

# Incidence and Predictors of Lost to Follow up Among Children Attending ART Clinic at Dessie Referral Hospital, Northeast Ethiopia: A Retrospective Cohort Study

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## Research

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# Abstract

**Background:** Despite, antiretroviral therapy could reduce the transmission of human immunodeficiency virus and related morbidity, loss to follow up is a main challenge among children living with human immunodeficiency virus. Therefore, the aim of this study was to assess the incidence and predictors of loss to follow up among under 15 years old children attending antiretroviral therapy clinic at Dessie referral hospital, North east Ethiopia.

**Methods:** A ten-year institution based retrospective cohort study was employed among 448 under 15 years' old children who were enrolled on antiretroviral therapy. Data were entered and cleared using Epi- data version 3.1 and then exported to STATA version 14 for further statistical analysis. Kaplan Meier survival curve was used to estimate the survival time and log rank test was used to compare the survival time between different categories of the explanatory variables. Multivariable Cox proportional hazards model was fitted to identify predictors of loss to follow up and p-value < 0.05 was considered as statically significant.

**Results:** The overall incidence rate of loss to follow up was 6.3 per100 children in years of observation. Being male (AHR=2.1, CI =1.37 ,3.34), age 1-5 years (AHR=1.6, CI=1.05,2.46), poor adherence to antiretroviral therapy (AHR = 6.6; CI=4.11,10.66), fair adherence to antiretroviral therapy (AHR= 2.2; CI = 1.13 ,4.20), regimen was not changed (AHR = 4.1; CI = 2.59 ,6.45), world health organization stage III and IV (AHR= 2.2; CI =1.40, 3.33) and height for age < -2 z score (AHR = 2.2; CI = 1.43, 3.44) were predictors of loss to follow up.

**Conclusion:** The incidence rate of loss to follow was high. Age 1-5 years, world health organization stage III and IV, poor and fair adherence to antiretroviral therapy, regimen was not changed, being male and stunted were higher risk for loss to follow up. Therefore, close monitoring to the higher risk groups for loss to follow up highlighted in this study could decrease the rate of loss to follow up. Improving the adherence of children to antiretroviral therapy and nutritional support for stunted children were also recommended.

## Background

Human immunodeficiency virus(HIV) is a virus that causes acquired immunodeficiency syndrome (AIDS) by reducing the body's immune system that fight infection by attacking cluster of differentiation 4 cells (CD4)(1). From the beginning of the epidemic, 74.9 million people have been infected with HIV virus and about 32 million people have died worldwide(2). Globally, 37.9 million people were living with HIV by the end of 2018. Of these, 1.7 million were children and 180, 000 children died due to HIV related illnesses in the same year(3).

Despite the burden of HIV epidemic is varying across countries and regions, an estimated of 0.8% adult populations (15–49 years) were living with HIV worldwide(4). Greater than two-third of the world population were found in Sub-Saharan Africa which is the most severely affected region in HIV epidemic (5).

Ethiopia is one of the Sub -Saharan Africa countries where HIV is challenging to decline across its different geographical area(6). Ethiopian demographic and health survey report showed that there is variation of HIV prevalence among region. For example, Gambella region (4.8%) and Addis Ababa (3.4%) have the highest HIV prevalence rate while Southern Nations, Nationalities and peoples regional states(0.4%) and Somali region (< 0.1%) have the lowest(7). According to Ethiopian public health institution, HIV related estimates 691, 362 were living with HIV by the end of 2019. Of these 45,824 were children. Besides, 20, 300 were newly infected and 8, 256 were died with HIV related illness(8).

Antiretroviral therapy (ART) is essential for children to survive a long period life through reducing viral load and disease progresses(9). Without access to life-saving ART and regular medical supervision, HIV-infected children are more vulnerable to negative outcomes including death (10).

Loss to follow up is a critical barrier for the successful of HIV care and treatment(11). A significant number of children drop out from the treatment cascade (12).Globally, an estimated of 14% and 28% children were LTFU from the treatment cascade at one and two years after ART initiating respectively (13). LTFU is a commonly problem reported in Africa especially in Sub-Saharan Africa where an estimated of 20–40% of children were LTFU (14, 15). Children on ART who become LTFU are more risk to develop drug-resistant virus than those who remain on ART. Due to this, it impair the quality of life and shorten the survival time of those children with LTFU from ART regimen(16, 17).

Several studies revealed that there was a significant number of LTFU among children. Studies done in resource limited settings in Asia and Africa showed that 69% of LTFU occurred in the first 3 and 6 months of ART(18). In South Africa 8.4 per100 children year of observation and 5 per 100 children year of observation of LTFU occurred in the first and second year respectively(19) and in Ethiopia 6.26 per 100 children years of observation (20).

LTFU could be affected by the complex inter play of self-care, community factors, care delivery and the drug itself (21). Age of the children < 2 years, 1–5 year, CD4 count < 350cells at ART initiation, WHO stage III/IV, weight for age  $\leq$  2, short duration of time on ART, hemoglobin level < 8 g/dl, handling by non-educated care giver and disclosure of HIV status were associated with LTFU (22), (23–27).

To decrease LTFU from ART program, several African regions including Ethiopia used different mechanisms. Give free services, decentralization of services, create awareness using religious or community leaders and other stake holders as counselor and phone calling or mobile short message for caregiver were used to retain children on the program(28)29).The health sector give response to HIV, it is one of the targets of Sustainable Development Goals (SDGs) which is settled by united nations general assembly to "end HIV epidemic" by 2030 (30).

In addition, Ethiopia is implementing several strategies to end HIV epidemic by 2030 such as, global HIV prevention Coalition(reduced new infection by70% by 2020), HIV strategic plan ( reduced HIV related death by 80% and enroll 85% of children living with HIV for ART by 2020) and target 90 (90% of all people know their HIV status, 90% of HIV positive people were accesses to treatment and 90 of all people receiving ART will have viral suppression by 2020) (8, 31, 32). To achieve this goal, assess incidence and predictors of LTFU have a vital role in retaining of children in ART program.

Furthermore, LTFU is a critical barrier for determining the clinical outcome in HIV treatment program and identifying modifiable factors of LTFU is fundamental for designing effective patient retention strategy (47). There is limited data regarding to predictors of loss to follow- up among children attending ART clinic especially in Amhara region and to evaluate the relation of the following factors with LTFU like parent status, parent HV status and adherence level. Therefore, the aim of this study was to determine LTFU after ART initiation among children attending ART clinic and identifying its predictors

## Methods

### Study setting

The study was conducted at Dessie referral hospital, North east Ethiopia. The hospital is located at Dessie town, which is 401 km far from the capital city of Addis Ababa. Dessie referral hospital is the only referral hospital in this north wollo with catchment population of seven million. The hospital provides ART service for peoples living with HIV since 1995E.C and the case-team comprises different trained health professionals.

#### Study design and period

A ten-year institution based retrospective cohort study was employed starting from January 2010 to January 2020.

## Sample Size Determination And Sampling Procedures

The sample size was determined using Epi info version 7.2 by considering the following predictors: underweight, hemoglobin level and taking cotrimoxazole in study conducted in Ethiopia (39) with 95% CI, 80% power and ratio of exposed to unexposed was 1:1,  $p_1$  = Percent of outcome among exposed and  $P_2$  = Percent of outcome among unexposed. Then taking cotrimoxazole given large sample and the final sample size was 488. After getting this sample size the medical registration numbers of all under15 year's old children who started ART from January 2010 to January 2020 were collected from the database. Then computer generating method was used to select random medical registration numbers.

#### Data collection instrument and procedure

Data extraction tool was developed from the standardized ART entry and follow up form of the Ethiopia ministry of health and currently used by ART clinic. First the patient record was observed and appropriate data extraction format was prepared in English version. Data collectors were used the data collection tool to collect the information from children's charts. Charts were retrieved using the children's registration number which was found in data base in the electronic system and one data clerk was support them by identifying registration number of the charts. Necessary data were extracted by reviewing children's ART cards. Lost to follow up was confirmed by reviewing medical registration in the hospital or registration by ART adherence supporter. The first laboratory result was taken as baseline data. The data were collected by four experienced Bachelor of Science degree in nursing who have been trained on comprehensive HIV care and involved in the patient follow up care. Pretest was done on ten percent of the sample at Dessie referral hospital. 1 master in nursing supervisor was closely supervised the entire data collection process. 1 day training was given for both data collectors and supervisor concerning the data collection tool and data collection process. Data quality was also assured through designing proper data collection tool and continuous supervision. Codes were given for checklists. All collected data were checked for completeness by data collectors and supervisor every day.

#### Operational definition

##### Loss to follow up

Defined as no visit in the past 30 days and above for ART patients and not documented as died or transferred out to another ART clinic(23).

##### Transferred out

Those patients who were transferred to other health care facilities

### **Event**

LTFU of children after the initiation of ART.

### **Censored**

Individuals who died while on ART or individuals transferred out to other health institution after the beginning of the study or individuals on ART at the end of the study

### **Duration on ART**

Defined as the time between the start date of ART and the date of last contact with the health facility during data collection.

## **Data analysis**

The data were checked for completeness, consistencies and then, coded and entered using Epi data version 3.1. Then the data were cleaned and analyzed using STATA version 14. Descriptive statistics was computed to determine frequencies and summary statistics (mean standard deviation and percentage). Data were presented using tables and figures. Antroplus software was used to generate Z scores (weight for age, height for age, weight for height and body mass index for age) to define nutritional status. The Kaplan Meier survival curve was used to estimate survival time after initiation of ART and log rank test was used to compare survival curves of different categorical explanatory variable. The Cox proportional hazard model was used to assess the predictors of LTFU. To see the effect of predictors on time of LTFU, bivariable Cox-proportional hazard regression model was fitted for each explanatory variable. Moreover, those variables having p-value  $\leq 0.25$  in the bivariable analysis was fitted to the multivariable Cox-proportional hazard regression model. Hazard ratio with its 95% confidence interval and p-values was used to measure strength of association and identify statistical significant result. Variables having P-value  $< 0.05$  were considered as statistically associated with LTFU. Cox proportional hazard model assumption was checked using scaled schoenfeld residual test (P-value greater than 0.05 was met the assumption) and graphically with log-log Cox adjusted survival estimate. The model fitness was checked using Cox –snell residuals test. Multicollinearity was checked with variance inflation factor.

## **Results**

### **Sociodemographic Characteristics Of Children On Art**

Among 488 children were used for analysis more than half of participants (52.9%) were male. Majority of the participants (76%) were came from urban area and more than two third (85.2%) of them were living with their parents. The median age of children at ART initiation was 8 years with SD  $\pm 3.8$  and IQR (6.4).

Table 1  
Baseline sociodemographic characteristics of children on ART at Dessie referral hospital, North east Ethiopia, 2020

Variable		Frequency	Percent
Sex of children	Male	258	52.9
	Female	230	47.1
Age of children	≥ 5 years	341	69.5
	1–5 years	125	25.6
	< 1 years	22	4.5
Relation of child to care giver	Parent	416	85.2
	Guardian	72	14.8
Religion of parent/care giver	Muslim	299	61.3
	Orthodox	171	35.0
	Other*	18	3.7
Residence	Urban	371	76
	Rural	117	24
Age of parent/ care giver	≥ 35 years	258	52.9
	< 35 years	230	47.1
Sex of parent/care giver	Male	125	25.6
	Female	363	74.4
Marital status of caregiver	Married	341	69.9
	Single	18	3.7
	Widowed	74	15.1
	Divorced	55	11.3
HIV status of parent/caregiver	Both parent positive	148	30.3
	Mother positive	241	49.4
	Father positive	29	5.9
	Father negative	7	1.4
	Care giver positive	1	0.2
	Care giver negative	24	4.9
	Unknown	38	7.8

\*= Includes catholic and protestant \*\* =Includes student and waiters

Variable		Frequency	Percent
Parent status	Both alive	348	71.3
	Only mother alive	57	11.7
	Only father alive	29	5.9
	Both died	33	6.8
	Un known	21	4.3
Occupation of parent /care giver	Farmer	94	19.3
	Merchant	92	18.9
	Government employ	94	19.3
	Daily worker	59	12.1
	House wife	145	29.7
	Other **	4	0.8
Place of delivery child	Health facility	237	48.6
	Home	251	74.4
* = Includes catholic and protestant ** =Includes student and waiters			

### Baseline clinical, laboratory and ART information of children on ART

During ART initiation (73 .2%) of children had opportunistic infection. Nearly half of (48.2%) children were eligible for ART treatment based on low level of CD4 count. (Table 2).

Table 2

Baseline clinical, laboratory and ART information of children on ART at Dessie referral hospital, Northeast Ethiopia, 2020

Variable		Frequency	Percent
Presence of OIs at base line	Yes	357	73.2
	No	132	26.8
Type of OIs	Pneumonia	66	18.9
	Pulmonary tuberculosis	29	8.1
	Upper respiratory tract infection	45	12.6
	Unexplained wasting and stunting	4	1.1
	Diarrhea	56	15.7
	Unexplained Fever	26	7.3
	Herpes zoster	44	12.3
	Oral candidacies	25	7
	Skin dermatitis	49	13.7
	Other*	13	3.64
Functional status $\geq$ 5 years (n = 341)	Working	324	95
	Ambulatory	10	2.9
	Bed ridden	7	2.1
Developmental status < 5 years (n = 147)	Appropriate	121	82.3
	Delayed	24	16.3
	Regressed	2	1.4
WHO staging	Stage I	134	27.5
	Stage II	171	35
	Stage III	166	34
	Stage IV	17	3.5
Hemoglobin level	$\geq$ 10 mg/dl	431	88.3
	< 10 mg/dl	57	11.7
CD4 count	$\geq$ 350 cells	227	46.5
	< 350 cells	261	53.5

\*=includes HIVwasting syndrome, extra pulmonary tuberculosis, parotid enlargement

\*\*= Fatigue and nausea

Variable		Frequency	Percent	
Eligibility criteria	Clinical (WHO staging )	50	10.2	
	CD4 count	235	48.2	
	Without criteria	139	28.5	
	DBS positive	28	5.7	
	Both clinical and CD4 count	36	7.4	
Base line regimen	4a(d4t-3TC-NVP)	116	23.8	
	4b(d4t-3TC-EFV)	51	10.5	
	4c (AZT-3TC-NV)	137	28.1	
	4d (AZT-3TC-EFV)	88	18	
	1e (TDF-3TC-EFV)	51	10.5	
	1 h(ABC-3TC-NVP)	9	1.8	
	1 g(ABC-3TC-EFV)	15	3.1	
	4 g(ABC-3TC-LPV/r)	17	3.5	
	Other (1c,4i,4j)	4	0.8	
Taking prophylaxis	Yes	452	92.6	
	No	36	7.4	
Type of prophylaxis	CPT	440	96.3	
	INH	13	2.8	
	Both CPTand INH	4	0.9	
Side effect	Yes	34	7	
	No	454	93	
Type of side effect	Anemia	16	47	
	Rash	14	41.2	
	Eye discharge	2	5.9	

\*=includes HIVwasting syndrome, extra pulmonary tuberculosis, parotid enlargement

\*\*= Fatigue and nausea

Variable		Frequency	Percent
	Other**	2	5.9
Regimen change	Yes	281	57.6
	No	207	42.4
Reason for change	Drug side effect	34	12
	New drug availability	104	36.8
	Drug stock out	82	29
	New tuberculosis	6	2.1
	Virologic failure	25	8.8
	Weight > 25 kg	32	11.3
Adherence level	Good	406	83.2
	Fair	38	7.8
	Poor	44	9
*=-includes HIVwasting syndrome, extra pulmonary tuberculosis, parotid enlargement			
**= Fatigue and nausea			

## Nutritional Information Of Children On Art

From all over of the study participants living with HIV 17.2% were stunted.

Table 3  
Nutritional information of children on ART at Dessie referral hospital, North east Ethiopia, 2020

Variable		Frequency	Percent
Weight for height/length (< 5 year)	Normal	122	83
	Wasted	25	17
Weight for age ( age < 10 year)	Normal	267	75.4
	Under weight	87	24.6
Body mass index for age ( $\geq$ 5 year )	Normal weight	299	87.7
	Thinness	42	12.3
Height /length for age (< 15 years)	Normal	404	82.8
	Stunted	84	17.2

# Incidence Of Loss To Follow Up After Art Initiation

From the 488 cohort of children on ART 301(61.68) were on ART at the end of study, 101(20.7%) were LTFU with (CI = 17.20,23.80), 75 (15.37%) were transferred out and 11(2.25%) were died. The overall loss to follow up incidence density rate (IDR) in the cohort was 6.3 per 100 children in years of observation with (95% CI = 5.21, 7.77).

## Cox proportional hazard ratio analysis for predictors of Loss to follow up

The relationship between the baseline variables and the risk of loss to follow up for children on ART was analyzed using Cox proportional hazard regression model. In bivariable analysis the Cox proportional hazard model showed that sex of child, age of child 1–5 years, residence, taking prophylaxis, change of regimen, CD4 count, WHO staging, hemoglobin level, adherence level and height for age were statistically significant predictors of loss to follow up. In multivariable analysis, all predictors found to be significant in bivariable were assessed and only sex of child, age of child between 1–5 years, WHO stage, adherence to ART, height for age and regimen change were found to be strong predictors of loss to follow up.

Children whose age between 1–5 years were increase the hazard of LTFU by 1.6 times as compared to those whose age  $\geq$  5 years (AHR = 1.6, CI = 1.05, 2.46). Children being male were 2.1 times more hazardous to LTFU than females (AHR = 2.1, 95% CI = 1.37, 3.34). The hazard of LTFU in children who had WHO stage III and IV were 2.2 times higher than those who had WHO stage I and II (AHR = 2.2, CI = 1.40, 3.33). Having poor adherence to ART was 6.6 times increase the hazard LTFU among children as compared to good adherence to ART (AHR = 6.6, CI = 4.11, 10.66) and also children had fair adherence to ART were 2.2 times more hazardous to LTFU as compared to those who had good adherence (AHR = 2.2, CI = 1.14, 4.20). The hazard of LTFU in children whose nutritional status was stunted (HFA < -2Zscore) were 2.2 times higher than their counterpart (AHR = 2.2, CI = 1.43, 3.44). Children whose regimen was not changed were 4.1 times more hazardous to LTFU as compared to those whose regimen was changed (AHR = 4.1, CI = 2.59, 6.45).

Table 4  
Cox regression analysis for predictors of lost to follow up among children on ART at Dessie referral hospital, Northeast Ethiopia, 2020

Variable	Status	CHR with CI	AHR with CI	P
	<b>LTFU Censored</b>			
Age ≥5 years	58(17%) 283(83%)	1	1	<b>0.030</b>
1–5 years	39(31.2%) 86(68.8%)	1.9(1.28,2.90)	<b>1.6(1.05, 2.46)</b>	0.426
< 1 years	4(18.2%) 18(81.8%)	1.2(0.43, 3.28)	0.6 (0.21,1.94)	
Sex male	71(27.5%) 187(72.5%)	2.4(1.55–3.65)	<b>2.1(1.37, 3. 34)</b>	<b>0.001</b>
Female	30(13%) 200(87%)	1	1	
Residence urban	66(17.8%) 305 (82.2%)	1	1	0.176
Rural	35(29.9%) 82(70.1%)	2(1.34–3.04)	1.3 (0.88,2.06)	
Taking prophylaxis	88(19.5%) 364 (80.5%)	1	1	0.718
Yes	13(36.1%) 23(63.9%)	2.7(1.52,4.91)	0.9(0.46 ,1.71)	
No				
Change of regimen	43(15.3%) 238(84.7%)	1	1	<b>0.000</b>
Yes	58(28%) 149(72%)	4.3(2.84–6.41)	<b>4.1(2.59 ,6.45)</b>	
No				
CD4 count	28(12.3%) 199(87.7%)	1	1	0.094
≥350cells	73(28%) 188(72%)	2 (1.28–3.06)	1.5(0.93, 2.41)	
< 350cells				
Hemoglobin	75(17.4%) 356(82.6%)	1	1	0.267
≥ 10 mg/dl	26(45.6%) 31(54.4%)	2.7(1.73, 4.23)	1.3 (0.81, 2.16)	
< 10 mg/dl				
Height/L for age	63(15.6%) 341(84.4%)	1	1	<b>0.000</b>
Normal	38(45.2%) 46(54.8%)	3.6(2.38,5.39)	<b>2.2(1.43, 3.44)</b>	
Stunted				
WHO stage	42(13.8%) 263(86.2%)	1	1	<b>0.000</b>
Stage I &II	59(32.2%) 124(67.8%)	2.1(1.43,3.16)	<b>2.2(1.40,3.34)</b>	
Stage III&IV				

Variable	Status		CHR with CI	AHR with CI	P
	LTFU	Censored			
Adherence	53(13.1%)	353(86.9%)	1	1	0.019
Good	12(31.6%)	26(68.4%)	2.8(1.50,5.26)	<b>2.2 (1.14,4.20)</b>	<b>0.000</b>
Fair	36(81.8%)	8(18.2%)	8.6(5.64, 13.21)	<b>6.6(4.11,10.56)</b>	
Poor					

## Discussion

The incidence rate of this study was 6.3 per 100 children years of observation (CI = 5.21, 7.77). Up on running the final cox proportional hazard model statistically significant predictors for LTFU were being male, WHO stage III and IV, age between 1–5 years, stunted, poor and fair adherence to ART and regimen was not changed.

The overall incidence rate of this study is in line with the study conducted in Addis Ababa Ethiopia 6.26 per 100 children in years of observation(20). On the other side, the result of this study is lower than the studies conducted in Tanzania 18.2 per100 children in years of observation, Uganda 12.6 per100 children in years of observation and in South Africa 10.8 per 100 children in years of observation ( 24,33,34). This difference might be due to socio-cultural difference. In addition, in Tanzania the study includes both pre ART (before ART) initiation and post ART initiation children and in Uganda the presence of high orphan children in the study.

In contrary, the result of this study is higher than studies conducted in Thailand 2.92 per 100 children in years of observation and India 4.4 per 100 children years of observation. This difference might be due to socio cultural and economic difference (35, 36). The other possible explanation is the presence more ART service decentralization in India. Additionally, in Thailand there is a difference in operational definition of LTFU (use 12 months to say LTFU) and study period difference (6 years). Plus to this, the result of this study is higher than studies conducted in Zimbabwe 4.92 per 100 children in years of observation, Kenya 3.29 per 100 children years of observation and Ethiopia 3.6 per 100 children years of observation (37, 38, 39). This is might be due to variation in implementation of retention in care strategy and also follow up period difference (5 years) and in Ethiopia the difference might be study period difference (six years).

In this study, LTFU before 18 months (with incidence rate of 6.6 per100 children years of observation) was higher than LTFU after 18 months of ART initiation (6.1 per100 children years of observation). This is due to the fact that at initial time they are risk for immune reconstitution inflammatory syndrome and drug side effect that increase the risk of death. The incidence rate of lost to follow up at first year (6.9 per 100 children years of observation) was higher as compared to the second year (5.9 per 100 children years of observation). This is in line with the study conducted in South Africa(19). This is might be health care workers give repeated counseling for caregivers about the benefit of ART treatment and consequence of discontinuation. The other possible explanation might be government give attention and create awareness for the community about the benefit of treatment and decentralization of ART services.

The cumulative incidence of this study was 20.7% (CI = 17.20, 23.80). This is in line with the studies conducted in West Africa 21.8%, Nigeria 19% and Ethiopia 17.9%(13 34, 37). However, this result is higher than studies

conducted in Asia 4.1%, Cote d'Ivoire 9.3%, East Africa 14%, South Africa 9% and Zambia 16% (16, 22). This might be due to economic and socio-demographic differences and variation in implementation of retention strategy. For example, in Zambia health care workers apply home-to-home visits. In contrast, the findings of this study are lower than studies conducted in Mozambique 38.7% and in Adama Ethiopia 34% (40, 41). This might be in the Mozambique study conducted in 10 rural districts and there was a challenging of transportation and poor health care infrastructure. In Adama Ethiopia study includes both pre-ART initiation and post-ART initiation.

In this study, the hazard of loss to follow up among children whose age between 1–5 years were 1.6 times higher than children whose age greater or equal to five years. This is supported by studies conducted in Thailand and Botswana (35, 41). This is due to this age group was more at risk for malnutrition and opportunistic infection that increase disease progression rapidly (42). This result is inconsistent with a comparative analysis study conducted in Asia and Africa and study conducted in South Africa (16, 19).

This study showed that being male was 2.1 times increasing the hazard of loss to follow up as compared to female. This is consistent with studies conducted in Kenya, South Africa and Brazil (19, 27, 37). This is due to most of 152 (59.4%) of males initiate ART with advanced stage of diseases (III and IV).

Having advanced clinical stage (WHO stage III and IV) at the time of ART initiation was significantly increased the hazard of loss to follow up among children. This is supported by studies conducted in West Africa, Malawi, Uganda, Botswana and Ethiopia (24, 41, 43, 44, 45).

The possible explanation might be children initiate ART in advanced stage increase the risk of opportunistic infections that cause morbidity and mortality that leads to unregistered death. Moreover, children at advanced stage may develop drug side effects especially within the first six months and further complicate disease progression (46).

On the other hand, the result of this study is inconsistent with studies conducted in South Africa and Kenya (34, 37). The possible explanation might be patients with stage I and II not feel sick enough to accept restrictive medical care (47). Additionally, in South Africa children in this stage were asymptomatic and health care workers were not given more attention than those had advanced disease (34).

Children whose nutritional status was stunted were more hazardous to loss to follow up as compared to those whose nutritional status was normal. This is supported with studies conducted in other parts of Africa country include Ethiopia (22, 26, 40). This could be due to the fact that stunted children may have had poor baseline health and poor ART compliance as compared to normal. In fact HIV by itself affects nutritional status and malnourished children more affected by HIV and increase disease progression (48, 49). Furthermore, stunted children may have had concomitant opportunistic infection that detained them back from the health facility for refill of drug and some may have died from such condition (50).

Regarding to adherence to ART, those having poor adherence to ART were about seven times increase the hazards of loss to follow up as compared to those having good adherence to ART. Also the hazardous of LTFU among children who had fair adherence to ART were 2.2 times higher than their counterpart. This is the fact that poor/fair adherence increase viral load duplication and decrease drug effectiveness. Because of this, further suppression of immune system and increase opportunistic infection that rapidly increase disease progression (51). The other possible explanation might be poor medication adherence cause HIV viral resistance

and subsequently treatment failure. Moreover, children depend on their caregiver to get their care due to this, if the child had poor improvement caregiver's might be feel hopelessness or carelessness and loss from treatment cascade.

Furthermore, children whose regimen was not changed were four times more hazardous to loss to follow up as compared to those whose regimen was changed. This is might be most of old regimens have side effects that cause advanced disease and complication that leads to death. For example AZT containing regimen cause anemia that increase the disease progress (52).

## **Conclusion**

The incidence rate of loss to follow was high. Age 1–5 years, world health organization stage III and IV, poor and fair adherence to antiretroviral therapy, regimen was not changed, being male and stunted were higher risk for loss to follow up. Therefore, close monitoring to the higher risk groups for loss to follow up highlighted in this study could decrease the rate of loss to follow up. Improving the adherence of children to antiretroviral therapy and nutritional support for stunted children were also recommended.

## **Abbreviations**

AIDS: Acquired Immune Deficiency Syndrome; ART: Antiretroviral Therapy; HIV: Human Immunodeficiency Viruses; LTFU: Lost to Follow UP; WHO: World Health Organization

## **Declarations**

### **Consent of publication**

Not applicable

### **Availability of data and materials**

The data sets used or analyzed for current study are available from cross ponding author on reasonable request

### **Competing interest**

No conflict between authors

### **Funding**

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### **Authors' contributions**

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