

A CROSS-SECTIONAL STUDY OF ADHERENCE TO ANTI-RETROVIRAL THERAPY AMONG PEDIATRIC PATIENTS OF HIV

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Abstract

Background: The aim of the study is to assess the level of adherence and factors influencing adherence to antiretroviral therapy (ART) among pediatric patients of HIV. **Materials and Methods:** After obtaining approval from the institutional ethics committee, a cross-sectional, observational study was conducted among 134 HIV/AIDS patients aged < 15 years. Patients who were on ART since 6 months were included in the study. Written and informed consent was obtained from the participant or the guardian. The study was conducted in the Department of Paediatrics, KIMS, Hubballi. The data was collected by self report by the care giver or the child regarding treatment adherence over the past month and ADRs experienced by them during the course of therapy, using a questionnaire. Confidentiality of patients was maintained throughout and after the study. **Result:** Of the 134 pediatric patients of HIV/AIDS, 73.8% participants had good adherence to ART with adherence percentage of > 95%. The most common cause of non-adherence was the failure at the patient's end to refill the drugs. Higher mean adherence percentage was seen among those who travelled <10 km to access ART. On assessing the association of adherence to factors affecting it, statistically significant association was seen with ADRs and clinical outcome of the disease. Higher mean adherence was seen when the responsibility of taking the medication was shared by the participant and one other caregiver. **Conclusion:** Adherence level observed in this study emphasizes the need for intervention to ensure good clinical outcome. Several factors were seen to influence adherence to ART among which, occurrence of ADRs was a significant one. The study also found that availability of a responsible care giver positively affects the outcomes of therapy. Hence educating the children and care givers about importance of adherence to ART can lead to better outcome of the therapy.

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is one of the most destructive epidemics the world has ever witnessed. 81,430 children were estimated to be living with HIV, and are on active care with antiretroviral therapy (ART) by the national programme according to the India HIV estimates 2020. Around 10% of the total new HIV infections in 2020 were estimated among children aged <15 years.^[1]

With the availability of antiretroviral drugs, there has been a decline in mortality and morbidity due to AIDS and these drugs have changed the disease pattern to a chronic manageable infection. Despite the great progress made in the field of pediatric HIV diagnosis and treatment, pediatric antiretroviral

treatment (ART) failure is an under-recognized issue that needs to be addressed.^[2] The current goals of HIV treatment in children include restoring, enhancing and preserving immune function, suppressing viral replication, preventing the emergence of viral drug-resistance mutations, reducing drug-related toxicity and improving long-term outcomes and quality of life.^[3]

Antiretroviral therapy (ART) for HIV disease is often highly demanding, which includes multiple medications that require frequent dosing^[4]. Adherence to antiretroviral therapy is critical for reducing the disease burden particularly among the children with HIV. Pediatric age group faces higher challenges to adherence since it has combined influence of the child, the care-giver and various other individual and social factors. Treatment

limiting drug toxicities can add to the complexity in the management of HIV by impairing patient adherence to treatment, leading to lower clinical outcomes and higher cost to the public health system.^[4,5] The effects of non-adherence range from individual disability to global threat due to development of treatment-resistant viruses. Maximum treatment outcomes can be achieved with good adherence to ART. The present study was done to assess compliance to ART drugs and factors affecting it among pediatric patients with HIV/AIDS.

MATERIALS AND METHODS

The study was conducted in the Department of Pediatrics at KIMS Hospital, Hubballi. Pediatric HIV patients aged less than 15 years who are accessing ART centre, KIMS Hubballi and fulfilling the inclusion criteria, constituted the study. 134 HIV/AIDS patients aged below 15 years who visited the Department of Pediatrics were included in the study.

Inclusion Criteria

- All patients below 15 yrs of age, diagnosed with HIV/AIDS on antiretroviral therapy visiting KIMS hospital, Hubballi.
- Patients on ART for a period of 6 months or more.
- Patients or the legal guardian of patients willing to give consent for the study.

Exclusion Criteria

- Patients on ART for a period of less than 6 months.

Clearance from the institutional ethics committee was taken before starting the study. Written and informed consent was taken after explaining the study, in their native language, from the participant / the legal guardian. A questionnaire containing questions relating to adherence was adopted from the Pediatric AIDS Clinical Trials Group (PACTG) questionnaire- Module I & II^[6,7] was used to collect the data. The participants along with their guardians were interviewed separately in private, in their vernacular language. The name of the participant was not recorded in the questionnaire in order to maintain the confidentiality. All the information collected was based on patient's self report.

Patients who had taken more than $\geq 95\%$ of the prescribed doses in the past month were considered as adherent. Patients who had missed doses were asked to provide the number of days the medication was missed and reasons for missing the medications. To minimize recall bias, adherence over previous month was recorded. Participants were also asked about the distance travelled to access ART and the person responsible for administration of medication. CD4 count at the start of treatment and the latest, WHO clinical stage of the disease at the start and the latest were recorded. Patient was also asked about any co-morbid conditions he/she was

suffering from, at the time of interview, like TB, HBV, HCV or any other disease states. Patients were asked for any adverse reactions experienced during the course of treatment. Confidentiality of patients was maintained throughout and after the study.

Statistical methods: Data was entered in Microsoft Excel 2007 and was analyzed as numbers & percentages. Chi square test, paired and unpaired student's t test were used for comparing attributes and variables of study. Probability value of <0.05 was considered as significant. Data was described in the form of tables and graphs. IBM SPSS software version 21 was used for calculations.

RESULTS

[Table1] shows that among 134 study participants, primary caregiver was solely responsible for administration of medication for 46 (34.3%) participants. 46 (34.3%) study participants themselves administered the medication. Study participant and caregiver jointly administered the medication in case of 32 (24%) participants. For 5 (3.7%), the study participant and one other person was responsible for administration. In case of 5 (3.7%) participants other than the options mentioned were responsible for medication administration.

It was noted that majority of the participants; 63 (47.0%) travelled around 10 to 50 KM while 58 (43.3%) travelled less than 10 KM and 13 (9.7%) travelled more than 50 KM to access ART care.

[Figure 1] At the start of treatment with ART, 41 (30.6%) were in WHO clinical stage I of disease, 25 (18.7%) were in stage II, 35 (26.1%) were in stage III and 32 (23.9%) were in stage IV. WHO staging at the start of treatment of 1 (0.7%) participant was unknown. While at the time of interview, latest WHO staging of 109 (81.3%) participants was stage I, 20 (14.9%) were in stage II, 3 (2.2%) were in stage III and 2 (1.5%) were in stage IV of the disease.

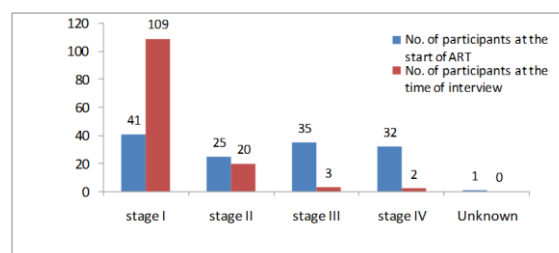


Figure 1: Comparison of WHO stage of study subjects

93 (69.4%) out of the 134 study participants had never missed a dose of ART in the past month. 41 (30.6%) participants had missed at least one dose of medicine in the past month.

[Figure 2] shows the number of study participants with different levels of ART adherence in 1 month prior to the interview. 99 (73.8%) participants had taken 95% and more of the prescribed medications

for that month, 18 (13.4) participants had taken 90% to 95% of the prescribed medications for that month and 17 (12.8%) participants had taken 90% and less of the prescribed medications for that month. The mean adherence in the study population was 94.2% with a standard deviation of 15.6%.

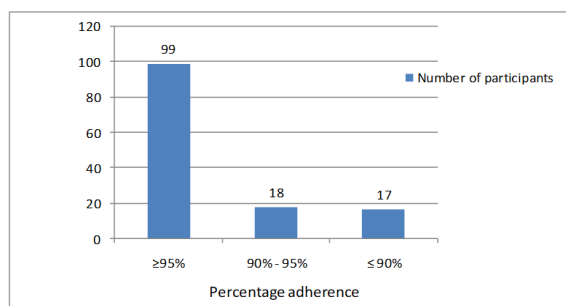


Figure 2: Degree of adherence to ART over the previous 1 month

The 134 study participants were asked about the causes of missing the medication. 58 (43.3%) participants responded to this question and gave various reasons for missing medication. Many participants gave multiple reasons and a total of 80 responses were recorded. Of the 80 responses obtained, 24 (30%) participants said that they ran out of drug and could not refill it on time, and this was the most common cause for missing the medication. 16 (20%) said that they missed the medication since they were away from home, 15

(18.6%) could not get the drug since there was no supply of their medication in the ART centre, and 8 (10%) participants had missed the medication because they were sick with other illness. Forgetting to take medication, falling asleep, unpalatability, physical effects caused by drugs, caretaker being unwell were few among the other reasons recorded. Of the 134 study participants, 39 (29.1%) participants reported to have experienced adverse drug reactions to ART. Majority of these i.e. 34 (87.2%) occurred in the first 2 months of therapy, while 4 (10.2%) reported ADRs after 6 months of ART therapy. Commonly encountered ADRs included nausea, vomiting, diarrhoea, rash & itching, lack of appetite, burning sensation in stomach and dizziness.

Association of adherence to the factors determining adherence was checked by independent sample t test. As per Table-2, statistically significant association was seen between adherence and the latest WHO clinical stage of the disease with a p value of <0.001. Participants with higher mean percentage of adherence to the therapy were in WHO clinical stage I and stage II of the disease at the time of interview. Significant statistical association with a p value of 0.04 was found between adherence and adverse reactions. Higher mean percentage of adherence was seen among participants with no adverse reactions to the therapy.

Table 1: Person responsible for administration of medication.

Person responsible for administration of medication	Number	Percentage
Primary caregiver solely responsible	46	34.3
Study participant solely responsible	46	34.3
Study participant and caregiver jointly	32	24
Study participant and other individual	5	3.7
Other	5	3.7
Total	134	100

Table 2: Association of adherence and the latest WHO staging and ADR

Latest WHO staging	SD	P value
I	94.9 (13)	<0.001
II	96.3 (11)	
III	83.3 (28)	
IV	50 (70)	
Adverse drug reaction	SD	P value
Yes	89.8 (25)	0.04
No	95.9 (8.9)	

p value based on independent sample t test, SD-standard deviation

DISCUSSION

Little is known about the impact of adherence on the response to therapy in children with HIV infection, and measures of adherence have not been widely applied to antiretroviral therapy trials in children^[8]. This study makes an effort to look into the various factors influencing adherence to ART among pediatric patients. In our study, data was collected using a questionnaire which was designed by modifying the Pediatric AIDS Clinical Trial Group (PACTG) questionnaire module 1 & 2. The PACTG

questionnaire has been validated for use as a part of standard practice in PACTG therapy studies. The PACTG questionnaire has been adopted for studies conducted in various countries with slight modifications^[8-10]. Patients who had taken more than 95% of the prescribed medications for that month were considered adherent, as such high degree of adherence is essential to ensure good clinical outcome.^[11] Our study showed that 73.8% participants had taken more than 95% of the medication in the previous month and were well adherent to treatment. 26.2% participants were non

adherent and they are at higher risk of failure of therapy. In a study conducted at New Delhi by Bhattacharya et al, good adherence was seen among 65.6% participants,^[12] while good adherence was seen among 73% children in a study conducted in Cape Town by Davies et al.^[13]

In our study the most common cause for missing the medication, as reported by the participant or the guardian was their failure to refill the medicines at the end of the month, once they ran out of medication (30%), as the patient was away from home or could not visit the ART centre on the required day. Schomaker et al in their study on HIV positive children found that irregular clinic visits led to worse outcomes than with regular follow-up.^[14] Poor palatability of the medication was identified as the most common problem (28.1%) in administering the medications to in a study by Davies et al.^[13]

Association of adherence to various factors by independent sample t test:

In our study, the age group of 0-2 yrs was found to have higher mean adherence to ART. Similar to our findings, a study by Williams et al,^[4] found that older age was associated with increased likelihood for non-adherence. Participants who travelled less than 10 KM to access ART were found to have higher mean adherence (95.7%) in our study. This shows that easy accessibility to ART centre is one of the important factors that determine good adherence.

In the current study, mean adherence was found to be high when the responsibility of taking the ART medication was shared by the participant and one other caretaker (99.4%). This finding is of importance because unlike adult patients, medication adherence among children is a complex issue influenced by various factors. Availability of a responsible care giver can improve treatment outcome among pediatric patients. In a study by Arika it was observed that prevalence of adherence was low among caregivers below 20 and those over 60 years of age implying that characteristics of care giver significantly influences the adherence to therapy.^[15]

In the present study, statistically significant association was seen between adherence and the WHO clinical stage of the disease. Higher mean adherence was seen among participants who were in WHO clinical stage II of the disease (96.3%), implying better clinical outcomes with higher degree of adherence to therapy.

In the present study, statistically significant association was seen between adherence and adverse drug reactions experienced by the participants. Mean adherence was higher among participants who had not experienced any adverse reactions during the course of therapy (95.9%). This finding shows that occurrence of adverse events can significantly reduce the adherence to therapy and hence affect the clinical outcome. Similar to our finding, in a study by Nsheha et al, adherence was worse among children who developed side effects to ART.^[16]

CONCLUSION

Exploring various aspects of pediatric HIV treatment is of great importance since they are vastly dependent on the care givers, unlike adult patients. Among various factors influencing treatment adherence, our study found that the distance travelled to access ART, the availability of responsible caregiver and drugs with lower adverse effects were important contributing factors for good adherence. This study underscores the importance of maintaining adequate level of adherence in order to achieve good clinical outcome.

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