with adherence primarily because almost all patient's felt treatment was beneficial in adherent and non-adherent group. The factors found significant on univariate analysis were analyzed by multivariate logistic regression.

Table 5: On applying logistic regression, four factors came out to be significantly associated with adherence, having less than college education (AOR-3.48), having WHO stage four disease at diagnosis (AOR-2.56) those with habit of alcohol consumption (AOR-2.45) and those without family support (AOR-2.38) were found to be more likely to be non-adherent, (p value taken significant at ≤ 0.05).

DISCUSSION

In the present study, most of the HIV infected patients (44.5%) were in the age group of 31-47 years with mean age of 39.22 ± 11.73 years comparable to the findings of other studies. [10,11,12]

The males outnumbered the females in this study. The male: female ratio in this study was 2.57:1. This was high as compared to ratios in other studies [14,15,16] This could possibly be explained by the fact that 59.7% of the study population in the present study was from rural areas where women do not have the accessibility to HIV testing services and probably lack awareness about HIV-AIDS. The present study found that the percentage of HIV positive individuals who were married were 68.1%, which was comparable to other studies [14,16,17,18]. The percentage of unemployed patients in the present study was 43.1% which is higher than 33%-34.8% found in other studies. [14,16,19] This increased number of unemployed people may be due to Covid related loss of work of many people. In the present study the per-

centage of literates was 77% which was comparable to other studies. [14,16,17] In the present study 24.37% patients were in stages III and IV as compared to 14.7% patients in the study by Raju B N et al. [18]

In the present study 71.98% patients showed optimum adherence of ≥ 95%. Other studies assessing adherence over a similar period showed 81% [15] and 89%. [14] The figures for optimum adherence in our ART center in the previous years was also between 81-83% and hence the low figure found in our study is probably a result of the impact of Covid Pandemic which resulted in decreased travel options, unemployment and resulting financial problems. In our study 27% were unskilled workers, 43.1% were unemployed and travel cost was mentioned as a burden by 51.8% patients. Studies assessing adherence for longer periods [16,17] showed lower prevalence and studies assessing adherence over a few days showed higher prevalence. [19,20,21] In our study only 5(1.4%) patients taking TB treatment at the time of interview in contrast to studies from Maharashtra by Giri P.et al [22] in 2011-12 where prevalence of TB was (17%) among HIV positive patients. The low prevalence in the present is probably because of Isoniazide Prophylaxis Therapy (IPT) which was being given to all patients. Among the factors affecting adherence male sex was found to be significantly associated with reduced adherence similar to the findings of Joshi B. et al. [17] Literacy was significantly associated with adherence in the present study comparable to other studies. [17,18] In the present study the group which had financial constraints were 1.61 times more likely to be non-adherent as compared others who had no constraints similar to other studies. [17] The present study shows that socio economic class affects the adherence with those from lower SEC having more chances of non-adherence and family support was found to be positively associated with adherence similar to other study. [23] The odds of being non adherent on using alcohol and tobacco was comparable to findings of Raju B.N. et al [17]. WHO stage at diagnosis was associated with adherence in the present study similar to another study [17] In the present study less than college education, alcohol addiction, lack of family support and advanced stages of disease at diagnosis were found significant in logistic regression.

Our study had few limitations. It assessed patients coming only to ART center. It did not include those people taking treatment for HIV from private hospitals. The possibility of recall bias cannot be ruled out in this study and adherence reported by recall method is usually over reported. No causal claims can be made as temporality could not be assessed.

RECOMMENDATIONS

The out-of-pocket expenditure, to reach ART center, is a problem which needs urgent attention. It not only causes people to miss /delay coming to the center but also in some cases the attendant takes medicine for the patient or any one of the spouses takes medicine for the other. So, all patients do not receive counseling and a complete check-up which is most important for maintaining adherence and proper follow up of the patient.

In case of selected patients with poor adherence (< 80%) and for missed and LFU cases there may be a role of treatment supporter similar to DOTS provider for a certain fixed period of time may be 6-12 months depending upon the individual patient.

Treatment for quitting addictions and screening patients for subclinical depression along with evaluation and treatment of all diagnosed patients will help to improve adherence.

People who are registered at a center near their homes and are working in other cities are more prone to miss treatment. This is because they do not want to be transferred to other center for fear that their HIV status may be disclosed at place of work or where they stay. They should be given the facility of taking treatment as 'in transit patients' without being transferred to the new center.

IEC/BCC activities to stop stigma and discrimination against PLHIV and linking them to ART services, social service schemes and employment schemes are effective long-term measures to improve adherence as well as quality of life of PLHIV.

CONCLUSION

The present study showed that 72% patients had ≥95% adherence to ART. Adherence requires support from friends and family members, dealing with alcohol addiction, improving education levels for young patients and taking care of travel cost for patients. This together with regular counseling about the importance of adherence to treatment will improve adherence.

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Key Messages: Free ART and regular counselling to ensure optimal adherence is very important to improve outcome of HIV positive patients. Equally important are giving travel allowance, helping them overcome addictions and depression and good social support.