

Level of Adherence and Factors Associated with Antiretroviral Therapy among HIV Infected Children in Selected Public Hospitals, Addis Ababa, Ethiopia

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Abstract

Background: Non-adherence to Antiretroviral Therapy (ART) has serious consequences both on the individual and the society. It diminishes the effectiveness of viral suppression, promotes viral resistance, and places the individual at risk of hospitalization, opportunistic infection, and HIV transmission.

Objective: To assess the level of adherence and factors associated with Antiretroviral Therapy among HIV infected children in selected public hospitals, Addis Ababa, Ethiopia.

Methods: A hospital based cross-sectional study was conducted on 380 under-fifteen years old children who had been taking ART for at least 6 months, and on their respective caregivers. It was conducted at pediatrics ART units of the selected hospitals from January to March, 2014. From five public hospitals that were giving the service, two were selected through simple random sampling technique. The data were entered into Epi Info 3.5.3 and analyzed using SPSS Version 20. The statistical association between the outcome and predictor variables were assessed by logistic regression model, using adjusted Odds Ratio with its 95% CI. *P*-value < 0.05 was considered statistically significant

Results: As 380 of the caregivers of the children were interviewed, a response rate of 95% was obtained. The level of adherence to ART was 355 (93.4%). The main reason for 7(28%) of the non-adherent participants skipping their treatment was forgetting. The factors that had statistical association with the adherence were the caregivers' with secondary and above educational status (AOR=4.17, 95%CI: 1.30, 13.32); the Child's age <5years (AOR=11.24, 95%CI: 1.32, 95.45); lack of nutritional support (AOR=0.40, 95%CI: 0.005, 0.308); and the children who were aware of their HIV sero-status (AOR=4.26, 95%CI: 1.48, 12.18).

Conclusion: The level of adherence to ART in the study area was suboptimal. The caregivers' educational status, the age of the children, lack of nutritional support, and non-disclosure sero-status were associated with non-adherence to ART. Since forgetting was the main reason reported for missing ART doses, use of reminders should be encouraged. The caregivers should inform the children about their sero-status. Additionally, the caregivers and the clinicians should look for various means to meet the nutritional requirements of the children. In general, a collaborative effort of all stakeholders is recommended to enhance adherence to ART among HIV infected children.

Key Words: *Adherence, ART, Care giver, HIV/AIDS*

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Introduction

HIV has always been a major health problem globally. In 2014 in sub-Saharan Africa, about 25.8 million people lived with the virus. In 2015, UNAIDS reported that among the children who were less than 15 years, 190,000 were newly infected ones (UNAIDS, 2015; WHO, UNICEF, UNAIDS, 2011). In the same year, there were 123,550 HIV infected children in Ethiopia, of whom 58,806 needed ART (AIDS Resource Center, 2015).

Adherence to ART is as important as access to it (CSA, 2011, 2012). To fully realize the therapy's life-extending benefits (Starace *et al.*, 2006), more than 95%, which is consistent and nearly perfect, adherence is recommended (Heyer *et al.*, 2006). Poor adherence to ART diminishes the effectiveness of viral suppression, promotes viral resistance, and places the People Living with HIV (PLHIV) at risks of hospitalization,

opportunistic infection, and HIV transmission (Mohammadpour *et al.*, 2010).

However, a child's adherence can be influenced by many factors which can be categorized as characteristics of the child, the caregiver, the family, and the regimen. Many of these complicate the measurement of pediatric adherence, as well (Haberer *et al.*, 2009; Ugwu *et al.*, 2013). Unlike adults, children rely upon their caregivers for their medicine. The caregivers may lack commitment or be busy with other activities (WHO, 2006). Poor palatability, lack of fixed dose, and side effects of the drugs hinder the children to take optimal doses (Federal Ministry of Health, 2008). Furthermore, parents' death and their unwillingness to disclose the status also limit the involvement of others into the care (Osterberg *et al.*, 2005).

Several studies have been conducted to determine the level of adherence and its associated factors. Studies conducted in South Africa and Nigeria reported that 94% and 86% of the children were adherent to ART, respectively (Davies *et al.*, 2015; Iroha *et al.*, 2010). A study in Addis Ababa also revealed that 93.3% of the children had 95% adherence level (Biresaw *et al.*, 2013). In Ethiopia, little has been known about the pediatric adherence to ART and its associated factors. There are also inconsistencies among the findings.

Therefore, this study tried to assess the level of adherence and factors associated with ART among HIV infected children in selected public hospitals, Addis Ababa, Ethiopia. Its findings would contribute to the body of knowledge in the problem area.

Methods and Materials

Study area, Design, and Period

A hospital based cross-sectional study was carried out in Addis Ababa, the capital city of Ethiopia. About 3 million population live in the city (CSA, 2015). In Addis Ababa City Administration, 9 public and 18 private hospitals; 24 public health centers and 3 private clinics deliver HIV care. However, only 5 of the public hospitals provide pediatric Antiretroviral Treatment (ART) services (AIDS Resource Center, 2015). For this study, two public hospitals, Saint Peter TB Specialized Hospital and Yekatit 12 Teaching Hospital, were randomly selected. Saint Peter TB Specialized Hospital provides care and treatment for patients with TB, Multi Drug Resistant Tuberculosis (MDR-TB), and HIV. This study was conducted from January to March, 2014, among under 15 years of age who were enrolled in ART program in both hospitals.

Study Participants

The study participants were under-fifteen years of age children living with HIV and taking ART for at least 6 months in pediatrics ART units of the selected hospitals during the study period. Caregivers of the children who were below 6 months of age and who were seriously ill were excluded. The sample size was determined using single population proportion formula. The final calculated sample size was 401.

Data Collection Procedure

Data were collected with an interviewer guided structured questionnaire adopted from different literatures and pre-tested on 10% of the children taking ART in Alert Hospital, Addis Ababa. Initially, it was prepared in English and then translated into Amharic by language experts. The data collectors were trained for two days about data quality and interviewing techniques. Two BSc. nurses conducted the interview in private rooms nearby the ART units. The principal investigator checked the data for completeness on daily basis.

Data Processing and Analysis

The outcome variable was adherence to ART, and adherence was defined as taking more than 95% of the prescribed doses; no dose of pill or suspension missed or delayed for more than or equal to 90 minutes in the past seven days (Markos *et al.*, 2016). The independent variables includes socio-demographic characteristics (Age, sex, ethnicity, educational status, marital status, and relationship of care giver with child, parents' vital status) of the caregivers, who were persons in charge of routinely administering antiretroviral drugs to the enrolled children. Moreover, the independent variable included the children's age and sex, the duration on ART, the recommended regimen, the CD4 count, the WHO clinical staging, the opportunistic infections' (OI's) prophylaxis, the nutritional support, and the disclosure status of the children.

The data were coded and entered into Epi Info 3.5.3 and analyzed using SPSS Version 20. Descriptive statistics were computed and presented in tables and graphs. Logistic regression model was used to determine the statistical association between the outcome and the predictor variables using adjusted Odds Ratio (OR) with 95% C.I. P-value < 0.05 was considered as a statistically significant association.

Ethical Considerations

The study was reviewed and approved by Institutional Health Research Ethics Review Committee (IHRERC) of Haramaya University, College of Health and Medical Sciences. Data collectors were ensured assent and consent from children and caregivers, respectively.

Results

Socio-demographic Characteristics of Caregivers and Children

Three hundred eighty caregivers of children on ART were interviewed, which was a 95% response rate, and their mean age was 39 (SD±12). One hundred thirty two (24.7%) of the caregivers belonged to Amhara ethnic group, followed by Oromo 76(20%). Out of all caregivers, 109 (28.7%) were unable to read and write. Two third of the children, 254 (66.8%), were male. More than half of them (52.2%) were between 5 and 9 years of age, and the mean age was 8 years (SD±3) (Table 1).

Clinical Markers and Treatment Related Characteristics

During the clinical record review, the CD4 count of 168 (44.2%) children ranged from 200 to 499 cells/mm³, 221 (58.2%) were in stage I of WHO clinical classification at base line, 113 (29.7%) were receiving fixed dose regimen of AZT-3TC-EFV (Zidovudine-Lamivudine-Efavirenz) and more than three fourth, 289(76.1%), were taking prophylactic drugs for opportunistic infections (OIs). Nearly half of the children, 180 (47.4%), received nutritional support from the clinics, and only 60 (15.8%) of the children were aware of their HIV sero-status (Table 2).

Level of Adherence

The study found out that 355 (93.4%) of the children were adherent to ART: they missed no dose or not delayed it for more than or equal to 90 minutes. Only 25 (6.6%) of the children missed doses of their drugs in the last 7 days of the study period. The main reason for 7 (28%) of the non-adherent participants skipping their treatment was forgetting.

Table 1. Socio-demographic characteristics of caregivers and HIV infected children on ART in Saint Peter TB Specialized and Yekatit 12 Teaching Hospitals, Addis Ababa, Ethiopia, 2014.

Characteristics	Frequency	%	
Caregivers age (in years)	18-40	192	50.5
	41-59	155	40.8
	>60	33	8.7
Sex	Male	180	47.4
	Female	200	52.6
Educational status	Unable to read and write	109	28.7
	Primary	98	25.8
	Secondary & above	173	45.5
Marital status	Single	51	13.4
	Married	254	66.8
	Divorced/Separated/Widowed	75	19.8
Ethnicity	Amhara	132	24.7
	Oromo	76	20.0
	Gurage	55	14.5
	Tigre	33	8.70
	Others	84	22.1
Monthly income (in USD)	<24.51	81	21.3
	24.56-73.54	159	41.8
	73.59-122.57	98	25.8
	>122.62	42	11.1
Kinship to child	Mother	123	32.4
	Father	96	25.3
	Grandmother/father	61	16.1
	Others	100	26.2
Child age (in years)	< 5	97	25.5
	5-9	198	52.2
	10-14	85	22.4
Child sex	Male	254	66.8
	Female	126	33.2

Table 2. Clinical markers and treatment related characteristics of HIV infected children on ART in Saint Peter TB Specialized and Yekatit 12 Teaching Hospitals, Addis Ababa, Ethiopia, 2014.

Variable		Frequency	%
CD4 count/ mm ³ (Recent)	< 200	80	21.1
	200-499	132	34.7
	>=500	168	44.2
WHO Clinical stage(Base line)	Stage I	221	58.2
	Stage II	132	34.7
	Stage III	27	7.1
ART used (Fixed dose)	ABC-3TC-EFV	93	24.5
	AZT-3TC-EFV	113	29.7
	AZT-3TC-NVP	22	5.8
	TDF-3TC-NVP	95	25.0
	Others	57	15.0
OIs prophylaxis (during interview)	Yes	289	76.1
	No	91	23.9
Duration on ART (month)	6-12	189	49.7
	13-24	108	28.4
	>25	83	21.8
Nutritional support	Received	180	47.4
	Not received	200	52.6
Aware of their HIV sero-status	Yes	60	15.8
	No	320	84.2

Note: OI: Opportunistic infection; ART: Antiretroviral Therapy; ABC: abacavir, 3TC: lamivudine, AZT: Zidovudine, EFV: efavirenz, NVP: nevirapine, TDF: tenofovir

Predictors of Pediatrics Adherence to ART

In this study, the children below 5 years were more likely adherent (AOR=11.24, 95%CI: 1.32, 95.45) than those above 10 years. The children with caregivers who attended secondary education and above were also more likely adherent (AOR= 4.17, 95% CI: 1.31, 13.32) than those who were illiterate. Lack of nutritional support decreased adherence to ART by 60% (AOR=0.40, 95%CI: 0.01, 0.31) than those children received nutritional support. Additionally, children who were aware of their sero-status were more likely to be adhered (AOR=4.26, 95%CI: 1.49, 12.18) to ART compared with their counter parts (Table 3).

Table 3. Predictors of ART adherence among HIV infected children on ART in Saint Peter TB Specialized and Yekatit 12 Teaching Hospitals, Addis Ababa, Ethiopia, 2014.

Variable	Adherence status		COR(95%CI)	AOR (95% CI)
	Adhered N (%)	Not adhered N (%)		
Educational status				
Unable to read and write	100(91.7)	9 (8.3)	1.00	1.00
Primary	88 (89.8)	10(10.2)	2.51(0.86-7.24)	2.54(0.80-7.96)
Secondary& above	167(96.5)	6(3.5)	3.16(1.11-8.98)	4.17(1.31-13.32) *
Child's Age (in years)				
<5	87(89.7)	10(10.3)	9.66(1.20-77.08)	11.24(1.32-95.45) *
5-9	184(92.9)	14(7.1)	6.39(0.82-49.40)	4.36 (0.52-36.09)
10-14	84(98.9)	1(1.2)	1.00	1.00
Duration on ART (in months)				
6-12	183(96.8)	6(3.2)	0.24(0.08-0.68)	0.37(0.11-1.16)
13-24	99(91.7)	9(8.3)	0.66(0.25-1.71)	0.91(0.31-2.64)
≥25	73(88)	10(12)	1.00	1.00
Nutritional support				
Received	179(99.4)	1(0.6)	1.00	1.00
Not received	176(88)	24(12)	0.41(0.00-0.30)	0.40(0.00-0.31) *
Aware of their sero-status				
Yes	51(85)	9(15)	3.35(1.40-7.99)	4.26(1.49-12.18) *
No	304(95)	16(5)	1.00	1.00

Note: * $P < 0.0$; COR: Crude Odds Ratio; AOR: Adjusted Odds Ratio

Discussion

Based on the caregivers' report of the last seven days before the interview, the pediatric adherence to ART was 93.4%. The main reason reported for missing doses of ART (28%) was forgetting.

Although the 93.4% adherence level in this study is compatible with a similar study finding in Addis Ababa (93.3%) (Biressaw *et al.*, 2013), it is below the recommended level (95%). However, it is less suboptimal than the adherence levels reported from Mekelle (83.4%) (Eticha *et al.*, 2014), Addis Ababa (86.9%) (Biadgilign *et al.*, 2008), and Nigeria (86%) and Malawi (72%) (Iroha *et al.*, 2010; Weigel *et al.*, 2009). The possible explanations for this suboptimal level of adherence to ART might be that the caregivers were not counseled for strict adherence before starting ART and during the follow up to suit their level of understanding and context.

The effect of forgetting on non-adherence to ART in this study (28%) is as much as the one found in Harar

and Dire Dawa (30%), and Wollo (28.4%)(Arage *et al.*, 2014; Zegeye *et al.*, 2015). Forgetting is reported as a main reason from Nigeria (55.2%) and Tanzania (59.5%) (Mghamba *et al.*, 2013; Ugwu *et al.*, 2013; Zubayr *et al.*, 2015). The possible explanation might be that the caregivers could not use phone alarm or might be busy with routine activities.

Being aware of HIV status was identified as determinants for adherence. The children who were told about their HIV status showed better adherence, and this is similar to the study findings in south Wollo, Harar and Dire Dawa, (Arage *et al.*, 2014; Zegeye *et al.*, 2015). However, a study in Addis Ababa showed contrary to this finding (Biadgilign *et al.*, 2008). Despite the controversies between pediatrics ART adherence and sero-status disclosure, children who were aware of their sero-status might be more concerned about their health and could understand the benefits of ART.

Besides, further investigations will be required to straighten out these contradictory results.

The current study revealed that lack of nutritional support decreased adherence to ART by 60%. The World Bank reported that nutritional interventions can optimize the benefits of ART and may increase compliance with treatment regimens (World Bank, 2008). A study in Uganda also reported that lack of nutrition was a significant barrier of adherence (Kitaka *et al.*, 2007). Provision of food and micronutrients improves outcomes (Fawzi *et al.*, 2004; Ndekha *et al.*, 2005; Villamor *et al.*, 2005). Additionally, Biadgilign *et al.* (2008) reported that those children received nutritional support from the clinic (66.3%) showed poor adherence. Therefore, the issue of nutritional support needs further exploration.

In this study, adherence to ART decreased with an increase in age of the children. A study done in Gonder also reported a similar finding (Dachew *et al.*, 2014). This might be due to fear of stigma. Therefore, encouraging disclosure with specific support might be central to increase children's adherence as they get older.

This study had some limitations. The use of caregivers' report of adherence to ART might lead to over estimation. Using a single method to assess adherence could not yield more reliable results. The social desirability and recall biases might not be completely eliminated. Besides, small sample size had shown some limited effect on the model we used.

Conclusion and Recommendations

The level of adherence to ART in the study area was suboptimal. It is comparable to other studies conducted in Ethiopia and other developing countries. Forgetting was the main reason reported for missing ART doses. The caregivers' educational status, the age of the children, lack of nutritional support, and non-disclosure sero-status were the statistically significant factors that showed association with non-adherence to ART.

Therefore, disclosure of HIV status to children is so controversial that further study are required. However, encouraging caregivers might be essential to disclose the HIV status to the children and use of reminder to minimize forgetting of caregivers to give ART. Case managers should link the caregivers with organizations that provide nutritional support. It is also worth mentioning that the caregivers should search for other means to meet the nutritional requirements of the children. Furthermore, a collaborative effort is

recommended to enhance adherence to Antiretroviral Therapy among HIV infected children.

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Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

BF carried out the study starting from conception to analysis and interpretation of data. SL participated in topic selection, data analysis, and interpretation and manuscript writing. AK participated in topic selection, reviewing the proposal, data analysis and commented on drafted manuscript. All authors read and approved the final draft of the manuscript.

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