



## Factors Affecting Adherence to Highly Active Anti-Retroviral Therapy in Pediatric HIV Cases: An Exploratory Study

### Paediatrics

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### ABSTRACT

**Background:** Inadequate adherence in Acquired immunodeficiency syndrome (AIDS) increases the risk of drug resistance and treatment failure. Adherence is a serious challenge for those receiving Anti-Retroviral Therapy (ART) especially children. Factors associated with pediatric ART adherence can be related to caregivers, children themselves, the medication/regimen, socioeconomic, or service delivery issues.

**Objective:** The present study was conducted to know the factors affecting adherence to ART in pediatric HIV/AIDS patients at tertiary care hospital.

**Methods:** The study was a hospital based cross – sectional study where 216 children registered at the pediatric ART clinic of a tertiary care hospital in Delhi and their caregivers were included in the study. Semi-structured, pretested interview schedule was used for data collection through face to face interview.

**Results:** Out of the 216 children, males outnumbered females in the ratio of 2.48:1. Approximately 90% of the study subjects had  $\geq 95\%$  adherence in last 3 months of the study. Independent risk factors in multivariate logistic regression analysis for non-adherence were: lower age of the child, female gender, non-parental caregiver and presence of illness in last six months.

**Conclusion:** Factors associated with non-adherence to ART were lower age, female, non-parental caregiver and presence of illness.

### KEYWORDS:

HIV/AIDS, adherence, female gender, non-parental caregiver

### Introduction

HIV (Human Immunodeficiency Virus) continues to be a major global public health issue, having claimed more than 39 million lives till 2014.<sup>[1]</sup> Children have higher rate of viral replication with resulting high viral load and higher rate of CD4 cell destruction.<sup>[2]</sup> According to United Nations Programme on HIV and AIDS (UNAIDS), the total estimated number of children under the age of 15 years living with this virus globally was 2.6 million at the end of 2014.<sup>[3]</sup>

In India, the estimated number of people living with HIV/AIDS were 0.21 million in 2013 according to UNAIDS. Of these children comprised 7% of total cases (0.14 million).<sup>[4]</sup> With the availability of ART since 2004, HIV infection, which was once considered a progressively fatal illness, has now become a chronic treatable condition in children, as in adults.<sup>[5]</sup>

In many families children act as caregiver for sick parents who have AIDS. Family which is most effective structure for responding to children's need is disrupted in most of the cases because of HIV infectivity of parents.<sup>[6]</sup>

Inadequate adherence increases the risk of drug resistance and treatment failure. Adherence is a serious challenge for those receiving ART especially children. Factors associated with pediatric ART adherence can be related to caregivers, children themselves, the medication/regimen, socioeconomic, or service delivery issues.<sup>[7]</sup> Parents may have poor understanding of the need to take the medication and they may be unwilling to disclose the child's HIV-positive status to the child or others involved in the care. This may create problems in administering doses while the parent is at work or the child at school.<sup>[8]</sup>

Adherence assessment in children with HIV/AIDS is a very pertinent issue that would ultimately impact upon the success of the programme and clinical outcome in the patients. Therefore, this study was conducted at the pediatric ART Clinic in a tertiary care teaching hospital in Delhi with the objective of assessing adherence to ART in HIV-infected children and their influencing factors.

### Subjects and Methods

#### Study design, settings and participants:

It was a hospital based cross-sectional study conducted over a period of one year from January to December 2015 in ART Centre of tertiary care teaching hospital in New Delhi, India. All children aged up to 14 years of age enrolled at ART centre constituted the study population. A total of 260 cases, which were registered at ART centre as on 31st December 2013 were enrolled for the study. However, 44 caregivers who refused participation were excluded from the study. So, total 216 pediatric HIV cases receiving treatment and care for HIV/AIDS at ART clinic were enrolled for study.

#### Data collection

The caregivers of the study subjects attending the pediatric ART clinic were interviewed after taking informed written consent. Assent was taken from children aged 7 to 14 years in addition to written consent from the parents or legal guardians. For children less than 7 years, only written consent from the parents or legal guardians was taken. Clinical and related laboratory reports of the subjects were accessed from the records at pediatric ART clinic. The interview was taken in a separate personal counsellor room and confidentiality was maintained at the time of interview.

### Study tools

A semi-structured interview schedule was designed, pretested and used for data collection to study socio-economic and demographic profile and treatment adherence for Highly Active Anti-Retroviral Therapy (HAART) regarding HIV/AIDS. Information regarding a) socio-demographic profile of child and caregiver i.e. age, gender, religion, educational status, area of residence, socio-economic status of the parents, parent's occupation, parents' HIV status b) information regarding factors affecting response to HAART like age of the child, socioeconomic status, caregiver's education, duration since initiation of ART were asked. Information about missed dose of ART last time, reason for non-adherence were also assessed.

Socio economic status was assessed by Modified B. G. Prasad Socio-economic status scale using updated current price index of 2015.[9] The schedule in English was translated in the local language (Hindi) and retranslated back to English for validation. It was pretested on 20 patients in similar setting. Appropriate modification was done after pretesting. Average time duration of each interview was approximately 20-25 minutes.

**Adherence:** Adherence to ARV treatment was assessed using the pill count method.

Number of tablets/dose actually taken by the patient for a particular time/period  $\times$  100

### Number of tablets/dose prescribed for this time/period

Adherence was classified as optimal ( $\geq 95\%$ ) and sub optimal ( $<95\%$  adherence).<sup>[7]</sup> A serial record of adherence calculated thus is maintained in a register for each child separately. Retrospective adherence of last 6 months was obtained from the records available in the ART centre. Mean adherence was calculated for the study period which was used for statistical analysis.

### Statistical analysis

Data were analyzed and statistically evaluated using SPSS software, version 17 (Chicago II, USA).<sup>[10]</sup> Quantitative data was expressed in mean, standard deviation while qualitative data were expressed in percentage. Statistical differences between the proportions were tested by chi square test or Fisher's exact test. 'p' value less than 0.05 was considered statistically significant. Further, Odds ratio and 95% confidence interval was used to quantify the risk factors. Univariate analysis was done and among those factors which were found to be significant with 'p' value  $\leq 0.1$  were entered in multivariate analysis.

### Ethical issues

All participants were explained about the purpose of the study. Confidentiality was assured to them. Assent was taken from subjects 7 years to 14 years along with informed written consent from their parents or caregivers. The study was approved by the Institutional Ethical Committee.

### Results

#### Socio-demographic profile of study subjects:

Out of the subjects surveyed, half (n = 104; 48.1%) of the children were in the age group of 10-14 years while only 38 (17.6%) were less than 5 years old (Mean age =  $8.62 \pm 3.82$  year). The majority of the study subjects were living in urban areas (n=137; 63.4%), belong to class IV socio-economic status (n=100, 46.3%) and were males (71.3%). The majority (n=178; 82.4%) of the study subjects were taken care of by their parents. More than one-fourth (n=62, 28.7%) of the fathers and half of the mothers (n=114, 52.8%) of the study subjects were illiterate. Less than five percent (n=8, 3.7%) of the fathers and most of the mothers (n=176, 81.5%) of the study subjects were unemployed.

Out of 216 subjects, 196 (90.7%) were on ART. Majority 174 (88.8%) of the study subjects had  $\geq 95\%$  mean adherence in the last 6 months by pill count method. Out of 196 study subjects, 22 (10.2%) had missed a

dose of ART medications in last week, while one fourth (n =54; 25%) of the study subjects missed the dose of ART medication more than one month back.

Non-Adherence to HAART was significantly associated with gender of child, age group of children and caregiver of child (Table 1).

Nearly two-third of the caregiver (n=140; 64.8%) informed that it takes more than 90 minutes to reach ART centre from their place of stay. According to the records nearly sixty percent (n=126, 58.3%) of the study subjects had an episode of illness in the last six months.

Non-adherence to HAART was significantly associated with distance from health facility, Duration of ART, illness and problems faced by the caregiver in giving medications to child (p = 0.001) (Table 2). After adjusting for other factors the independent predictors for non-adherence were lower age of the child [AOR = 4.99 (95% CI: 1.25, 19.99)], non-parental caregivers [AOR = 6.07(95% CI: 1.67, 22.0)], female children [AOR = 7.109 (95% CI 1.98, 25.47)] and presence of illness in past six months [AOR = 7.36 (95% CI: 1.38, 39.1)] (Table 1 and 2).

### Discussion

The present study was a hospital based cross sectional study conducted to assess adherence to ART in HIV-infected children using the pill count method and to assess the factors that influence adherence in 216 HIV positive children, taking treatment and care from ART centre of tertiary care teaching hospital in Delhi. The caregivers of the study subjects attending the pediatric ART clinic were interviewed after taking informed written consent.

Adherence to treatment was good and comparable to that reported in other studies from India and abroad conducted by Dachev et al<sup>[11]</sup>, Seth et al<sup>[12]</sup>, Arange et al<sup>[7]</sup>, Nyogea et al<sup>[13]</sup>, Bhattacharya.<sup>[14]</sup>

High level of adherence to HAART can be attributed to counselling sessions given to the study subjects/caretakers at each visit, visible clinical improvement experienced as a result of ART, satisfaction on part of the caregivers regarding the quality of services at the ART centre and use of reminders to take medications.<sup>[15,16]</sup>

### Factors associated with non-adherence to HAART

In univariate analysis, lower age of children (<5 years), female gender of child, non-parental caregivers, distance to ART centre more than 90 minutes, lesser duration of ART (<2 years), presence of other illness and encountering problems while administering medications to children were found to be significantly associated with non-adherence to ART.

A study done by Arange et al<sup>[7]</sup> reported that those children who had to travel longer distances to reach ART centre were non adherent to ART. Buchanan et al<sup>[17]</sup> conducted a study in United States which showed that greater levels of non-adherence was reported among parents/caregivers who faced problems in administering medications to the child. A study by Nyogea et al<sup>[13]</sup> also reported that child with non-parent caregivers had poor adherence. Association of age of children with non-adherence has been shown by other studies also.<sup>[11,17]</sup>

### Conclusion and recommendations

It can be concluded from the study that approximately 90% of the study subjects had  $\geq 95\%$  adherence in last 6 months of the study. Non-adherence to HAART was significantly associated with younger age of child, female gender, non-parental caregiver, presence of co-morbid conditions and with lesser duration of ART. Independent risk factors for non-adherence were: lower age of the child, female gender, non-parental caregiver and presence of illness in last six months.

It is recommended that there is a critical need for targeted intervention strategies to increase the level of adherence to one hundred percent.

For better adherence, innovative counselling techniques need to be used to counsel caregivers about the advantages and benefits of high level of drug adherence in addition to placing a mechanism for follow up and tracing them by mobiles, and home visits. Monitoring and evaluation of adherence strategies are important components of any ART program and should be strengthened for identifying the key factors that influence adherence.

**Limitation**

This study used pill count method to measure adherence which is a relatively easy to perform and objective method. However, there could be manipulation of the pills by participants and wrong reporting. This ART centre is a centre of excellence and the results may not be generalizable to other ART centres.

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**Table 1: Socio-demographic factors affecting adherence to HAART (n=196)**

	Mean Adherence	Chi-square value, 'p' value	Adjusted Odds Ratio (AOR) 95% CI, 'p' value	
	<95(n=22)	≥ 95 (n=174)		
<b>Age group</b>				
Less than 5 years (n =32)	8 (25.0)	24 (75.0)	$\chi^2=7.283$ p = 0.01**	4.99 [1.25-19.99] p = 0.023**
≥5years (n =164)	14 (9.3)	150 (90.7)		
<b>Gender of child</b>				
Male (n =140)	9 (6.4)	131 (93.6)	$\chi^2=11.31$ p = 0.002*	7.11 [1.98-25.47] p = 0.003*
Female (n =56)	13 (23.2)	43 (76.8)		
<b>Age of the caregiver</b>				
≤ 40 years (n =156)	17 (10.9)	139 (89.1)	$\chi^2=0.82$ p = 0.78	
> 40 years (n =40)	5 (12.5)	35 (77.5)		
<b>Sex of the caregiver</b>				
Male (n =88)	14 (15.9)	74 (84.1)	$\chi^2=3.51$ p = 0.06	
Female (n =108)	8 (7.4)	100 (92.6)		
<b>Relation with the child</b>				
Parents (n =158)	11 (6.9)	147 (93.1)	$\chi^2=14.85$ p = 0.001*	6.07 [1.67-22.0] p = 0.006*
Relative (n =38)	11 (28.9)	27 (71.1)		
<b>Religion of caregiver</b>				
Hindu (n =160)	20 (12.5)	140 (77.5)	$\chi^2=1.422$ p = 0.23	
Others (n =36)	2 (5.6)	34 (94.4)		
<b>Education status of caregiver</b>				
Illiterate (n =79)	68 (86.1)	11 (13.9)	$\chi^2=0.968$ p = 0.361	
Literate (n =117)	106 (90.6)	11 (9.4)		
<b>Socioeconomic status</b>				
Class I, II and III (n =74)	8 (10.8)	66 (89.8)	$\chi^2=0.02$ p = 0.88	
Class IV and V (n=112)	14 (11.5)	108 (88.5)		

\*Significant at p value <0.01; \*\* Significant at p value <0.05

**Table 2: Other factors associated with non-adherence to HAART in study subjects**

	Mean Adherence	Chi-square value, 'p' value	Adjusted Odds Ratio (AOR) 95% CI, 'p' value	
	<95 (n=22)	≥ 95 (n=174)		
<b>Time to reach ART centre</b>				
≤ 90 minutes (n=68)	2 (2.9)	66 (97.1)	$\chi^2=7.1$ p = 0.008	2.71 [0.53-13.74] P = 0.229
> 90 minutes (n=128)	20 (15.6)	108 (84.4)		
<b>Duration of ART</b>				
≤ 24 months (n = 42)	11 (26.2)	31(73.8)	$\chi^2=12.01$ p = 0.002*	0.28 [0.07-1.08] P = 0.06
>24 months (n=154)	11 (7.1)	143(92.9)		
<b>Problems faced by the caregivers</b>				
Yes (n = 160)	22 (12.9)	148 (77.1)	$\chi^2= 3.79$ p = 0.001*	
No (n =26)	0 (0)	26 (100.0)		
<b>Illness in past six months**</b>				
Present	20 (17.9)	92 (82.1)	$\chi^2=11.53$ p = 0.001*	7.36 [1.38-39.1] p = 0.01**
Absent	2 (2.4)	82 (97.6)		

\*Significant at p value <0.01

\*\* Illness includes Lower Respiratory Tract Infection/ Pneumonia, Upper Respiratory Tract Infection, diarrhoea, CSOM, pyoderma/ scabies etc.

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