

## Determinants of Non-Adherence to Antiretroviral Therapy Among HIV Infected Children Aged Less Than 15 Years in DebreMarkos and Felegehiwot Referral Hospitals, Northwest Ethiopia

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### Abstract

#### Background

Non-adherence to antiretroviral therapy is a major challenge to HIV/AIDS care. For antiretroviral therapy to be effective, high level of adherence is required. So far, there is no study on determinant of non-adherence to antiretroviral therapy in the study area. Therefore, this study was conducted to identify determinants of non-adherence to antiretroviral therapy among HIV infected children in DebreMarkos and Felegehiwot referral hospital.

## Methods

Case-control study design was employed on total of 220 samples in Debremarkos and Felegehiwot referral hospital. Data was collected by using a structured pre-tested questionnaire and by data abstraction format from ART registration chart. Data was entered in to EPI data statistical version 3.1 software and then exported to SPSS Windows version 20 for analysis. Binary logistic regression analysis was conducted to find out association between dependent and independent variables. Multivariate logistic regression analysis was done to identify independent factors for non-adherence.

## Result

Fifty five case and 165 controls were included in the study. The study showed that factors like duration of HIV diagnosis to ART initiation [AOR=2.379, 95% CI(1.150-4.921)], duration on ART use [AOR = 3.128; 95% CI (1.036-9.444)], types of ART drug [AOR = 4.752, 95% CI (1.620-13.937)], educational status of the care giver [AOR = 0.25, 95% CI (0.076-0.831)], follow up schedule [AOR=2.567(1.148-5.740)] and difficulty during taking the drug [AOR=5.867, 95% CI(2.200-15.645)] were the major identified significant factors for none adherence to ART treatment in the study area.

## Conclusion

The wider the interval of follow-up appointment the higher chance of non-adherence to ART. Early initiation of ART after diagnosis HIV is protective against non-adherence. Therefore, the capacity to effectively manage the above critical factor is crucial in the success of antiretroviral therapy.

## Introduction

Globally there were approximately 36.7 million people living with HIV (PLHIV) at the end of 2015 with 2.1 million people becoming newly infected with HIV. Sub-Saharan Africa is the most affected region, with 25.6 million PLHIV and accounts for two-thirds of the global total of new HIV infections. According to Ethiopian Public Health Institution (EPHI) estimates and projections for Ethiopia for 2017, the national HIV prevalence is 1.16% [1]. Furthermore, in 2012, 260,000 children less than 15 years were newly infected and 210,000 died from AIDS-related causes. In the last decade, HIV has emerged as one of the leading causes of childhood mortality and morbidity in sub-Saharan Africa [2].

WHO recommends antiretroviral therapy (ART) for all people with HIV as soon as possible after diagnosis without any restrictions of CD4 counts and strict adherence towards their medication is mandatory. Adherence is defined as the extent to which a patient takes a medication in the way intended by a health care provider. It is double burden in pediatric patients due to their age standard ART consists of fixed dose combination (FDC) of ART drugs to maximally suppress the HIV virus and stop the progression of HIV disease [3]. With regard to ART drugs, an adherence level of 95% or more is required in order to obtain successful outcome [4].

The ultimate goal of antiretroviral therapy is to achieve maximal and durable suppression of virus replication [5]. However, sub-optimal adherence to ART can lead to incomplete viral suppression, emergence of resistant viral strains and treatment failure. Non-adherence can also result in resistance to first-line ART and in such cases, patients often must switch to significantly more expensive second-line regimens which are more difficult to procure and more difficult for patients to access [6,7]. Switching to second-line therapy for children results in a more costly lifetime ART regimen, and is a major financial concern and human resource burden [8].

Many factors lead children's to non-adherent to their treatment plan due to frequent dosing and are supplied in formulations that may be difficult for children to tolerate (large pills, bitter-tasting liquids, and gritty powders). Children fail to tolerate adverse effects of ART medications, since it is more frequent and severe. Antiretroviral syrups, which used in young children, require refrigeration. Some households don't have any sort of refrigeration, and even those that do have, may not have enough space to store large quantities of these formulations [9]. Adherence is also influenced by factors associated with the disease and its treatment, with the relationship between the patient and the healthcare provider and with patients themselves, such as socio-economic status which is often based on employment or occupational status in addition to educational level and income [10].

Children rely on a caregiver, who often is also infected, to administer medication. These challenges may be exacerbated in resource-limited settings (RLS) that are most affected by the HIV epidemic. Often elderly family members have to care for children whose biological parents have passed away, and end up being burdened with multiple dependents while being frail themselves [11]. According to WHO report, the types of factors have been identified as barriers to optimal ART adherence; namely; regimen characteristics, patient characteristics [30]. Drug stock-outs, can hamper adherence with ART [12]. The study conducted in South Africa; transport affects the patient's access and adherence to ART treatment and economy play an important role in determining the kinds of services that patients receive, the economic strains they experience, and their vulnerability to dropping out of treatment [13].

In Ethiopia in 2016 around 398,277 adults and 21,686 children under the age of 15 are taking ART. Based on the spectrum estimate the 2017 ART need is 665,116 for adults and 57,132 for children under 15 years of age. Recently ART service is being available in more than 1224 Health facilities of which around 909 are Health centers. On the basis of the new spectrum estimate for 2016, ART coverage for adults (age 15+) has reached 61% but the coverage remains low (33%) for children (age <15) living with HIV (1). In addition to low coverage in age group less than 15 years in the country factors determining have not been studied in the study area. Therefore, the purpose of this is to identify determinants of non-adherence to ART among HIV infected children aged less than 15 years in Debremarkos and Felegehiwot Referral Hospitals, northwest Ethiopia.

## Methods

### Study Setting

This study was conducted in Debremarkos and Felegehiwot referral hospitals which are found in Amhara regional state, Ethiopia. The hospitals have been giving services such as HIV counseling and testing, provision

of ART, treatment of opportunistic infections; prevention of mother to child transmission, TB/HIV co infection treatment, and care for HIV exposed infants. The numbers of children on ART at Debremarkos and Felegehiwot Referral Hospitals was 323 and 305 respectively.

### **Study Design**

An institutional based unmatched case-control study was conducted from February to March 2018.

### **Study Population**

All children under 15 years with their primary care givers who are on ART at Debremarkos and Felegehiwot Referral Hospital ART clinic during data collection were source population. All HIV positive children under 15 years who had at least one month start ART before a data collection period was considered as a study population of this study. All cases who had follow-up during the data collection period were included in the study whereas controls were included by systematic random sampling techniques in every other K<sup>th</sup> appointees.

The sample size was calculated using STATCALC program of EPI version 7 Software. The minimum number of cases and controls required to achieve a 95% confidence level and power of 80%. Four controls were taken for each case. The minimum require sample size calculated using by inserting the above assumptions was 213, by adding 5% non-response rate the total sample size was 223.

### **Data Collection**

The tool was prepared after reviewing literature. It was prepared in English and then translated to Amharic and retranslated back to English to ensure its consistency. The questionnaire contains information on socio demographic related variables, drug regimen related variables, and health care delivery related variables and reason for non-adherence variables. Medical record was reviewed to identify clinical markers like CD4 count and WHO clinical staging.

The data were collected using clinical record review and interview. Three BSc nurses and three expert case managers working in ART clinics supervised by two BSc nurse experienced professionals. Baseline information was filled out from ART registration and follow-up forms. One day training on the objective of the study, confidentiality of information and interviewing techniques was given.

The outcome variable was non- adherence to ART and explanatory variables were: Patient or family /care giver related factors, medication and clinical related factor, health care delivery system related factor and social or environmental factors.

### **Data Analysis**

Data were coded and entered in to EPI data statistical version 3.1 software and then exported to SPSS Windows version 20 for further analysis. Descriptive statistics was computed for each variable. Bivariate logistic regression was used to check variables associated with the dependent variable. Those variables found

to have p-values of  $\leq 0.2$  was fitted to multivariable logistic regression to control the effects of confounders. Odds ratios with 95% CI are computed and variables having p-values less than 0.05 in the multiple logistic regression models was considered significantly associated with the dependent variable.

### **Operational Definitions**

Non-Adherence (cases): patients who had a history of they took less than 95% missing the prescribed doses or fixed hours (missing 1 doses out of 7 doses or 2 doses out of 14 doses) all of scheduled regimens which supposed to take in a week.

Adherence (controls): were near-perfect ( $>95\%$ ) take to dose of all regimens as prescribed with fixed hours which supposed to take in a week.

Primary Care giver: People 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 was obtained from the Ethical Review Committee of the Debreworkos University, college of health science. Permission letter was obtained from Debreworkos and Felegehiwot Referral Hospital. Each caregiver/subject was adequately informed about the purpose of the study and written informed assent was obtained from the parents/guardians. Interviews were conducted in private rooms and confidentiality was kept. They were informed to withdraw from study at any time and/or to refrain from responding to questions if they were not interest to participate by any reason.

## **Result**

### **Socio-Demographic Characteristics**

A total of 220 HIV-positive children 55 (25%) cases and 165 (75%) controls) who had at least one month ART follow up participated in the study with response rate of 99.4%. Among the study participants 50.45% (30 cases and 81 controls) were male. Majority of 90.9% (50 cases and 150 controls) were above the age of five years. Furthermore, majority of 78.6% (47 cases and 126 controls) of the children's care takers were females. The mean age  $\pm$  (SD) of the children at the time of data collection were 9.3years ( $\pm 3.25$ ). The mean age  $\pm$  (SD) of the caregiver at the time of data collection were 35.5 ( $\pm 8.39$ ). The reported length of time the children stayed on ART ranged from 4 month to 149 months and the mean were 70.5 months. Those who were unable to read and write accounted for 34.0% (24 cases and 51 controls). Regarding occupation, 30.9% (16 case and 52 controls) were merchant and 68.2% (38 cases and 112 controls) of the caregivers were married. Seventy-nine percent of (44 cases and 130 controls) reported an average monthly family income of greater than 500ETB (Table 1).

**Table 1:** Socio-demographic characteristics of the study participants North West region, East and West Gojjam zone in Debreworkos and Felegehiwot Referral Hospitals, 2018

Variables	Response	Frequency	
		Controls N (%) n=165	Cases N (%) n=55
Age of child	<5 years	15(9.1%)	5(9.1%)
	5-9 years	63(38.2%)	19(34.5%)
	10-14 years	87(52.7%)	31(56.4%)
Sex of child	Male	81(49.1%)	30(54.5%)
	Female	84(50.9%)	25(45.5%)
Educational level of the child	Attending formal education	136(82.4%)	46(83.6%)
	Not attending formal education	29(17.6%)	9(16.4%)
Age of the caregiver	20-30years	65(39.4%)	16(29.1%)
	31-40 years	69(41.8%)	29(52.7%)
	41-50 years	18(10.9%)	8(14.5%)
	>50 years	13(7.9%)	2(3.6%)
Sex of the caregiver	Male	39(23.6%)	8(14.5%)
	Female	126(76.4%)	47(85.5%)
Educational status of the caregiver	Unable to read and write	51(30.9%)	24(43.6%)
	Read and write only	20(12.1%)	7(12.7%)
	Elementary school	29(17.6%)	5(9.1%)
	Secondary school	34(20.6%)	14(25.5%)
	College and above	31(18.8%)	5(9.1%)
Residence of the care giver	Urban	112(67.9%)	34(61.8%)
	Rural	53(32.1%)	21(38.2%)
Marital status of the care giver	Single	9(5.5%)	2(3.6%)
	Married	112(67.9%)	38(69.1%)
	Divorced	4(2.4%)	1(1.8%)
	Widowed	40(24.2%)	14(25.5%)
Occupation of the caregiver	Farmer	49(29.7%)	12(21.8%)
	Employee	40(24.2%)	7(12.7%)
	Merchant	52(31.5%)	16(29.0%)
	No job	20(12.1%)	11(20.0%)
	Others	4(2.4%)	9(16.4%)

Relation with the child	Mother	96(58.2%)	31(56.4%)
	Father	24(14.5%)	7(12.7%)
	Sister	12(7.3%)	2(3.6%)
	Brother	12(7.3%)	4(7.3%)
	Grand mother	13(7.9%)	8(14.5%)
	Others	8(4.8%)	3(5.5%)
Information on parents of the child	Both parents alive	74(44.8%)	26(47.3%)
	Only father alive	15(9.09)	5(9.1%)
	Only mother alive	33(20.0%)	7(12.7%)
	Both are died	43(26.1%)	17(30.9%)
Use of memory aids	Yes	158(95.8%)	30(54.5%)
	No	7(4.2%)	25(45.5%)
HIV status of the caregiver	Positive	122(73.9%)	37(67.3%)
	Negative	43(26.1%)	18(32.7%)
Average monthly family income	<500	35(21.2%)	11(20.0%)
	>500	130(78.8%)	44(80.0%)

### Medication Related Factors

The majority of 46.8% (27 cases and 76 controls) of children in this study were on AZT+3TC+NVP based Regimen at baseline and similar with the baseline, about 51.8% (24 cases and 90 controls) children were currently on AZT-3TC-NVP based regimen. About 55% of the children in this study were on ART for greater than 60 months. Regarding on types of ART drugs 88.2% (45 cases and 150 controls) of the children was on first line regimen (Table 2).

**Table 2:** Medication-related factors of non-adherence in North West region, East and West Gojjam zone in Debremarkos and Felegehiwot Referral Hospital, 2018

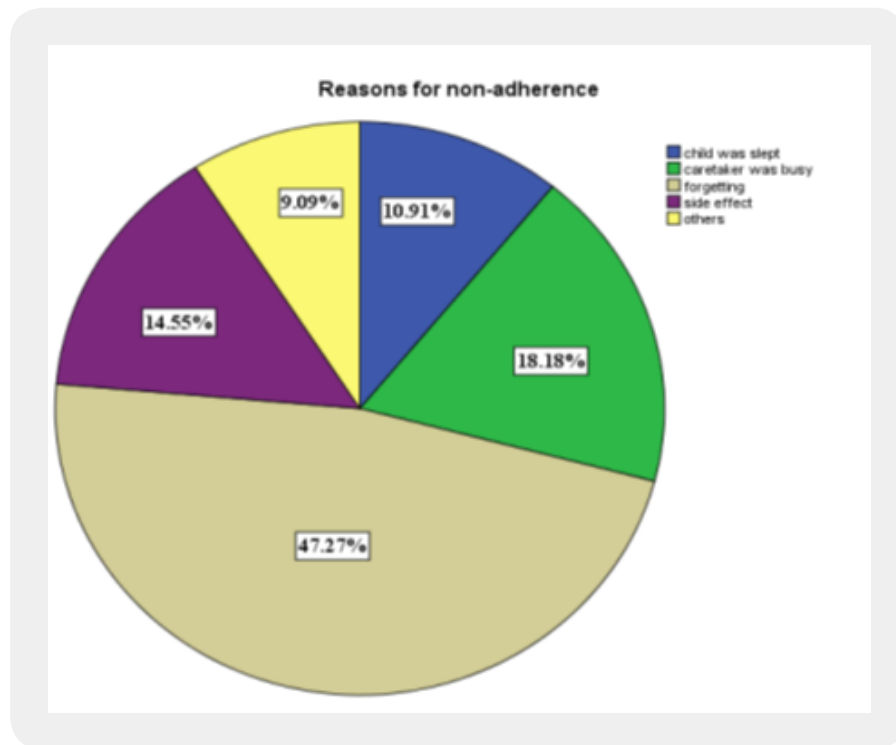
Variables	Response	Frequency	
		Control N(%) n=165	Case (%) n=55
Base line ART regimen	ABC-3TC-NVP	7(4.2%)	3(5.5%)
	ABC-3TC-EFV	8(4.8%)	2(3.6%)
	AZT-3TC-NVP	76(46.1%)	27(49.1%)
	AZT-3TC-EFV	37(22.4%)	13(23.6%)
	D4T-3TC-NVP	23(13.9%)	4(7.27%)
	D4T-3TC-EFV	11(6.7%)	3(5.5%)
	Others	3(1.8%)	3(5.5%)

Current ART regimen	ABC-3TC-NVP	6(3.6%)	6(10.9%)
	ABC-3TC-EFV	8(4.8%)	3(5.5%)
	AZT-3TC-NVP	90(54.5%)	24(43.6%)
	AZT-3TC-EFV	36(21.8%)	10(18.2%)
	AZT-3TC-LPV/r	10(6.2%)	5(9%)
	AZT-3TC-ATV/r	3(1.8%)	3(5.5%)
	TDF-3TC-EFV	9(5.5%)	2(3.6%)
	Others	3(1.8%)	2(3.6%)
Duration of HIV positive test to initiate ART	Within month of test	95(57.6%)	25(45.5%)
	1-12 month	46(27.9%)	17(30.9)
	>1 year	24(14.5%)	13(23.6%)
Duration on month of ART	<36 month	42(25.5%)	8(14.5%)
	36-59	31(18.8%)	18(32.7%)
	>60 month	92(55.8%)	29(52.7%)
Type of ART currently use	First line	150(90.9%)	45(81.8%)
	Second line	15(9.1%)	10(18.2%)
Baseline CD4 count	<200	17(10.3%)	5(9.1%)
	200-499	47(28.5%)	18(32.7%)
	>=500	101(61.2%)	32(58.2%)
Current CD4 count	<200	7(4.24%)	2(3.6%)
	200-499	23(13.9%)	13(23.6%)
	>=500	135(81.8%)	40(72.7%)
Baseline WHO staging	I	34(20.6%)	12(21.8%)
	II	54(32.7%)	16(29.1%)
	III	70(42.4%)	23(41.8%)
	IV	7(4.2%)	4(7.3%)
Current WHO staging	I	163(98.8%)	53(96.4%)
	II	0(0%)	1(1.8%)
	III	2(1.2%)	0(0%)
	IV	0(0%)	1(1.8%)
Cotrimoxazole before start ART	Yes	114(69.1%)	33(60%)
	No	51(30.9%)	22(40%)
Cotrimoxazole with ART	Yes	150(90.9%)	50(90.9%)
	No	15(9.1%)	5(9.1%)
Difficulty during taking ART	Yes	14(8.5%)	21(38.2%)
	No	151(91.5%)	34(61.8%)



### Respondents' Reason for Missing Prescribed Pills

Forgetting, care taker being busy, side effect, the child was slept, and others, were the most common reasons mentioned by of care givers of the children who were missed their doses respectively.



*Figure 1: Reasons for non-adherence among Under 15 children at Debre Markos and Felege Hiwot Referral Hospital, 2018*

### Health Care Delivery System-Related and Social/Environmental Factors

The majority of patients 87.7% (44 cases and 149 controls) disclosed their status to family members and for other peoples. Sixty nine percent (35 cases and 117 controls) of individuals were more often living less than 47km away from the ART clinic and 89.5% (50 cases and 147 controls) were spending their time more than 2 hours in the health facility (Table 3).

**Table 3:** Health care delivery system-related factors and Social/environmental factors of non-adherence in North West region, East and West Gojam zone in Debre Markos and Felege Hiwot Referral Hospital, 2018

Variables	Response	Frequency	
		Control N(%) n=165	Case N(%) n =55
Anyone know the child HIV status	Yes	149(90.3%)	44(80.0%)
	No	16(9.7%)	11(20.0%)
Childs HIV status disclosure	Yes	58(35.2%)	20(36.4%)
	No	107(64.8%)	35(63.6%)
Waiting time in the facility during follow up	<2 hrs	18(10.9%)	5(9.1%)
	>=2 hrs	147(89.1%)	50(90.9%)
Lack of transport	Yes	15(9.1%)	8(14.5%)
	No	150(90.9%)	47(85.5%)
Distance from ART clinic(KM)	<47km	117(70.9%)	35(63.6%)
	>=47km	48(29.1%)	20(36.4)
Shortage of ART on follow up	Yes	21(12.7%)	13(23.6%)
	No	144(87.3%)	42(76.4%)
Received nutritional support	Yes	24(14.5%)	4(7.3%)
	No	141(85.5%)	51(92.7%)

### Determinants of Non-Adherence to Antiretroviral Therapy

HIV positive children who had received ART medication used after 1 year of diagnosis of HIV were 2.4 times more likely to not adhere as compared to those who had received ART medication within a month [AOR=2.379, 95% CI (1.150-4.921)]. Patients who had more than 36 month ART follow-up were 3.1 times more likely to not adhere as compared to those who had <36 months follow-up [AOR = 3.128, 95% CI (1.036-9.444)]. The odds of non-adherence were 4.8 times more likely occur to those who had on second line drug as compared to those who had on first line drug [AOR = 4.752, 95% CI (1.620-13.937)]. The odds of non-adherence were 75% times less likely to occur among the care giver those who had elementary school as compared to those who had unable to read and write. HIV positive children who had taking medication for two month were 2.6 times more likely to being non-adherent as compared to those who had taking the drugs monthly [AOR=2.57(1.15-5.74)]. In addition, the odds of non-adherence were 5.9 times more likely to those who had difficulty during taking the drug as compared to the counterpart [AOR=5.87,95% CI (2.20-15.64)] (Table 4).

**Table 4:** Bi-variable and multivariable analysis between explanatory variables and non-adherence to ART among participants in Debre Markos and Felege Hiwot Referral Hospital, North West Ethiopia, 2018

Variables	Responses	Adherence status		Odds Ratio with 95% CI	
		Control	Case	COR	AOR
Age of the caregiver	20-30	65	16	1.00	
	31-40	69	29	1.71(0.85-3.42)	
	41-50	18	8	1.81(0.67-4.89)	
	>50	13	2	0.62(0.13-3.05)	
Sex of the care giver	Male	39	8	1.00	
	Female	126	47	1.82(0.79-4.18)	
Educational status of the caregiver	unable to read and write	51	24	1.00	1.00
	Read and write only	20	7	0.74(0.21-2.01)	
	Elementary school	29	5	0.37(0.13-1.06)	0.25(0.076-0.83)
	Secondary	34	14	0.88(0.39-1.93)	
Anyone know the child HIV status	College and above	31	5	0.34(0.12-0.99)	
	Yes	149	44	1.00	
Duration of HIV + test to ART initiation	No	16	11	2.33(1.01-5.38)	
	Within month of test	95	25	1.00	1.00
	1-12 month	46	17	1.40(0.57-2.32)	
Base line ART regimen	>1 year	24	13	2.06(1.27-4.42)	2.38(1.15-4.92)
	ABC-3TC-NVP	7	3	1.00	
	ABC-3TC-EFV	8	2	0.25(0.27-2.32)	
	AZT-3TC-NVP	76	27	0.36(0.07-1.87)	
	AZT-3TC-EFV	37	13	0.35(0.63-1.96)	
	D4T-3TC-NVP	23	4	0.24(0.04-1.39)	
	D4T-3TC-EFV	11	3	0.29(0.24-2.11)	
Current ART regimen	Others	3	3	0.24(0.06-2.05)	
	ABC-3TC-NVP	6	6	1.00	
	ABC-3TC-EFV	8	3	0.38(0.07-2.14)	
	AZT-3TC-NVP	90	24	0.27(0.08-0.90)	
	AZT-3TC-EFV	36	10	0.29(0.07-1.05)	
	AZT-3TC-LPV/r	10	5	0.62(0.13-3.05)	
	AZT-3TC-ATV/r	3	3	0.79(0.08-5.02)	
TDF-3TC-EFV	9	2	0.32(0.05-1.11)		

	Others	3	2	0.48(0.13-1.80)	
Duration on ART	<36 month	42	8	1.00	1.00
	36-59month	31	18	3.05(1.21-8.19)	3.13(1.04-9.44)
	>=60 month	92	29	1.66(0.69-3.92)	
Type of current ART drug	First line	150	45	1.00	1.00
	Second line	15	10	2.22(0.93-5.29)	4.75(1.62-13.94)
Shortage of ART Medicine	Yes	21	13	2.12(0.98-4.59)	
	No	144	42	1.00	
Schedule of ART follow up	Monthly	128	36	1.00	1.00
	Two monthly	33	18	1.94(0.98-3.84)	2.57(1.15-5.74)
	Three monthly	4	1	0.89(0.09-8.20)	
Received nutritional support	Yes	24	4	1.00	
	No	141	51	2.77(0.72-6.56)	
Difficulty during taking the drug	Yes	14	14	3.68(1.63-8.34)	5.87(2.20-15.64)
	No	151	41	1.00	1.00

## Discussion

This study also tried to examine the different variables associated with child non-adherence to ART. Clinical record review, interview were used to identify Non-adherence factors along with the caregiver characteristics. In this study, such as, educational status of the care giver, duration on ART, type of ART drug, schedule for follow up and duration of HIV diagnosis to ART initiation, difficulty during taking the drug; were found to be independent determinant factors with non-adherence to ART.

Caregivers of non-adherent children reported that missed doses were most often due to forgetfulness; care taker was busy, drug side effects, and others. This finding in the current study is consistent with a study [7,14-17], which found that missed doses were most commonly due to forgetfulness. The odds of non-adherence was 75% times less likely to occur among those who had elementary schools as compared to those who had unable to read and write, these finding is supported by the study conducted in Fiche hospital [14]. This finding of non-adherence was not being related to the age and sex of the child and it was not in agreement with reports from other studies [7,14-18]. The possible explanations for such differences could be possible progressive improvement of patient care and management systems with time; and difference in study design.

This study showed that patients who had 36-59 month on ART follow-up were 3.1 times more likely to not adhere as compared to those who had less than 36 months follow-up [AOR=3.12,95% CI (1.04-9.44)]. This finding is inconsistent with study conducted in India and Nigeria [6,7]. The possible reason could be these studies were included those patients who had less than 6 months' duration on ART. On top of the treatment duration of the patients, the accessibility of health facilities, living conditions, socio-demographic characteristics of the population in south India and Nigeria is differ from Ethiopia which might have effect on the adherence status of the patient. And when the duration of ART increases there might be treatment

fatigue and side effect can get worse the longer a drug is taken, tend to neglect their ART regimen over a period of time.

The odds non-adherence were 4.8 times more likely occur to those who had on second line drug as compared to those who had on first line drug [AOR = 4.75, 95% CI (1.62-13.94)]. This finding is consistent with done in Mekelle [16]. The possible explanation for this might be children on second line regimen due to formulation of the drug in (size, taste, pill burden) and unavailability of the drug which is too expensive is make it to non-adherent for ART.

HIV positive children who had taking medication every two monthly were 2.6 times more likely to non-adhere as compared to those who had taking the drug monthly [AOR=2.57, 95% CI (1.15-5.74)]. This finding is not significantly associated with adherence in other studies in Fiche Hospital [14]. The possible reason for this could be, in current study patients follow-up appointment were: monthly, every two month and every three month appointment, but in Fiche Hospital appointment was below monthly and monthly.

HIV positive children who had received ART medication used after one year of diagnosis of HIV were 2.4 times more likely to not adhere as compared to those who had received ART medication within one year [AOR=2.38,95% CI (1.15-4.92)]. The possible explanation for this might be the delay of early linkage by health care provider to the chronic follow up, poor counseling of the care giver about importance of early initiation, poor awareness of the caregiver towards the ART drugs and poor care system. The odds of non-adherence were 5.9 times more likely to those who had difficulty during taking the drug as compared to the counterpart [AOR=5.87,95% CI (2.20-15.64)]. The possible explanation for this might be the formulation of drug in (size, taste), treatment fatigue, pill burden of the drug makes it difficult to take the medicine inappropriately.

## Limitation of the Study

None inclusion of socio-cultural and behavioral related factors towards non-adherence is one limitation. Health related effect on non-adherence may be affected to some extent by social desirable; however, it was minimized by different strategy like interviewing in private rooms. And also adherence assessment was based on the caregiver self-report through interview which may have social desirability bias and recall bias.

## Conclusion

In conclusion, the non-adherence was more likely occur to those who had on second line drug as compared to those who had on first line drug. HIV positive children who had taking medication every two monthly were more likely to non-adhere as compared to those who had taking the drug monthly. HIV positive children who had received ART medication used after one year of diagnosis of HIV were more likely to not adhere as compared to those who had received ART medication within one year. The non-adherence were more likely to those who had difficulty during taking the drug as compared to the counterpart. This study also showed that patients who had 36-59 month on ART follow-up were more likely to not adhere as compared to those who had less than 36 months follow-up. Therefore, the wider the interval of appointment the higher chance of non-adherence to ART. Early initiation of ART after diagnosis HIV is protective against non-adherence.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Data Availability

All the necessary data are available.

## Sources of the Fund

The study was conducted by self sponsor.

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