

## Adherence to Highly Active Antiretroviral Therapy and Predictors of Non-Adherence among Pediatrics Attending Ambo Hospital ART Clinic, West Ethiopia

Kebede Alemu, Jimma Likisa\*, Minyahil Alebachew, Goboze Temesgen, Gurmu Tesfaye, Hunduma Dinsa

Ambo University, College Of Medicine and Health Sciences, Department of Pharmacy, Clinical Pharmacy Course and Research Team

\*Corresponding author: Jimma Likisa, Ambo university, college of medicine and health sciences, department of pharmacy, clinical pharmacy course and research team Pobox 19, Ambo, Ethiopia; Tel:+251917305585; Email:jimmapharm@gmail.com

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### Abstract

**Background:** ART increases the length, quality of life, and productivity of the people living with HIV (PLWH). The effectiveness of ART relies on a strict adherence to it. But such data are lacking in the study area. Therefore, the objective of this study is to assess adherence to ART and factors affecting non-adherence among pедиатrics who are on follow up at Ambo Hospital ART clinic, Ethiopia.

**Method:** Hospital based cross-sectional study design involving 120 participants (patients and their) care giver. The study was conducted from April to May 2014. Data analysis was done using SPSS version 20.0.

**Results:** In this study, 84.2% of the participants had taken their prescribed ARV drugs fully for the past 7 days. Considering individuals who had ever missed their dose regardless of time reference, overall adherence rate is 66.7% was obtained. Most frequently mention a reason of missing their dose in the last one week was forgetting (40%). After controlling the effects of other variables, two variables namely sex of the child and WHO stage were found to be significantly associated with adherence to ART in children.

**Conclusion:** Adherence rate obtained in this study is lower than what is required. Forgetfulness, ADRs, and quarrel among family were most frequently mentioned barriers of adherence. Female patients and early WHO stages were independent predictors of non-adherence to medication in this study. Therefore, much works have to be done to optimize adherence to ART in order to make our patients fully advantageous from their treatment.

**Keywords:** Adherence rate; ART; Ambo; Ethiopia

**Abbreviations:** AIDS: Acquired Immunodeficiency Syndrome; ART: Antiretroviral Therapy; HAART: Highly Active Antiretroviral Therapy; HIV: Human Immune Deficiency Virus; PLWH: People Living With HIV; SPSS: Statistical Package for Social Sciences; WHO: World Health Organization

## Introduction

Human Immunodeficiency Virus (HIV) infection is one of the most destructive epidemics the world has ever witnessed. According to 2010 WHO global report on AIDS epidemic estimates the number of people living with HIV was 34 million, of these 22.9 million were from Sub Saharan African. Children continue to be born with HIV worldwide; however, sub-Saharan African is the most affected. Ninety percent of estimated 3.4 million children less than 15 years living with AIDS were from sub Saharan African [1]. Children less than 15 years newly infected with AIDS were 390,000. Although children under the age of 15 years represented about 14.8% of 22.9 million people living with HIV in Sub-Saharan African, they accounted for 13.8% of the 1.8 million deaths and HIV/AIDS account for 9% of mortality in children aged below five years [2].

Even though it doesn't cure, highly active antiretroviral therapy (HAART) has remained the only available option in reducing HIV/AIDS-related morbidity and mortality. It has long been found to be effective in reducing viral load, improving immune function, and improving the quality of life of PLWH [3-5]. However, successful long-term treatment of HIV requires strict adherence to the Highly Active Antiretroviral Therapy (HAART) regimen [6].

To optimally benefit from such treatment, WHO recommends at least 95% of adherence to ART [2]. In contrast, suboptimal adherence rates had been reported in Africa; 88% in South Africa [9], and 80% in Atlanta [10]. Similar trend is observed in Ethiopia; 83% at two hospitals in Oromiya [11], 88.3% in Yirgalem Hospital [12], and 81.2% in three hospitals in Addis Ababa [13].

## Statement of the Problem

The importance of adhering to ART has been widely publicized and accepted as a critical element in the success of ART. There is limited data on adherence to antiretroviral therapy worldwide, few studies of HIV-infected children show adherence to antiretroviral drugs as a major problem in pediatric antiretroviral therapy. Adherence to antiretroviral drug in children and adolescents is a problem due to multiple factors which include high pill burden, poor palatability, side effects, long term toxicity, forgetfulness and caretaker factors [16-18]. Consequences of non adherence to antiretroviral drugs include increase in viral load, decrease of CD4 cell count, disease progression, ARV drugs resistance, risk of transmitting resistant viruses and limitation of future treatments options [2,5]. Therefore, high level of adherence is very crucial to maximize the usefulness of antiretroviral therapy. To our knowledge, no published work in the study area has been found on assessing level of adherence to ART and its associated factors among pediatrics for which reason the current study was designed.

## Significance of the study

With improved diagnostic tests, HIV status of many children can be confirmed early and starting ART early. ART is life-long, therefore it is important to assess level of adherence and look for factors affecting it in children. This is one of the significance of the present study.

Another significance of this study is that this study it had identified barriers of adherence which is used for designing effective intervention to maximize adherence to ART among pediatrics. Moreover, identifying associated factors of adherence in children will contribute to improved adherence to ARV.

Data from this study is useful to health planners such as those at the Ministry of Health and non-governmental organization working on ART rollout program. This finding, therefore, enable such bodies to design better programmes to alleviate the problem of non-adherence to ARV in children and serves as resource for new research on identified gap.

Lastly, this paper will be used as important literature for future researchers who want to undertake similar study.

## Methods and Materials

### Study design

- A facility based cross-sectional study was conducted

### Study area and period

Study was conducted from April to May 2014 in Ambo Hospital at ART clinic. Ambo Hospital is found in ambo town which is located at 126km to the west of Addis Ababa. It is the town in which different nations and nationalities from Ethiopia are living. In the town there are different health facilities providing health services for the population in the town and the local communities. Accordingly, there are two health centers and one general hospital in the town. Currently, one health center and the hospital are giving ART provision service for people living with HIV (PLWH). In the hospital, there is separate ART clinic at which care and follow up is given for PLWH. As of April 2014, there are 166 children on ART at this clinic.

### Source population

- All children and adolescents who are on ART at ambo hospital ART clinic.

### Study population

- All children and adolescents who were on ART at Ambo Hospital ART clinic who were included in this study fulfilling the inclusion criteria.

### Inclusion and exclusion criteria

#### Inclusion criteria

- Age less than 14 years in case of child
- Willingness to participate
- Available during data collection period
- On first line regimens

#### Exclusion criteria

- Have major disability such as deafness
- Severely ill patients

### Sampling technique

There was no such technique used as we considered all pediatrics on ART.

## Sample size determination

This was not done as we took all patients who fulfilled inclusion criteria. In this way we included 120 patients in this study from the total of 166 patients who are currently on ART at this clinic. From total 30 patients were excluded as they are on 2nd line regimes, 6 patients were severely ill at the time of data collection, 2 patients were deaf, and the remaining 8 patients didn't come during data collection period.

## Data collection technique and procedures

Data was collected using structured questionnaires through exit interview. The questionnaires were for the purpose of this study which contains three main parts; socio-demography of the patients, clinical characteristics of the patients and finally medication taking behaviours of the patient. Data was collected by one druggist and one clinical nurse working in Art clinic.

## Data analysis

Data was entered and cleaned before actual analysis. Analysis was done using SPSS version 20.0. Descriptive data were generated and placed in terms of frequency and percentage. Association between variables was assessed using chi-square(x2) test. Predictors of non-adherence were identified using bivariate and multivariate logistic regression analysis. The result was placed in the form of odds ratio (OR) and p-value. In all cases,  $p < 0.05$  was considered to be significant.

## Data quality assurance

A pre-test was conducted at Ambo Health Centre on 10 patients. One day training was given for data collectors to ensure maximum quality of data collected. Supervision was made by principal investigator on daily base.

## Operational definitions

Non-adherence: Patients' and care givers' self-report of ever missing at least two doses regardless length of time since the missed dose(s).

## Care giver

A person who lives with the child and participates in the child's daily care and take the responsibility in giving the child medication and bring the child to clinic.

## Ethical consideration

Ethical clearance to carry out this study was obtained from Ambo University College of Health Science, Department of pharmacy. Formal letter was written to ambo hospital administration to secure permission to undertake the study. In addition, each participant was assured of confidentiality, informed consent was also obtained from the respondents who participated in answering of the interviewer administered questionnaire.

## Limitation of the study

Adherence assessment was based on patients' or care givers' self-report which could bias the result. Beside this, we considered anyone who have ever missed their dose as non-adherent regardless of number of missed dose and time since missed

dose which could lead to over or under estimation of adherence.

## Results

### Socio-demographic Characteristics of the child and care giver

A total of 120 children respondents were included in the study. As shown in table 1, majority 48(40%) of the children were above 10 years. The mean age of the children was 9.5 years (1 to 17 years). Gender wise there is no much difference in which case 50.8% of the children were girls. A majority (64.4%) of the caregivers were protestant by religion. Concerning the educational status of the Care giver, 42.5%, were in primary school. Regarding occupation, 47 (39.2%) were merchant and 24(20%) were working as a government employee. Four hundred four (86.7%) of the caregivers were married and 16 (13.3%) were single. 95(79.2%) of the primary caregivers were biological parents of the children. About 59 (49.2%) of the respondents had household income levels above 500ETB.

Variables	Freq	Percent
Sex Of Child		
Male	59	49.2
Female	61	50.8
Age of the child		
<5 years	30	25
5-10 years	42	35
>10years	48	40
LVG Condition of Child		
With Parent	83	69.2
Other than Parent	37	30.8
Sex of care giver		
Male	27	22.5
Female	93	77.5
Residence of CG/child		
Urban	93	77.5
Rural	27	22.5
Marital status of CG		
Ever Married	104	86.7
Single	16	13.3
Religion of CG or child		
Protestant	76	64.4
Orthodox	37	30.8
Muslim	7	5.8
Occupational status of CG		
Farmer	24	20
March	47	39.2
Employee	24	20
Job less	25	20.8
Incomes of CG <200ETB		
200-500 ETB	36	30
>500 ETB	59	49.2

**Table1:** Socio-demographic Characteristics of the child and care giver in Ambo general hospital, Ethiopia, April-May 2014

CG: care giver, ETB: Ethiopian birr, ever married includes divorced, separated, married, LVG: living condition of the child

## Clinical Characteristics of the Child and Care Giver

Table 2 shows the clinical characteristics of the child and its care giver. Accordingly, most of the children 74(61%) were in stage III based on WHO classification. Majority (35%) of the children in this study had CD4 count of > 350 cells/mm<sup>3</sup>. Very few (17.5%) of the children had their HIV status disclosed. The largest proportion (49.2%) of children in this study was on AZT+3TC+NVP based regimen. About 48% of the children in this study were on ART for greater than 48 months. Children on cotrimoxazole prophylaxis were 77.5% while only 24.2% of the children were on INH prophylaxis.

Variables	Category	Freq	Percent
Child HIV status disclosure	Yes	21	17.5
	No	99	82.5
Care givers HIV status	Positive	85	70.8
	Negative	35	29.2
Care giver on ART	Yes	90	75
	No	30	25
Provider estimate of adherence	Good	79	65.8
	Fair	23	19.2
	Poor	18	15
Current regimen	D4T+3TC+NVP	34	28.3
	D4T+3TC+EFV	2	1.7
	AZT+3TC+NVP	59	49.2
	AZT+3TC+EFV	25	20.8
TB history	Yes	47	39.2
	No	73	60.8
Hospitalization history	Yes	57	47.5
	No	63	52.5
Cotrimoxazole prophylaxis	Yes	93	77.5
	No	27	22.5
INH prophylaxis	Yes	29	24.2
	No	91	75.8
TB developed on INH, HAART or both	Yes	13	10.8
	No	107	89.2
CD4 category	<100	7	5.8
	100-250	39	32.5
	251-350	32	26.7
	>350	42	35
WHO stage	1	10	8.3
	2	25	20.8
	3	74	61.2
	4	11	9.2
Length of time on ART	<12	17	14.2
	41997	16	13.3
	25-48	29	24.2
	>48	58	48.3

**Table 2:** Clinical Characteristics of the Child and Care Giver, Ambo Hospital, Ethiopia, April- May 2014

In this study, 84.2% of the participants had taken their prescribed ARV drugs fully for the past 7 days. Few participants (15.8%) did not adhere to ART. But when we considered individuals who had ever missed their dose regardless of time reference, it was observed that overall adherence rate is 66.7%. Most frequently mention reasons of missing their dose in the last one week was forgetting (40%), and some were due to ADR (25%). Moreover, quarrel among family as well as mental problems were also found to be responsible for significant proportion of reasons for missed dose during this period constituting 17.5% and 10% respectively [Table 3].

Variables	Category	freq	Percent
Ever Missed Dose	Yes	40	33.3
	No	80	66.7
Missed Dose in the last week	Yes	19	15.8
	No	101	84.2
Most common Reasons for non- adherence	Forgetting	16	40
	ADR	10	25
	Quarrel among family	7	17.5
	Mental problem	4	10
	Pill burden	3	7.5

ADR: adverse drug reactions

**Table 3:** Adherence Rate among Pediatrics, Ambo Hospital, Ethiopia, April-May 2014

## Factors affecting adherence to ART

After controlling the effects of other variables, two variables namely sex of the child and WHO stage were found to be significantly associated with adherence to ART in children. As shown in Table 4, female children are 3.9 times less likely to adhere to their prescribed dose. Similarly, children who started their treatment at earlier WHO Stages (that mean I, II) were more likely to become non-adherent to their ART regimens. For instance, child who started ART at WHO stage 4 had adherence rate of about 95% while the one who started treatment at stage 2 had adherence rate of 87.2%. However, factors such as living condition of the child, primary care giver, HIV status of care giver, and whether care giver is on ART or not in case of HIV positive care givers were found to affect adherence only in univariate analysis (without adjusting for confounding factors).

## Discussion

Adherence to Antiretroviral therapy is very crucial in order to maximize the benefit of the drugs. Inadequate adherence is associated with immunological, virological failure, drugs resistance and treatment failure. The objective of this study was to determine proportion of good adherence. This study also tries to examine the different variables associated with child adherence to antiretroviral therapy in Ambo Hospital. Clinical record review, clinical markers and socio demographic and adherence factors were assessed along with the caregiver characteristics to determine the predictors of adherence. The findings of this study were discussed in comparison to previ-

Variables	Adherence	Non Adherence	P-value	OR	P-value	AOR
Sex Of Child						
Male	45	14	0.03	1		1
Female	35	26		2.4	0.007	3.9
Living Condition Of Child						
With Parent	60	23		1		
Other than Parent	20	17	0.05	2.2		
Primary Care						
Biological	67	27		1		
Non- biologic	12	13	0.03	2.7		
HIV Status of Care Giver						
Negative	18	17		1		
Positive	62	23	0.025	0.39		
Care on ART						
Yes	63	23		1		
No	14	16	0.009	3.13		
WHO Stage						
1	4	6		1		
2	19	6	0.05	0.21	0.033	0.128
3	47	27	0.16	0.38	0.076	0.22
4	10	1	0.026	0.67	0.032	0.055

AOR: Adjusted Odd Ratio

**Table 4:** Factors affecting Adherence to Antiretroviral Therapy among Pediatrics , Ambo Hospital , Ethiopia, April-May 2014

ously available literatures elsewhere in the world.

In this study, we found adherence rate of 84.2% considering patients who missed at least two doses in the last one week. This is lower than the recommended adherence level of at least 95% to fully benefit from ART as per the recent who guideline. Similarly, it is lower than the study conducted in Soweto, South Africa (88%) and in Yirgalem Hospita (88.3%) as well as study conducted at five hospitals in Addis Ababa (86%) in Ethiopia [12,9]. However, the adherence rate obtained in this study is almost similar to an adherence rate of 83% which was reported in two hospitals of Oromia Regional State [11], and 81.2% in three hospitals in Addis Ababa [13].

Again, when we compared the proportion of individuals who missed at least one dose which is 33.3% in our study, it is higher than the 20% reported in community setting in Atlanta [10], having missed at least one dose of ART.

It is established that non adherence is one of the reasons for failure of achievement of the global treatment successes [5]. The consequence of non adherence may result in an able to cure, complications such as sever disease and drug resistance, patients remain infectious [6-8]. The significant proportion of non adherence rate identified in this study and other similar studies in Ethiopia as well as other part of the world indicated that much work have to be done by responsible stake holders to achieve the standard adherence level of 95% to avoid problems mentioned above.

There are many barriers to HIV medication adherence and children/adolescents and their caregivers do not perceive them consistently [16,18]. In general, in this study forgetfulness was

the most common reasons for poor adherence to the medication. Similarly, study conducted in USA as part of sub study of multicentre cohort study, showed that the most frequently reported barrier by either the caregiver or youth was “forgot” [18]. The finding is also supported by the study conducted in eastern Ethiopia where the main reasons for non- adherence was forgetting (47.2%) [21]. Therefore, adherence counseling and health information dissemination need to include strategies to minimize forgetfulness using memory aids such as pill boxes, written schedule, and watch bell.

Development of ADRs and existence of quarrel among family were another barriers of adherence indentified in this study. This is similar to the report from India and Uganda [17,20]. Therefore, there should be strategy to ensure family stability such as identifying the source of quarrel and devising effective intervention as well as giving due attention to identify and manage ADRs to optimize adherence is mandatory.

In the present study, mental problems like depression, hopelessness and others accounted for 10% of reasons of non-adherence to the current antiretroviral therapy regimens. Similarly, in USA, it has been reported that patients with symptoms mental problem like depression were found to have higher rate of non-adherence to the same regimens [18].

Adherence behavior is influenced by many factors, which may be categorized as characteristics of the child, the caregiver(s) and family, the regimen, and society and culture [19]. In this study, we found that female sex and early WHO clinical stages of the disease increased the risk of non- adherence to medication significantly and independently. This is similar to the

study of Arun and co-worker in India [20] and Uganda, Kampala [17]. Study in South Africa and Addis Ababa also supported this finding. The fact that female children are less likely to adhere to their regimes could be because of the fact that females are more likely to be busy with home activities as well as sensitive to family issues like quarrel among their family and hence developmental problems compared to boys. Regarding the earlier WHO clinical stages of the disease, such patients are relatively free of signs and symptoms of the disease and hence my give little attention to their medication as compared to their counter parts that are at advanced stage (such as stage 4) of the disease.

However, factors such as primary care giver of the child, living condition of the child, HIV sero- status of the care giver and whether care givers are on ART or not affected adherence only in bivariate analysis. This is in contrast to the findings that were reported previously in other studies from Ethiopia [11,12]. Therefore, there is a need for further study to explore the effect of such variables on medication adherence in this population.

## Conclusion

Adherence rate in this study was lower than that is the recommended by WHO to be optimal. Forgetfulness was the most common reasons for poor adherence in this study. Being female and starting ART at early WHO stage (such as WHO stage 1 and 2) were found to increase the risk of non-adherence significantly and independently. In line with these findings we would like to recommend the following points. Much works have to be done by responsible stake holders to achieve the standard adherence level of 95% to avoid problems non-adherence. Adherence counseling and health information dissemination need to include strategies to minimize forgetfulness using memory aids such as pill boxes, written schedule, and watch bell. There should be strategy to ensure family stability such as identifying the source of quarrel and devising effective intervention as well as giving due attention to identify and manage ADRs to optimize adherence is mandatory. Lastly, special attention should be given to female patients and those who started their treatment at early stages of WHO clinical stages to optimize adherence rate among pediatrics population.

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