An Evaluation of Factors Affecting Non Adherence to Anti-Retroviral Therapy

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Abstract :

　Introduction : Non adherence has been considered as one of the factors responsible for emergence of resistance to ART. There are many factors (like patient related, regimen related, social/environmental and adverse effect related factors) thought of responsible for non adherence to ART. The current study focuses on the assessment of factors affecting non adherence to ART. **Objective :** To assess the factors affecting non adherence to ART. **Method :** This is a prospective study involving 200 people living with HIV/AIDS. The non adherence was measured using pill count method and factors responsible, were assessed using a pre structured performa. **Results :** Higher non adherence was seen amongst > 60 years age group, females, unemployed, illiterate, living as widow/widower and belonging to lowest socio economic class. **Conclusion :** As evident from results from the study, the socio demographic groups showing higher non adherence should be provided special attention and motivation through special counseling sessions. Devices like alarm clock can be used to remind patients about medication.

Key words : Anti Retroviral Therapy, Non adherence, Adherence

Introduction :

　A major worry with scaling up of antiretroviral therapy (ART) in settings with restricted resourcesis the emergence of drug resistant viral strains due to suboptimal adherence and the transmission of these resistant viral strains in the population. There are many factors thought of responsible for non adherence to ART. Apart from the quality of services provided by the health care system, many socio cultural factors also play part in determining the attitude of patients towards ART. This attitude is ultimately reflected in patients' adherence to ART and their CD4 count response and virological response. Recent surveys of knowledge, attitude and behavior regarding treatment adherence have provided insight into patient and service provider's perceptions of many factors influencing the practice of medicine taking. [1, 2]Other factors that seem to have a stronger relationship to treatment adherence than demographics include: 1) patient's knowledge of the treatment plan and regimen; 2) presence and management of side effects/symptoms; 3) cultural and health beliefs towards disease and treatment; 4) presence or absence of a social support system; and 4) specific co-morbidities such as substance abuse and mental health problems.[3]

Following are the hypothesized predictors of ART adherence.

- **Patient related Factors :** It is expected that patients who have more-positive attitudes toward ART, greater self-efficacy toward adherence and higher literacy levels will be more adherent with ART.

- **Regimen Factors:** The patients receiving less complex antiretroviral regimens and regimens that fit less well with the other daily activities will be less adherent.

- **Social/Environmental Factors:** The patients with more social support to be more adherent. Ease of availability of ART at affordable cost at the nearest center also aids adherence.

- **Adverse effects:** The side effects of Anti retro viral drugs vary from mild form (which hardly influences patient's attitude towards drug) to severe form (which may compel the patient to stop that drug). Following are some important adverse effects developing at various stages of therapy.

NON ADHERENCE AMONG CHILDREN

There were 2.5 million children living with HIV in world and 4, 20,000 children were newly infected in year 2007. [4] Adherence may be more complex in children compared to adults due to many factors including reliance on care giver who may themselves be ill or may not be the child's parent, complex dosing regimens, lack of availability of paediatric fixed dose combinations, poor drug palatability, difficulty with taking tablets/capsules and interference with daily routine. [5, 6] Adherence estimates of 50 to 75% have been reported, well below the required 95% to achieve optimal viral suppression. [6, 7] Health service challenges as well as individual factors such as poor socio economic circumstances, poor literacy and the prohibitive cost of liquid drug formulations necessitating tablet/capsule administration to very young children can be additional potential barriers.

Method :

Present study is unique in the sense that no similar prospective study has been done in the past, in Gujarat, to assess the factors affecting non adherence among patients on ART. The vacuum created by lack of such studies, prompted and motivated authors to conduct the present study.

This is a prospective study conducted at ART centre, Civil Hospital, Ahmedabad spanning over 18 months in duration. There is no previous data available on prevalence of non adherence in Gujarat. At the time of initialization of study, total number of patients enrolled at the ART centre was around 2000. In the current study, 10% of total patients enrolled at ART centre, were taken as sample size which is 200. Currently this ART centre (which is centre of excellence) is providing ART and other services like Integrated Counseling & Testing Centre (ICTC) Prevention of Parent to Child Transmission (PPTCT) laboratory investigations and dietary advices free of cost.

A cohort of 200 PLHA on ART was selected from PLHA attending ART centre. The study sample was selected by stratified random sampling technique. The strata used were male: female: paediatric age group in proportion of 6:3:1 respectively. The inclusion and exclusion criteria are as follow.

Inclusion Criteria

1. Only those patients who have never been non adherent during their treatment were included. Adherence of past treatment was ensured by past record of pill count recorded in white card of the patient.

2. Only those patients whose treatment has been started in the ART Centre, Civil Hospital, Ahmedabad were included in the study.

Exclusion Criteria

1. Those patients whose ART has been started in the other setup were not included.

2. Children without a known permanent & identifiable care taker were not included in the study

Method of Data Collection :

After receiving approval from ethical committee, PLHA were enrolled in the study by using above mentioned selection method. Informed consent was ensured before enrolment of each PLHA.

Along with enrolment, base line data about each sampled PLHA was collected using preformed and pre tested baseline data form. These patients were interviewed at monthly interval, every time they visit ART centre for next 18 months. The follow up data collection was done by either face to face interview or telephonic interview.

At the time of follow up, adherence to ART was measured by pill count method (monthly).

Pill count method at ART Center, Civil Hospital, Ahmedabad

The ART drugs were supplied as one tablet fixed dose combination containing the 3 drugs. The patients were instructed to swallow a single tablet of such a combination every 12 hours. The time of 12 hourly doses were determined according to patients' comfort. They were always dispensed an intact bottle containing 60 tablets. The patients were also advised to come back for refill at least 2 or 3 days before exhaustion of the dispensed doses (Usually on 28th day). The doses remaining with the patients were compared with the total doses dispensed to him/her

at the time of last visit. By this comparison number of doses missed by the patient can be known.

Attrition of cohort during 18 months of study period

Data was collected for next 18 consecutive months from the date of initiation. At the time of last follow up, 177 of all the enrolled PLHA were attending the ART centre. There was attrition of 23 subjects in during the study, which is 11.5% of original sample size. Out of these 23 subjects, 2 patients expired, 9 were lost to follow up and 12 PLHA were transferred to other ART centres, during the study period.

Definitions of non adherence

It has been known that <95% adherence is associated with significant resistance to ART. In pill count method non adherence is measured by dividing number of doses missed by patient during last month or time since last follow up by total number of doses dispensed to the patient. The relationship between number of missed doses and level of adherence is mentioned below. [8]

No. of missed doses	Level of adherence
≤ 3	≥95%
4 -12	94-80%
>12	<80%

In current study subjects are divided into 2 categories at the end of study.

1) Those who have never missed more than 3 doses in any month during the entire period **(Adherent)** and

2) Those that missed more than 3 doses on at least 1 occasion during study period **(Non adherent)**.

These categories make bases of division of study population into adherent and non adherent groups according to pill count method.

Results:

**Table 1 : Socio-demographic factors affecting level of adherence**

Characteristics	Adherent N(%)	Non-Adherent N(%)	Total N(%)
Age groups			
0-10	6(75.0)	2(25.0)	8(4.5)
10-20	4(66.7)	2(33.3)	6(3.4)
20-30	27(69.2)	12(30.8)	39(22.0)
30-40	53(76.8)	16(23.2)	69(39.0)
40-50	31(75.6)	10(24.4)	41(23.2)
50-60	8(80.0)	2(20.0)	10(5.6)
60-70	2(50.0)	2(50.0)	4(2.3)
Gender			
Females	36(72.0)	14(28.0)	50(28.2)
Males	95(74.8)	32(25.2)	127(71.8)
Education			
Graduate and Above	15(68.2)	7(31.8)	22(12.4)
Secondary and Higher Secondary	58(84.1)	11(15.9)	69(39.0)
Primary	43(72.9)	16(27.1)	59(33.3)
Illiterate	15(55.6)	12(44.4)	27(15.2)

Employment status			
Yes	98(77.2)	29(22.8)	127(71.8)
No	33(66.0)	17(34.0)	50(28.2)
Marital status			
Married	89(76.7)	27(23.3)	116(65.5)
Single	17(70.8)	7(29.2)	24(13.6)
Widow/widower	12(63.2)	7(36.8)	19(10.7)
Divorced/Separated	12(70.6)	5(29.4)	17(9.6)
Live in	1(0.8)	0(0)	1(0.6)
HIV Status of Partner/Parent			
Partner Negative	61(75.3)	20(24.7)	81(45.8)
Partner Positive	50(74.6)	17(25.4)	67(37.9)
Both Parents Positive	2(100.0)	0(0.0)	2(1.1)
Only Mother Positive	0(0.0)	1(100.0)	1(6.0)
Status of Partner Unknown	18(69.2)	8(30.8)	26(14.7)
Total	**131(74.0)**	**46(26.0)**	**177(100)**

As per the table 1, highest prevalence of non-adherence (50%) was found in the age group of 60-70 years of age followed by 10-20 years of age group (33.3%). Almost similar level of non-adherence is seen among both the genders (28% in females and 25.2% in males) (X^2=0.14, DF=1, p>0.05). Peak of the (44.4%) non adherence was seen among illiterates. Non adherence among illiterates was 17.4%. No statistically significant difference was found between levels of non-adherence with employment. (χ^2=2.32, DF=1, p>0.05). It was found that maximum non adherence was amongst widows/widowers (36.8%). (χ^2=2.18, DF=4, p>0.05). As evident from the table, when HIV status of the partner was unknown, higher non adherence and less adherence were seen, compared to others.

Figure 1: Level of non-adherence in various socioeconomic classes[*]
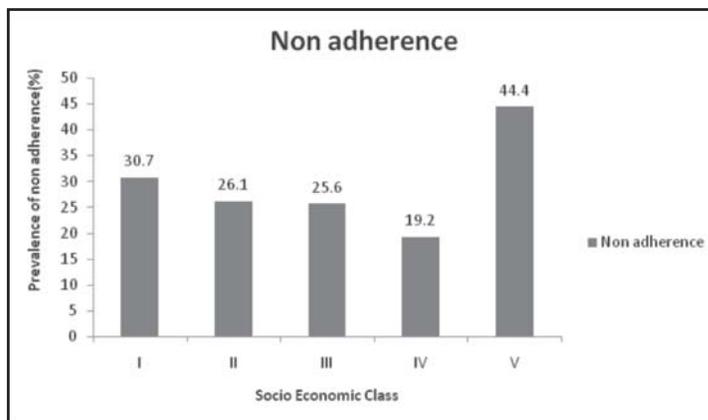
* Modified Prasad Classification

Maximum (44.4%) prevalence of non adherence was seen in SE class V, followed by class I (30.7%).

No significant relation was found between SE class and level of non adherence.

Table 2 : Treatment related factors affecting level of adherence

Regimen	Adherent n (%)	Non-Adherent n (%)	Total n (%)
Stavudine+Lamivudine+Efavirenz	5(62.5)	3(37.5)	8(4.5)
Stavudine+Lamivudine+ Nevirapine	31(75.6)	10(24.4)	41(23.2)
Zidovudine+Lamivudine	2(66.7)	1(33.3)	3(1.7)
Zidovudine+Lamivudine+Efavirenz	7(53.8)	6(46.2)	13(7.3)
Zidovudine+Lamivudine+Nevirapine	86(76.8)	26(23.2)	112(63.3)
Previous changes in Regimen			
Yes	104(73.2)	38(26.8)	142(80.2)
No	27(77.1)	8(22.9)	35(19.8)
Duration since diagnosis			
<6 months	19(73.0)	7(27.0)	26(14.7)
6-12 moths	19(73.0)	7(27.0)	26(14.7)
12-60 months	71(71.7)	28(28.2)	99(55.9)
>60 months	22(84.6)	4(15.3)	26(14.7)
Duration since treatment			
<6 months	47(67.1)	23(32.9)	70(39.5)
6-12 moths	24(77.4)	7(22.5)	31(17.5)
12-60 months	59(78.7)	16(21.3)	75(42.4)
>60 months	1(100)	0(0)	1(0.6)
Total	131(74.0)	46(26.0)	177(100)

Highest level of non adherence (46%) was seen among those who were on the regimen containing Zidovudin+Lamivudin+Efavirenz. Most 112(63.3%) PLHA were on regimen Zidovudin + Lamivudin + Nevirapine. Level of non adherence among them was 23.2%. There is 26.8% of non adherence among those whose ART regimen has been changed in the past, while prevalence of non adherence among those, whose ART regimen was not changed in the past is 22.9 % (X^2=0.22, p=0.06). Highest non adherence was seen amongst those who has been perusing treatment for less than 6 months (32.9%). (Table-2)

Discussion :

The present study had sample size of 200 patients of HIV, enrolled and attending ART centre, Civil Hospital, Ahmedabad. Out of 200, 177 could be followed till the end of study. This constitutes attrition of 11.5% of sample. Overall 131(74.0%) patients were completely adherent and never missed >3 doses/month during entire study period. 46(26.0%) patients had missed >3 doses/month at some point of time. They were defined as non-adherent. A study done in Pune and Delhi by Sarna A et al also found similar non adherence of 24.1%. [9]Although they followed different monitoring method for measurement of adherence. In another prospective study involving self-pill count also showed that level of non-adherence among the sample population is 21.9%.[10]

The level of non-adherence was found higher among females in the study done by Sarna A et al (18.4%). Similar finding is seen in the current study as well, in form of higher prevalence of non-adherence among females (28.4%). This can be explained by higher level of illiteracy (24.6%) among females of sample population. Illiteracy may become barrier between knowledge of importance of adherence to ART and their practices. As per the table 1, highest prevalence of non-adherence (50%) was found in the age group of 60-70 years of age followed by 10-20 years of age group (33.3%). Previous study conducted in Cuba by Carlos Aragonés BEng MS et al

showed highest non adherence amongst <25 years age group.[7]

Non adherence was found higher (34.0%) among those who were unemployed. Different result was seen in study done by Walshe L et al. Level of adherence among unemployed was higher (48.7%) than employed (33.7%). Highest level of non-adherence was among widows/wodowers (36.8%). Similar results were also noted in the study done in Sub Saharan Africa (33.3%). [11]Those whose partner or parents HIV status was unknown were more (30.8%) non adherent than who were aware. This may show their attitude of neglecting the illness and importance of knowing the status of partner. This may be reflected in their behaviour of missing doses as well.

The regimen containig "Zidovudine + Lamivudine + Efavirenz" was associated with higher level of non-adherence. Different results were found in a study conducted by Arun Kumar. [12]The mentioned study showed highest non adherence with regimen "Stavudine+Lamivudine+Efavirenz" It was observed in the current study that changes in the regimen leads to higher chances of non-adherence. Contrasting result was seen in study conducted at Cuba.[13]

Conclusion and Recommendations :

Current study could examine possible factors like age, gender, level of education, HIV status of partner, drug regimens, duration of treatment etc. Higher non adherence is seen among people with above mentioned characteristics. So such patients need more social support and motivation. Regular home visit can help to solve the issue among these patients. Increase in number of counseling session can also be beneficial to such patients. Daily or weekly pillboxes, timers with alarm, pagers, SMS on mobile or other devices can be used to remind patients with geriatric age group. Patients with low level of education may find conventional method of explanation about dosing, as difficult. For such patients, visual aids and audio/video information sources may be more beneficial. Apart from this, PLHA should be encouraged for education. Because of that, children living with HIV/AIDS can be also be

benefited, if financial, social and mental supports are provided for education. Overall increase in education level can result in increase in adherence level.

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