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# Incidence of loss to follow-up and its predictors among HIV-infected under-five children after initiation of antiretroviral therapy in West Amhara Comprehensive Specialized Referral Hospitals, Northwest Ethiopia: a multicenter retrospective follow-up study

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## Abstract

**Background** Loss to follow-up (LTFU) among under-five children from HIV care profoundly affects the treatment outcomes of this vulnerable population. It is a major factor that negatively affects the benefits of antiretroviral therapy (ART). Current information about LTFU among HIV-positive under-five children on ART is essential for effective treatments. To far, nevertheless, limited research has been done in Ethiopia to address this issue. Thus, this study aimed to assess the incidence and predictors of LTFU among HIV-infected under-five children receiving ART in West Amhara Comprehensive Specialized Referral Hospitals.

**Methods** A multicenter institution-based retrospective follow-up study was conducted among 435 HIV-infected under-five children on ART selected by simple random sampling from January 1, 2010 to December 31, 2019, and data were collected between December 1, 2021, and January 31, 2022. A standardized data extraction tool adapted from the ART entry and follow-up forms was used. The event of interest for this study was LTFU, whereas the absence of LTFU was censored. Before being transferred to STATA version 14 for analysis, the data were entered into Epi-Data version 3.1. The Kaplan–Meier curve was used to estimate an individual's survival-free probability at each specific point in time. The Cox proportional hazards model was used to identify predictors of LTFU.

**Results** Among the 420 records included in the final analysis, 30 (7.14%) of the individuals were LTFUs. The incidence rate of LTFU was 3.4 per 1000 person-months of observation (95% CI: 2.43–4.87). The survival probabilities of children after 12, 24, 36, and 48 months were 0.97, 0.92, 0.88, and 0.77, respectively. The independent predictors of LTFU were HIV infection in under-five children who lived in rural areas (AHR = 3.64; 95% CI: 1.41, 9.37), poor adherence to ART (AHR = 4.37; 95% CI: 1.59, 12.02), not receiving cotrimoxazole preventive therapy (AHR = 3.75; 95% CI: 1.39, 10.08),

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not receiving isoniazid prophylaxis (AHR = 3.4; 95% CI: 1.29, 9.01), and having a severe WHO clinical stage (AHR = 5.43; 95% CI: 1.38, 11.43).

**Conclusion and recommendation** The incidence of loss to follow-up was high, especially in the first two years after ART initiation. The risk of LTFU was greater for those who were rural residents, had poor adherence, lacked cotrimoxazole preventive therapy, not given isoniazid prophylaxis, and presented with WHO clinical stages III and IV. Therefore, clinicians should emphasize for cotrimoxazole preventive therapy and isoniazid prophylaxis, for those living in rural areas, who present with poor adherence and WHO clinical stages III and IV.

**Keywords** Antiretroviral therapy, Under-five children, Loss to follow-up, Predictors, Ethiopia

## Introduction

Human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) continues to be one of the main causes of morbidity and mortality in the world's population. Globally, 39 million people are HIV-positive as of 2022. Approximately 1.3 million people contracted (newly infected) HIV, while 630,000 people died from AIDS-related diseases in the same year. By the end of 2022, there were 760,000 new HIV infections, approximately 380,000 deaths from AIDS-related illnesses, and 25.6 million HIV-positive people living in Africa. Overall, 20.8 million HIV-positive people, 500,000 new HIV-infections, and 260,000 AIDS-related deaths occurred in Eastern and Southern Africa [1, 2].

Loss to follow-up was defined as not taking ART for three months (90 days) or longer following the last visit that was documented and not reporting or recording the patient's death or transfer to another healthcare facility on their medical records or logbooks [3]. Because children are unable to obtain healthcare services without caregivers, they are more likely than adults to acquire LTFU from HIV care [4]. Loss to follow-up impacts individuals in all communities worldwide and is a significant factor in the global illness burden. It has a detrimental impact on patients' clinical and immunological outcomes. It also has a high risk of medication resistance, transmission, morbidity, and mortality from HIV/AIDS and its consequences [5].

Loss to follow-up among HIV-infected children on ART faces a significant challenge. This is a considerable obstacle to the effectiveness of the program, which negatively impacts the immunological benefits of ART and drug adherence. Additionally, it increases drug toxicity, resistance and AIDS-related morbidity and mortality[6]. Although ART significantly improves the survival status and quality of life of HIV-infected children, LTFU from HIV care has a substantial impact on the treatment outcomes of vulnerable groups [7]. Although ART is recommended for all HIV-infected children regardless of CD4 count and WHO clinical stage, LTFU levels are particularly high in Ethiopia, along with the continuum of care, which is challenging because of their dependence on a caregiver [8].

According to studies, a considerable proportion of children from their ART clinic were found to have LTFU. Approximately 14% and 28% of children worldwide were left behind from the treatment cascade at one and two years following the initiation of ART, respectively [9]. A Study conducted in Asia and Africa showed that 69% of LTFU occurred in the first six months of ART initiation [10]. The incidence rate of LTFU in Myanmar was 4.7 per 100 person-years of observation [11], and Asia and Africa 4.1 per 100 person-years of observation [12]. Other studies done in South Africa showed that the incidence rates of LTFU were 7.5 and 10.8 per 100 person-years of observation [13, 14]. Studies done in Ethiopia showed that the incidence rate of loss to follow-up was 6.3 per 100 person-years of observation [15], 6.2 events per 100 child-years of observation [16] and, 6.26 per 100 person-years of observation [17].

The most commonly reported contributing factors for LTFU among HIV-infected children are advanced WHO clinical disease stage, malnutrition, younger age, lack of contact information for caregivers, fear of stigma, forgetfulness, scheduling conflicts, lack of access to transportation, privacy concerns, not disclosing HIV status, inadequate follow-up at the ART clinic, and not disclosing HIV status [9]. Similarly, living far from medical facilities, not having access to transportation, feeling stigmatized, not disclosing HIV status, being bedridden, and not realizing that ART is a lifelong medication are common risk factors that increase LTFU among HIV-infected children in Ethiopia [18].

A variety of tactics have been employed by numerous nations, including Ethiopia, to overcome LTFU from ART programs. Providing free HIV/AIDS and ART services is one of them. Other strategies include decentralizing services to lower facility levels, talking about raising awareness among religious and community leaders and other stakeholders, and using phone calls or brief messages on mobile devices to stay on the program [3, 19]. A religious leader is someone who leads and guides a group of people who share a common faith, plays a prominent

role within their community, improves the participation of their congregation in interventions, and thus promotes positive health outcomes. A community leader can influence societal attitudes and norms, improve health outcomes, mobilize demand for services, and reach those who are hard for formal health systems to reach, support the strengthening of the health system, and foster an atmosphere that makes access easier.

Ethiopia is implementing several strategies to end the HIV epidemic by 2030. For example, the Joint United Nations Program on HIV/AIDS (UNAIDS) launched three "95–95-95" targets for HIV/AIDS. These three "95–95-95" targets suggest that 95% of all HIV-infected people should know their HIV status, 95% of all HIV-infected people who know their status should receive treatment, and 95% of all people receiving ART should achieve viral suppression [20]. HIV-positive persons should start taking their HIV drugs in order to accomplish this goal, and the health care system should be strengthened in order to avoid LTFU when a patient is linked to the ART clinic.

In HIV treatment programs, LTFU is a significant challenge that complicates therapeutic outcomes. Determining whether LTFU was caused by modifiable or non-modifiable causes is essential to develop a patient effective retention plan. This study will be important for policymakers, clinicians and subsequent researchers to reduce HIV-related morbidity and mortality associated with LTFU and to achieve the ambitious plan by the year 2030 of ending the HIV pandemic in Ethiopia. There is limited evidence regarding to the incidence of loss to follow-up and its predictors among HIV-infected under-five children attending ART clinics in Ethiopia. Therefore, we assessed the incidence and predictors of LTFU among HIV-infected under-five children after the initiation of ART in Northwest Ethiopia.

## Methods and materials

### Study design, area and period

A multicenter institution-based retrospective follow-up study was carried out on under-five children who started ART between 2010 and 2019 in comprehensive specialized referral hospitals in West Amhara, Northwest Ethiopia. There are five comprehensive specialized referral hospitals in West Amhara, Northwest Ethiopia. These are the University of Gondar Comprehensive Specialized Referral Hospital (UoGCSH), Felege Hiwot Comprehensive Specialized Referral Hospital (FHCSH), Debre Tabor Comprehensive Specialized Referral Hospital (DTCSRH), Debre Markos Comprehensive Specialized Referral Hospital (DMCSRH), and Tibebe Ghion Comprehensive Specialized Referral Hospital (TGCSRH). The Tibebe Ghion Comprehensive Specialized Referral Hospital was excluded because it was recently opened and still does not provide ART services. The four included hospitals were UGCSRH, FHCSRH, DTCSRH, and DMCSRH, which are 300 km, 565 km, 660 km, and 738 km from Addis Ababa, the capital city of Ethiopia, respectively. These hospitals were chosen because they offer care services and follow-up for ART to a large number of patients in the area. In the Amhara region and its surrounding areas, the four hospitals serve almost 20 million people with inpatient and outpatient care. Apart from standard medical services, all four institutions offer long-term HIV treatment. Approximately 910 HIV-positive children under the age of five have started receiving ART at these locations to far; 648 of these children were receiving active ART during the study period.

### Source population

All under-five children with HIV-infection who had ever registered in pediatric ART clinics and begun ART in the study hospitals.

### Study population

Randomly selected under-five children with HIV-infection who took ART during the follow-up period.

### Inclusion criteria

All HIV-infected children under the age of five who were enrolled in the study hospital's pediatric ART clinic from 2010 to 2019 and who had been on ART medication for at least three months were included.

### Exclusion criteria

Children under the age of five with incomplete records of age and ART initiation date at the time of data collection were excluded.

### Sample size determination

The sample size was determined by using STATA version 14 statistical software for Cox proportional hazard regression. Since, we had used Cox proportional hazard regression for satistical analysis, we calculaed sample size by considering this software. The minimum required sample size was estimated based on the significant predictors of loss to follow-up in HIV-infected children on ART in the previous literature [16]. The identified predictors were relation of caregiver with a child, WHO clinical stage, regimen substitution, adherence to ART and TB treatment history. We chose regimen substitution as it offered the largest sample size and had the lowest hazard ratio (1.74). The probability of failure (event) in the previous literature was taken to be 0.219 [16]. STATA software calculations were performed by the assumptions of using a 95% confidence interval, 80% power, 5% level of significance, and after adding 10% contingency for incomplete

records (missing), yielding a total sample size of 435 for this study. The medical records of under-five children who received treatment throughout the study period were taken from the ART registry, and all four comprehensive specialized referral hospitals offering ART treatments were included. At this stage, a sampling frame was created, and the overall sample size and the total number of children receiving ART were contrasted. Subsequently, 435 study participants in total were chosen by means of a computer-generated random sample technique.

### Sampling technique and procedure

Initially, a stratified sampling technique was used to allocate samples proportionally to each study hospital and then a simple random sampling technique was used to select the samples from each hospital. Based on the unique source populations of each of the selected hospitals, a proportionately allocated sample was established. Each hospital's unique ART registration book, which is part of the Health Management Information System (HMIS), was used to gather patient medical registration numbers. These numbers were then entered into Microsoft Excel, which was then copied and pasted into SPSS version 23 independently in each hospital. Using SPSS, a random medical registration number was generated for every patient. A proportionate share of the computed sample size was collected among the four comprehensive specialty referral hospitals (Fig. 1).

### Data collection tools and procedures

After reviewing the medical records of some children with HIV, a standardized data extraction checklist was created for data extraction. Structured checklists that were created and adjusted in accordance with the charts were used to extract data from the charts. Data on HIV-infected children who began ART between January 2010 and December 2019 and got follow-up care at the study hospitals was obtained. The socio-demographic, clinical, laboratory, treatment, and outcome-related data needed for the assessment were collected using the created data abstraction tool. Using the patient's medical registration number, the medical records of eligible HIV-positive children receiving ART were first collected from the card room. Two senior BSc nurses supervised the four BSc nurses who collected the data. Then, basic socio-demographic, clinical, treatment and outcome related variables of HIV-infected children under the age of five were extracted from the selected charts. The most recent laboratory test results and clinical information were considered baseline values prior to initiating ART. On the other hand, follow-up data was gathered regarding characteristics including adherence level, history of OIs, regimen changes, and treatment failure history. Furthermore, pertinent patient information that was not contained in the patient's chart was obtained from the ART smart care file. Lastly, using randomly chosen reviews of previously retrieved medical information, the principal investigator verified the coherence between the records and the data gathered.

### Variables

#### *Dependent variable*

The outcome of this study was the loss to follow-up after ART initiation.

#### *Independent variables*

The independent variables that were used to affect the loss to follow-up of under-five children on ART were the following.

*Socio-demographic factors:* These included age and sex of the child, age and sex of the caregiver, residence, relationship of the caregiver to the child, and status of the parents.

*Baseline clinical, laboratory, and immunological factors,* such as WHO clinical stage, TB and its treatment status, hemoglobin level, CD4 count/percentage, ART regimen change, nutritional status (underweight, wasting, stunting), OIs, eligibility criteria for ART, cotrimoxazole preventive therapy (CPT), isoniazid preventive therapy (IPT), ART regimen change, treatment failure, adherence to ART, and history of OIs.

### Operational definitions

*Advanced WHO clinical stages:* HIV-positive children under the age of five had clinical stages III and IV when they were enrolled in ART [21].

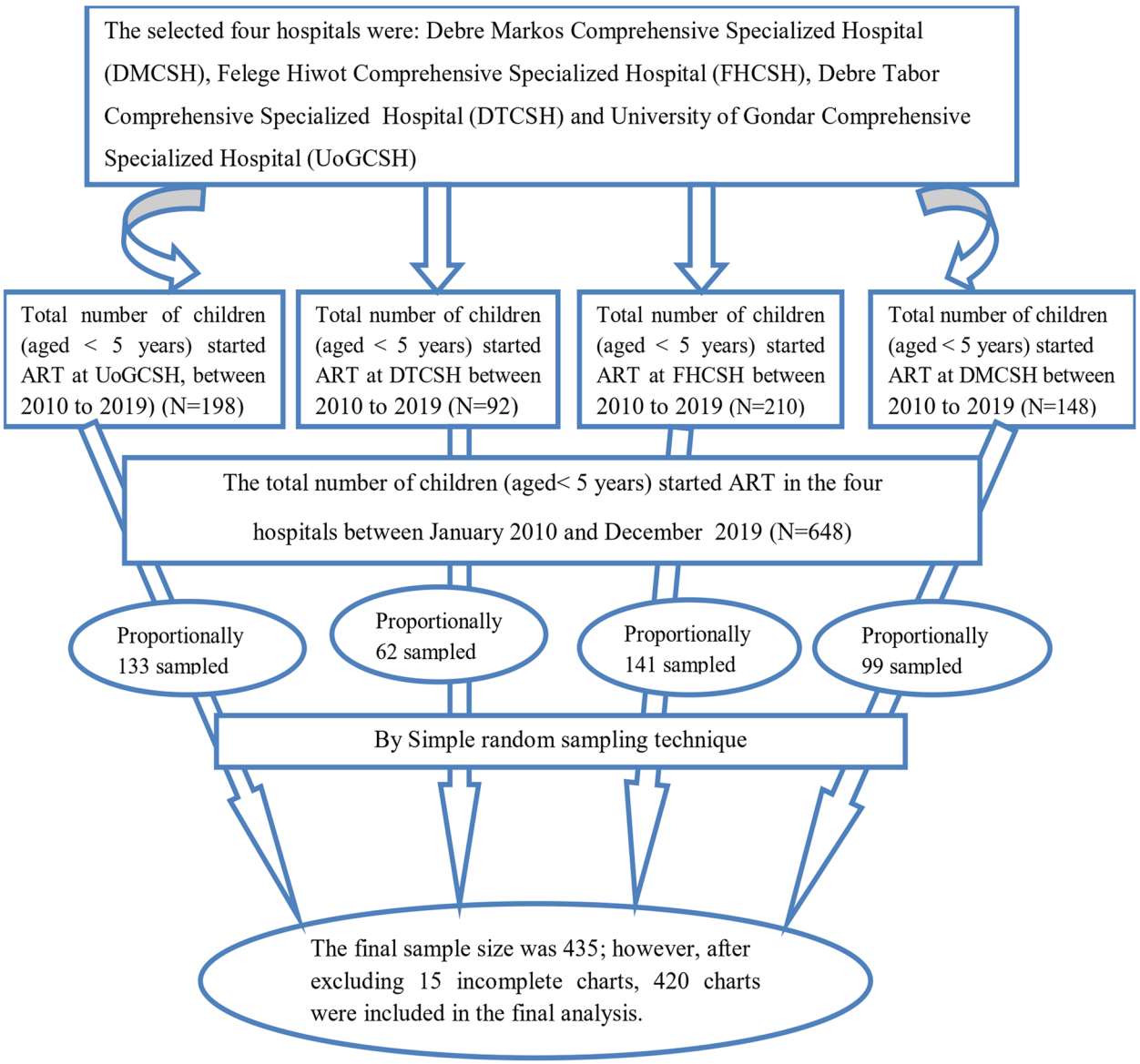
*Anemia:* Hemoglobin level less than 10 mg/dl [22].

*Event:* The event of interest for this study was the LTFU of HIV-infected under -five children after the initiation of ART.

*Censored:* Participants who died or were still alive under ART at the end of the follow-up period or who were formally transferred (refer) to other health facilities. The status of the patients (censored or LTFU) and other relevant data were available in the HMIS ART registration book, patient charts, and ART smart care files.

*Time to event:* The time interval (months) between ART initiation and the occurrence of LTFU.

*Follow-up time:* The follow-up time was calculated in months from the date of ART initiation until the date of event (LTFU) or censoring (death, transfer to other health facilities, or being alive at the end of their fifth year).




Footnote: proportion was calculated as follows: the total number of HIV-infected < 5 children on ART at a given hospital multiplied by our calculated sample size (435), and then divided by the total number of HIV-infected < 5 children started ART in the four hospitals between January 2010 to December 2019 (648). For example, for FHCSH, it was calculated as: 210*435/648 =141.

**Fig. 1** Sampling procedure used to assess LTFU and its predictors among HIV-infected under-five children receiving ART, Northwest Ethiopia, 2022

*Incidence rate of LTFU:* The rate of child LTFU during the follow-up time to the total person-months of observation.

*Mild WHO clinical stages:* HIV-positive under-five children in stages I and II of their baseline clinical stages at the time of ART enrollment [21].

*Moderate underweight:* children having a weight for age Z score (WAZ) < − 2 Standard Deviation (SD) [23].

*Severe underweight:* children having WAZ < − 3 SD [23].

Moderate stunting: children having a height for age Z score (HAZ) < − 2 SD [23].

*Severe stunting*: children having HAZ < −3 SD [23].

*Moderate wasting*: children having a weight for height Z score (WHZ) < −2 SD [23].

*Severe wasting*: children having WHZ < −3 SD [23].

*Opportunistic infections:* When, throughout the follow-up period, an HIV-positive children experienced any kind of OI following the start of ART [24].

*Treatment Failure; Clinical Failure:* Advanced or severe immunodeficiency (WHO clinical stages III and IV, excluding TB) demonstrated by a new or recurring clinical event following six months of successful treatment. *Immunologic failure:* At least two CD4 readings below the cutoff (CD4 count of less than 10%, or < 200 cells/$mm^3$). The CD4 + T-cell count was measured at baseline and every six months during follow-up. *Virologic failure*: when there were two consecutive assessments of the viral load during a three-month period that were larger than 1000 copies/ml with adherenced support between measurements [25].

*Loss to follow-up:* Children who have missed their follow-up or drug pick-up appointments for three months and more after last appointment date and had not been classified as dead or transferring out [3, 26, 27].

*Transferred out:* Children who were formally referred (taken) to various medical institutions [26].

*Incomplete card (chart):* when the patient's chart did not contain the indication for the dependent variable and/or 5% of the independent variables.

A child's developmental status was categorized as *appropriate* (ability to meet age-appropriate milestones), *delayed* (inability to meet age-appropriate milestones), or *regressed* (loss of age-appropriate achievements) [28].

*CD4 counts or percentages (%): below the threshold* if the child had CD4 cell counts < 1500/mm3 or 25% for age < 12 months, CD4 cell counts < 750/mm3 or < 20% for age 12–35 months, or CD4 cell counts < 350/mm3 or < 15% for age 36–59 months [29].

*Adherence: Good* (> 95%) if the percentage of missed doses was ≤ 2 doses of 30 doses or ≤ 3 doses of 60 doses; *Fair* (85–94%) if the percentage of missing doses was between 3 and 5 of 30 doses or 4–9 of 60 doses; *Poor* (< 85%) if missed doses were 6 doses of 30 doses or 10 and above doses of 60 doses, as documented by the ART physician [30].

### Data quality assurance and control

To assure the quality of the data, a one day training and orientation was provided to both the supervisors and the data collectors regarding the objectives of the study, how to extract pertinent data, and how to protect patient confidentiality. Every day, the supervisors also checked that the data was complete and consistent. The gathered data were examined and verified for completeness prior to entry, and any data that was incomplete being removed. To reduce data entering errors, Epi-Data were utilized during data entry.

### Data processing and analysis

A descriptive analysis was done to present the frequency of each variable. The Kaplan–Meier survival curve was used to estimate the LTFU-free (survival) probability of HIV-infected children at each specified time of ART. Plotting was performed with the likelihood of survival on the Y-axis and time on the X-axis. Since no one had experienced the event at time = 0 at the beginning of the study, the likelihood of survival was 100%, and the graph began at probability = 1.0 (100%). Log rank tests were used to compare the LTFU-free survival time between categories of each explanatory variable. The log rank test is a nonparametric test that compares estimates of the difference between groups at each observed event time. Graphical and Schoenfeld residual global proportional hazard tests were used to assess the proportional hazard assumption of the model. A *P*-value of > 0.05 on the Schoenfeld residuals of the proportional hazard (PH) test was used to ascertain whether the proportional hazard assumption was satisfied or violated, yielding a *P* value > 0.05 for each independent variables and an overall global test *P* value of 0.7929, which indicated that the assumption was fulfilled (Supplementary Table 1). The multicollinearity among independent variables was checked using the variance inflation factor (VIF); as a result, there was no multicollinearity because the value of the VIF for each independent variable was < 7. A bi-variable (simple) Cox proportional hazard model was used to identify candidate variables for multivariable Cox regression. A multivariable Cox proportional hazard model was used to identify predictors associated with loss to follow-up in HIV-infected children. Variables with a *p*-value less than 0.25 in the bi-variable analysis were considered in the multivariable Cox regression analysis. Additionally, variables having a *P*-value less than 0.05 in the multivariable Cox regression analysis with an AHR of 95% CI were deemed significant predictors of LTFU. Furthermore, the outcome status was computed by dividing the total number of occurrences of event (LTFU) to the total number of observations during the follow-up period. The incidence density was measured by person-months of observation.

## Results

### Socio-demographic characteristics

After reviewing the records of 435 HIV-infected children, 420 records were included in the final analysis, 15 of which were excluded due to incomplete data (missing). Approximately half (213, 50.71%) of the study participants were females. Two-thirds of the participants

(66.43%) were from urban areas. The baseline median age of the under-five children was 33.5 months (IQR: 19.5–47.5), the median age of the caregivers was 31 years (IQR: 27–37), and the majority of the parents (77.14%) were both alive (Table 1).

### Baseline and follow-up clinical, immunological, laboratory, and treatment-related characteristics

More than half (63.10) of the study participants had baseline opportunistic infections. In terms of developmental milestones, 360 (86.75%), 47 (11.32%), and 8 (1.93%) of the study participants were appropriate, delayed, and regressed, respectively. Two hundred (47.62%) of the participants initiated ART at WHO clinical stages III and IV. Approximately half (50.95%) of the children were screened for tuberculosis (TB) in the past (before the start of ART). The eligibility criteria for the initiation of ART were mainly determined by the CD4 + cell count and WHO clinical stage (42.96%), followed by the test and treatment strategy (27.1%). Furthermore, more than half (55.71%) of the children had CD4 counts below the threshold. Moreover, 47 (11.19%) of the participants had anemia at baseline. Eighty-four (20%) of under-five children on ART had a history of treatment failure. During the follow-up period, 322 (76.67%) and 57 (13.57%) participants had good and fair adherence, respectively; 41 (9.76%) had poor adherence by the end of the follow-up period. Regarding prophylaxis use, 372 (88.57%) of the participants were ever on cotrimoxazole preventive therapy (CPT), whereas 226 (53.81%) were not receiving isoniazid preventive therapy (IPT). Regarding nutritional status, 19.76%, 19.29%, and 20.48% of HIV-infected children were severely underweight, wasted and stunted, respectively. One-third (33.57%) of HIV-infected children had a history of ART regimen changes. Two hundred (47.62%) HIV-positive children had opportunistic infections (OIs) during the follow-up period (Table 2).

In this study, there was a significant difference in residence ($P=0.005$), CD4 + T cells ($P=0.044$), ART adherence ($P<0.001$), CPT ($P=0.006$), Hgb ($P=0.005$), and WHO clinical stage ($P=0.001$) between LTFU and non-LTFU patients (Table 3).

### Survival characteristics after initiation of ART

The study participants were followed for a minimum of 3 months to a maximum of 48 months, which provided a total of 8813.5 person-months of observation (734.46 person-years of observation/PYO), and the median follow-up time was 19 months (IQR = 11–32). At the end of the follow-up period, 319 (75.95%) of the children were alive, 30 (7.14%) were lost to follow-up, 46 (10.95%) were

**Table 1** Baseline socio-demographic characteristics of HIV-infected under-five children receiving ART in West Amhara Comprehensive Specialized Referral Hospitals, Northwest Ethiopia, 2022

| Variables | Category of variables | Frequency | Percent (%) |
|---|---|---|---|
| Sex of the child | Male | 207 | 49.29 |
| | Female | 213 | 50.71 |
| Age of the child | < 12 months | 56 | 13.33 |
| | 12–59 months | 364 | 86.67 |
| Status of parents | Both alive | 324 | 77.14 |
| | mother alive but father dead | 33 | 7.86 |
| | Mother dead but father alive | 19 | 4.52 |
| | Both dead | 44 | 10.48 |
| Sex of caregiver | Male | 98 | 23.33 |
| | Female | 322 | 76.67 |
| Age of care giver in years | 18–30 | 190 | 38.10 |
| | 31–40 | 160 | 38.31 |
| | 41–50 | 46 | 10.95 |
| | > 50 | 24 | 5.71 |
| Residence | Urban | 279 | 66.43 |
| | Rural | 141 | 33.57 |
| Relationship of caregiver for the child | Parent | 354 | 84.29 |
| | Sister/brother | 10 | 2.38 |
| | Uncle/aunt | 22 | 5.24 |
| | Grandparent | 23 | 5.48 |
| | Others | 11 | 2.62 |

**Table 2** Baseline and follow-up clinical, immunological, laboratory, and treatment-related characteristics of HIV-infected under-five children receiving ART in West Amhara Comprehensive Specialized Referral Hospitals, Northwest Ethiopia, 2022

| Variables | Category of variables | Frequency | Percent (%) |
|---|---|---|---|
| Opportunistic infection | Yes | 265 | 63.10 |
| | No | 155 | 36.90 |
| Developmental status | Appropriate | 362 | 86.19 |
| | Delayed | 48 | 11.43 |
| | Regressed | 10 | 2.38 |
| WHO clinical stage | Mild( stage I &II) | 220 | 53.38 |
| | Sever (stage III &IV) | 200 | 47.62 |
| Past TB test | Not determined | 206 | 49.05 |
| | Positive | 24 | 5.71 |
| | Negative | 190 | 45.24 |
| CD4 count or percent | Below the threshold | 234 | 55.71 |
| | Above the threshold | 186 | 44.29 |
| Hemoglobin level | Anemic(< 10 g/dl) | 47 | 11.19 |
| | Non-anemic (≥ 10 g/dl) | 373 | 88.81 |
| ART eligibility criteria | Immunologic/CD4 | 44 | 10.50 |
| | WHO stage | 81 | 19.33 |
| | Both WHO& Immunologic | 180 | 42.96 |
| | No criteria/Test and start | 114 | 27.21 |
| Treatment failure | Yes | 84 | 20 |
| | No | 336 | 80 |
| ART adherence | Good | 322 | 76.67 |
| | Fair | 57 | 13.57 |
| | Poor | 41 | 9.76 |
| Regimen change | Yes | 141 | 33.57 |
| | No | 279 | 66.43 |
| CPT | Given | 372 | 88.57 |
| | Not Given | 48 | 11.43 |
| IPT | Given | 194 | 46.19 |
| | Not Given | 226 | 53.81 |
| Underweight | Normal | 252 | 60.00 |
| | Moderate (WAZ < − 2) | 85 | 20.24 |
| | Severe (WAZ < − 3) | 83 | 19.76 |
| Stunting | Normal | 276 | 65.71 |
| | Moderate (HAZ < − 2) | 58 | 13.81 |
| | Severe (HAZ < − 3) | 86 | 20.48 |
| Wasting | Normal | 268 | 63.81 |
| | Moderate (WHZ < − 2) | 71 | 16.90 |
| | Severe (WHZ < − 3) | 81 | 19.29 |

*OI* Opportunistic infections, *ART* Antiretroviral therapy, *Hgb* Hemoglobin, *CPT* Cotrimoxazole Preventive Therapy, *INH* Isoniazid, *CD4* Cluster of Differentiation 4, *WAZ* Weight for Age Z-score, *WHZ* Weight for Height Z-score, *HAZ* Height for Age Z-score, *WHO* World Health Organization

transferred to other health facilities, and 25 (5.95%) died due to HIV/AIDS (Fig. 2).

The incidence rate of LTFU was 3.4 per 1000 person-months of observation (95% CI: 2.43–4.87) during the follow-up period. The median time to LTFU was 14 months (IQR = 11–20). Based on the actuarial life table, the estimated survival probability of under-five children on ART after the last month of follow-up was 77.1% (95% CI: 59.5–87.8). The survival probabilities of children after 12, 24, and 36 months were 0.97, 0.92, and 0.88, respectively (Table 4).

The overall Kaplan–Meier survival function estimate showed that most LTFU occurred in the first two years after ART initiation. Among the total 30 LTFUs, 10 (33.33%) and 12 (40%) occurred in the first and second years of ART initiation, respectively, and then declined steadily throughout the follow-up period (Fig. 3).

### Log rank test for the equality of survival function

The log-rank test ($x^2$) of the equality of hazard and mean survival duration was performed for the different categories of explanatory variables (Table 5).

The test results indicated that there was a statistically significant difference in survival experience among the categories of variables, such as place of residence, drug adherence, CPT, INH prophylaxis, and WHO clinical stages, respectively (Figs. 4, 5, 6, 7 and 8).

### Predictors of HIV-infected under-five children who were loss to follow-up

In the bi-variable Cox proportional regression analysis, age of the child, age of caregiver, sex of the child, sex of caregiver, status of parents, residence, OI at baseline, CD4 count or percentage, underweight, wasting, stunting, ART adherence, CPT, INH prophylaxis, OI during the follow-up period, baseline hemoglobin (Hgb) level, and baseline WHO clinical stage were found to have P-values < 0.25. These variables were candidate variables for multivariable Cox proportional hazard analysis. According to the final multivariable Cox proportional regression analysis, residence, ART adherence, CPT, INH prophylaxis, and WHO clinical stage were found to be predictors of LTFU at the 5% level of significance. The risk of LTFU among HIV-positive under-five children who lived in rural areas was 3.6 times greater (AHR = 3.64; 95% CI: 1.41, 9.37) than that among those who lived in urban areas. The risk of LTFU among under-five children with poor adherence to ART medication was 4.4-fold greater than that among those with good adherence (AHR = 4.37; 95% CI: 1.59, 12.02). Moreover, the risk of LTFU among HIV-infected under-five children who had never taken CPT was 3.8 times greater (AHR = 3.75; 95% CI: 1.39, 10.08) than that among those children

**Table 3** Chi-square test for patient characteristics who initiated ART in West Amhara comprehensive specialized referral hospitals, Northwest Ethiopia, 2022

| Variables | Categories | LTFU (%) | Censored (%) | $X^2$ value (df) | *P*-value |
|---|---|---|---|---|---|
| Age of the child | < 12 months | 6(20) | 50(12.82) | 1.2426 (1) | 0.265 |
| | 12 -59 months | 24(80) | 340(87.18) | | |
| Age of caregiver | 18–30 years | 12(40) | 178(45.64) | 2.3899 (3) | 0.496 |
| | 31–40 years | 10(33.33) | 150(38.46) | | |
| | 41–50 years | 5(16.67) | 41(10.51) | | |
| | > 50 years | 3(10) | 21(5.38) | | |
| Sex of the child | Male | 11(36.67) | 196(50.26) | 2.0583 (1) | 0.151 |
| | Female | 19(63.33) | 194(49.74) | | |
| Sex of caregiver | Male | 10(33.33) | 88(22.56) | 1.8060 (1) | 0.179 |
| | Female | 20(66.67) | 302(77.44) | | |
| Status of parents | Both alive | 20(66.67) | 304(77.95) | 3.0419(3) | 0.385 |
| | mother alive but father dead | 3(10) | 30(7.69) | | |
| | Mother dead, but father alive | 3(10) | 16(4.10) | | |
| | Both dead | 4(13.33) | 40(10.26) | | |
| Residence | Urban | 13(43.33) | 266(68.21) | 7.7273 (1) | 0.005 |
| | Rural | 17(56.67) | 124(31.79) | | |
| OI at baseline | Yes | 23(76.67) | 242(62.05) | 2.5555 (1) | 0.110 |
| | No | 7(23.33) | 148(37.95) | | |
| CD4 count | Above the threshold | 8(26.67) | 178(45.64) | 4.0648 (1) | 0.044 |
| | Below the threshold | 22(73.33) | 212(54.36) | | |
| ART adherence status | Good | 14(46.67) | 308(78.97) | 23.1648 | < 0.001 |
| | Fair | 6(20) | 51(13.08) | | |
| | Poor | 10(33.33) | 31(7.95) | | |
| Underweight | Normal | 15(50) | 237(60.77) | 2.2530 (2) | 0.324 |
| | Moderate(WAZ < − 2) | 6(20) | 79(20.26) | | |
| | Severe (WAZ < − 3) | 9(30) | 74(18.97) | | |
| Wasting | Normal | 17(56.67) | 251(64.36) | 0.7159 (2) | 0.699 |
| | Moderate(WHZ < − 2) | 6(20) | 65(16.67) | | |
| | Severe (WHZ < − 3) | 7(23.33) | 74(18.97) | | |
| Stunting | Normal | 13(43.33) | 262(67.18) | 5.2885 (2) | 0.071 |
| | Moderate(HAZ < − 2) | 7(23.33) | 52(13.33) | | |
| | Severe (HAZ < − 3) | 10(33.33) | 76(19.49) | | |
| CPT | Yes | 22(73.33) | 350(89.74) | 7.4111(1) | 0.006 |
| | No | 8(26.67) | 40(10.26) | | |
| INH prophylaxis | Yes | 10(33.33) | 184(47.17) | 2.1487(1) | 0.143 |
| | No | 20(66.67) | 206(52.82) | | |
| OI's during follow-up | Yes | 23(76.67) | 225(57.69) | 2.5555(1) | 0.110 |
| | No | 7(23.33) | 165(42.31) | | |
| Baseline Hgb | Anemic(< 10 g/dl) | 8(26.67) | 39(10) | 7.7862 (1) | 0.005 |
| | Nonanemic(≥ 10 g/dl) | 22(73.33) | 351(90) | | |
| WHO clinical stages | Mild (stage I & II) | 6(20) | 214(54.87) | 13.5810 (1) | < 0.001 |
| | Advanced (stage III&IV) | 24(80) | 176(45.13) | | |

*LTFU*: Loss to follow-up; *ART*: Antiretroviral therapy, $X^2$ chi-square; *df* degree of freedom, *OI* Opportunistic infections, *Hgb* Hemoglobin, *CPT* Cotrimoxazole Preventive Therapy, *INH* Isoniazid, *CD4* Cluster of Differentiation 4, *WAZ* Weight for Age Z-score, *WHZ* Weight for Height Z-score, *HAZ* Height for Age Z-score, *WHO* World Health Organization

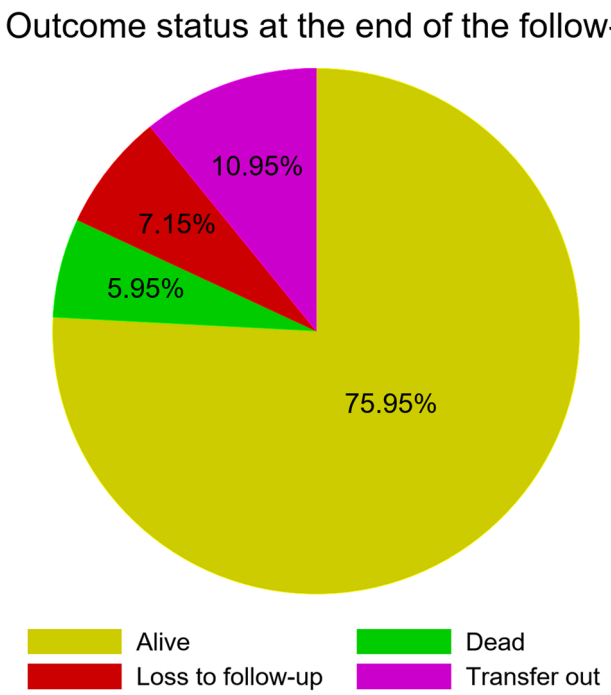



**Fig. 2** Overall outcome status of HIV-infected under-five children receiving ART, Northwest Ethiopia, 2022

**Table 4** The cumulative survival probability among HIV-infected under-five children receiving ART in West Amhara Comprehensive Specialized Referral Hospitals, Northwest Ethiopia, 2022

| Interval | | Big total | Deaths | lost | Survival | std. error | [95% conf. int.] | |
|---|---|---|---|---|---|---|---|---|
| 0 | 6 | 420 | 1 | 18 | 0.9976 | 0.0024 | 0.9829 | 0.9997 |
| 6 | 12 | 401 | 9 | 125 | 0.9710 | 0.0090 | 0.9468 | 0.9843 |
| 12 | 18 | 267 | 8 | 45 | 0.9393 | 0.0141 | 0.9047 | 0.9616 |
| 18 | 24 | 214 | 4 | 56 | 0.9191 | 0.0170 | 0.8783 | 0.9466 |
| 24 | 30 | 154 | 2 | 29 | 0.9059 | 0.0192 | 0.8604 | 0.9371 |
| 30 | 36 | 123 | 3 | 61 | 0.8765 | 0.0249 | 0.8177 | 0.9173 |
| 36 | 42 | 59 | 2 | 33 | 0.8353 | 0.0371 | 0.7468 | 0.8949 |
| 42 | 48 | 24 | 1 | 22 | 0.7710 | 0.0706 | 0.5954 | 0.8777 |
| 48 | 54 | 1 | 0 | 1 | 0.7710 | 0.0706 | 0.5954 | 0.8777 |

who had ever taken CPT. Furthermore, the hazard of LTFU in under-five children without INH prophylaxis was 3.4 times greater (AHR = 3.4; 95% CI: 1.29, 9.01) than that in children with INH prophylaxis. Finally, 5.4 times (AHR = 5.43, 95% CI: 1.38, 11.43) more likely to have LTFU in severe WHO clinical stages (stage III and IV) than in mild WHO clinical stages (stages I and II) (Table 6).

The Cox-Snell residual plot was used to assess the Cox proportional hazard regression model's goodness of fit. Based on the Cox-Snell residuals plot, the Nelson-Aelon hazard line had almost a 45-degree alignment with the reference line (Cox-Snell residual), indicating that the model was well fitted (Supplementary Fig. 1).

## Discussion

This institution-based retrospective follow-up study was conducted in comprehensive specialized referral hospitals in West Amhara, Northwest Ethiopia, to assess LTFU and its predictors among HIV-infected under-five children after ART initiation. In this study, the overall incidence rate of LTFU was 3.4 per 1000 person-months of observation (95% CI: 2.43–4.87) during the follow-up period. Our finding was in line with studies performed

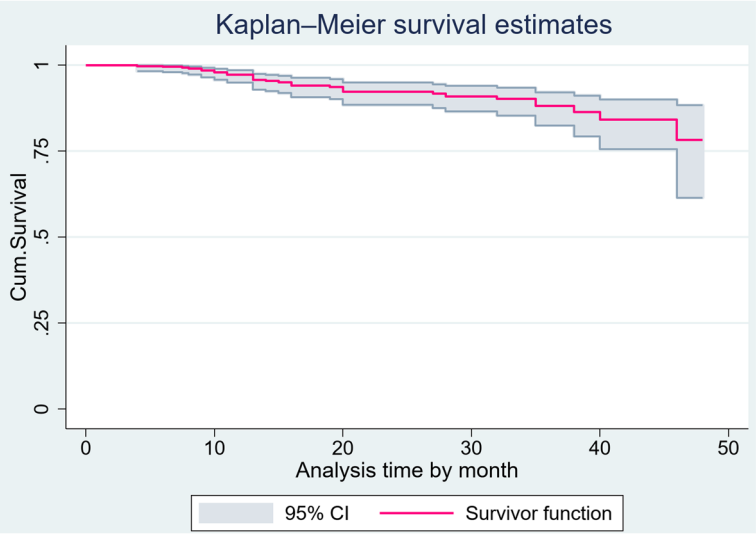



**Fig. 3** Kaplan–Meier survival curve of LTFU-free estimate among HIV-infected under-five children receiving ART, Northwest Ethiopia, 2022

in Ethiopia (3.3 per 100 child years) [6], Myanmar (4.7 per 100 child years) [11], and Asia and Africa (4.1 per 100 child years) [12]. However, this finding was lower than that reported in studies conducted at Dessie Referral Hospital, Northeast Ethiopia [15], Tanzania [31] and South Africa [13, 14]. The variations might be due to differences in the clinical characteristics of the study participants and study settings, as our study included four comprehensive specialized referral hospitals. The above disparity could be attributable to differences in ART enrollment periods, as a prior study in Tanzania and South Africa looked at children who started ART earlier (before 2012) and had different treatment eligibility criteria. Based on evidence that early ART initiation lowers HIV-related complications and LTFU in children, the WHO has advised starting ART at a younger age for pediatric patients starting in 2013, irrespective of their clinical or immunologic status [32]. The discrepancy might also be due to socioeconomic and cultural differences, such as differences in study time, because governments may have devised intervention strategies to alleviate the problem and develop health care policies. In addition, in Tanzania, the study included both pre-ART-initiated and post-ART-initiated children.

HIV-infected children from rural areas were at greater risk of LTFU than were their urban counterparts. Living in a rural area increased the risk of LTFU by 3.6 times more than living in an urban area. This finding is in line with other previous studies conducted in Ethiopia [7, 17, 33], Malawi [9] and Asia and Africa [12]. The possible reason could be that children living in rural areas travel long distances to obtain access to ART. Studies suggest that patients who live far from a medical center are more likely to experience LTFU [34, 35]. Children living in rural areas could have difficulties accessing favorable transportation; as a result, they could miss their appointments. Additionally, caregivers may forget to bring their children to the ART clinic at each visit. Furthermore, as most rural mothers lack formal education, the caregiver's educational background has a big impact on LTFU. Hence, individuals frequently turn to traditional treatments or faith-based therapy since they lack education [36]. Moreover, children from rural areas were more likely to experience LTFU. This could be due to factors such as a longer commute to a treatment facility, a lack of accessible transportation, and a lack of caregivers to accompany them to the clinic. As such, it is important to ensure that children from these areas have access to high-quality ART care services at nearby clinics. Our findings highlight the need to provide extra care, specialized clinical treatment, counseling, and support to children who travel long distances in their near-by residency.

This study also indicated that children who had poor ART drug adherence were at greater risk of LTFU than were those who had good adherence. Individuals with poor adherence had a 4.4-fold greater risk of receiving LTFU than those with good adherence. This is because poor adherence increases viral load duplication and decreases drug effectiveness, thus further suppressing the immune system and increasing opportunistic infection and disease progression [37]. The relationship between ART drug adherence and LTFU is well understood to be bidirectional. The common reasons for poor ART adherence among people living with HIV were the use of traditional or herbal medicine, dissatisfaction with healthcare services, depression, discrimination and

**Table 5** Mean survival duration stratified by categorical variables among HIV-infected under-five children receiving ART in West Amhara Comprehensive Specialized Referral Hospitals, Northwest Ethiopia, 2022

| Variables | Categories | Mean survival duration Months(95% CI) | Long rank $x^2$ -value | *P*-value |
|---|---|---|---|---|
| Age of the child | < 12 months | 41.83(37.03, 46.35) | 2.49 | 0.114 |
| | 12 -59 months | 43.79(42.56, 45.02) | | |
| Age of caregiver | 18–30 years | 44.91(43.24, 46.58) | 11.05 | 0.011 |
| | 31–40 years | 43.92(42.09, 45.75) | | |
| | 41–50 years | 35.27(32.21, 38.33) | | |
| | > 50 years | 29.29(23.19, 35.39) | | |
| Sex of the child | Male | 44.94(43.21, 46.67) | 1.50 | 0.220 |
| | Female | 42.89 (41.14, 44.64) | | |
| Sex of caregiver | Male | 36.82(34.44, 39.19) | 3.35 | 0.067 |
| | Female | 44.83(43.54, 46.17) | | |
| Status of parents | Both alive | 45.02(43.78, 46.27) | 6.55 | 0.088 |
| | mother alive but father dead | 42.13(37.25, 46.99) | | |
| | Mother dead, but father alive | 37.88(34.22, 41.54) | | |
| | Both dead | 33.49(28.60, 38.38) | | |
| Residence | Urban | 45.72(44.51, 46.92) | 13.37 | < 0.001 |
| | Rural | 38.334(35.21, 41.46) | | |
| OI at baseline | Yes | 42.63(40.96, 44.30) | 2.65 | 0.104 |
| | No | 45.69(44.03, 47.36) | | |
| CD4 count | Above the threshold | 45.69(44.12, 47.25) | 2.82 | 0.093 |
| | Below the threshold | 42.56(40.82, 44.29) | | |
| ART adherence status | Good | 45.48(44.19, 46.76) | 21.96 | < 0.001 |
| | Fair | 42.13(38.58, 45.69) | | |
| | Poor | 35.48(29.57, 41.39) | | |
| Underweight | Normal | 44.59(42.96, 46.22) | 1.58 | 0.454 |
| | Moderate(WAZ < − 2) | 43.59(40.99, 46.19) | | |
| | Severe (WAZ < − 3) | 41.85(38.74, 44.96) | | |
| Wasting | Normal | 44.83(43.40, 46.26) | 2.19 | 0.335 |
| | Moderate(WHZ < − 2) | 42.88(39.81, 45.96) | | |
| | Severe (WHZ < − 3) | 41.73(38.09, 45.38) | | |
| Stunting | Normal | 44.98(43.44 46.51) | 2.22 | 0.330 |
| | Moderate(HAZ < − 2) | 42.24(38.7 45.77) | | |
| | Severe (HAZ < − 3) | 42.21(39.47, 44.96) | | |
| CPT | Yes | 45.07(43.90, 46.25) | 26.74 | < 0.001 |
| | No | 30.38(25.69, 35.07) | | |
| INH prophylaxis | Yes | 45.75(44.41, 47.09) | 9.80 | 0.002 |
| | No | 40.84(38.64, 43.04) | | |
| OI's during follow-up | Yes | 43.54(41.71, 45.36) | 1.38 | 0.240 |
| | No | 43.41(41.83, 44.99) | | |
| Baseline Hgb | Anemic(< 10 g/dl) | 36.19(31.47, 40.92) | 8.81 | 0.003 |
| | Nonanemic(≥ 10 g/dl) | 44.87(43.62, 46.12) | | |
| WHO clinical stages | Mild (stage I & II) | 46.62(45.53, 47.71) | 13.99 | < 0.001 |
| | Advanced (stage III&IV) | 41.10(38.96, 43.25) | | |

$x^2$ chi – value, *OI* Opportunistic infections, *LTFU* Loss to follow-up, *ART* Antiretroviral therapy, *Hgb* Hemoglobin, *CPT* Cotrimoxazole Preventive Therapy, *INH* Isoniazid, *CD4* Cluster of Differentiation 4, *WAZ* Weight for Age Z-score, *WHZ* Weight for Height Z-score, *HAZ* Height for Age Z-score, *WHO* World Health Organization, *CI* confidence interval

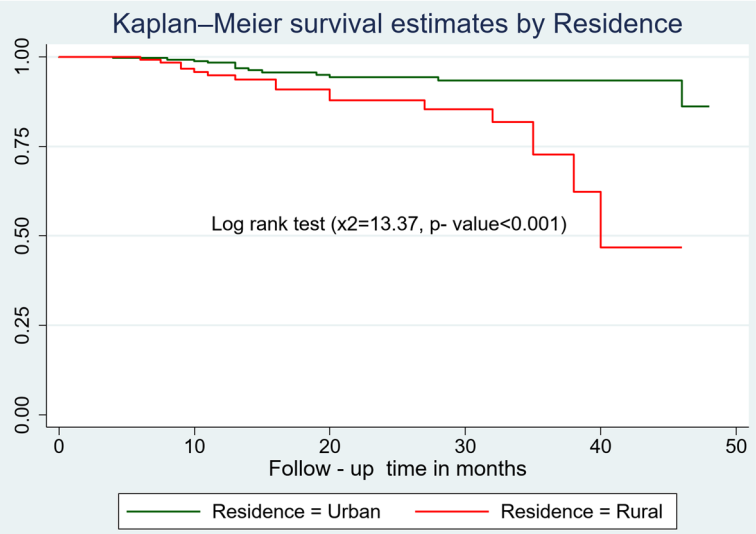



**Fig. 4** Kaplan–Meier survival curves to compare LTFU among HIV-infected under-five children receiving ART between urban and rural residences, Northwest Ethiopia, 2022

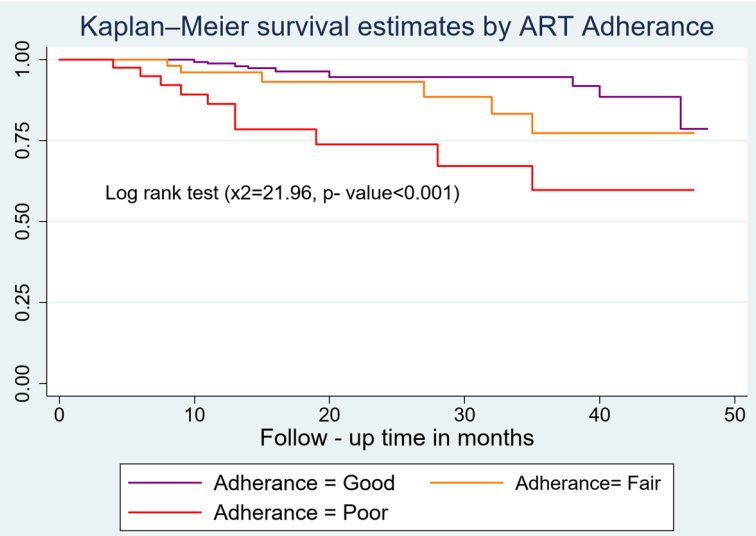



**Fig. 5** Kaplan–Meier survival curves to compare LTFU among HIV-infected under-five children receiving ART between good, fair, and poor ART drug adherence, Northwest Ethiopia, 2022

stigmatization, and poor social support [38]. The adherence status of the child to medications throughout the follow-up period was an important predictor, in agreement with the majority of studies. This finding was in line with studies conducted at Dessie Referral Hospital, Northeast Ethiopia, and Debre Markos Comprehensive Specialized Referral Hospital, Northwest Ethiopia [7, 15]. A possible explanation could be that treatment failure due to HIV viral resistance is caused by noncompliance with drug regimens. Furthermore, because children rely on their caregiver for care, caregivers may experience feelings of pessimism, carelessness, and loss as a result of the therapy cascade if the child shows no change [15]. Moreover, the strong relationship between adherence and LTFU may be involved. The elements that could lead to inadequate adherence will indirectly cause people to stop attending their routine check-ups. The main causes of poor adherence, according to the results of a qualitative study performed in Uganda, were poverty, the existence of drug side effects, depression, inadequate peer support and counseling, and stigma and discrimination; these variables may indirectly lead to a greater incidence

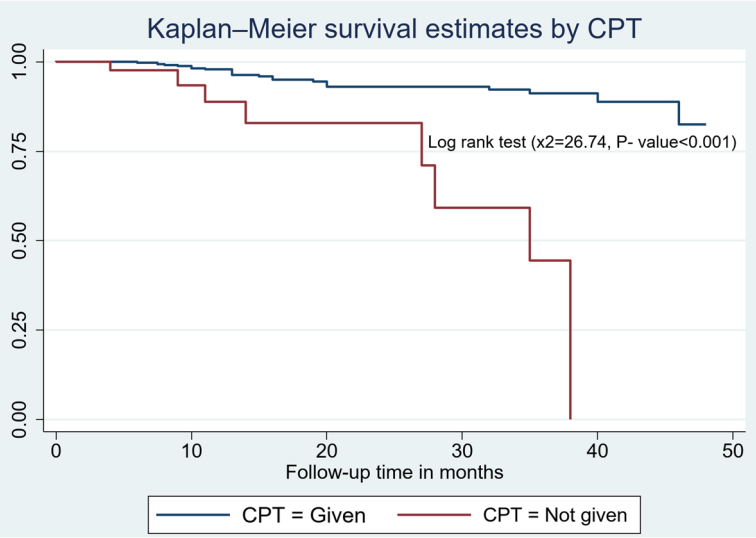



**Fig. 6** Kaplan–Meier survival curves to compare LTFU among HIV-infected under-five children receiving ART between CPT users and non-users, Northwest Ethiopia, 2022

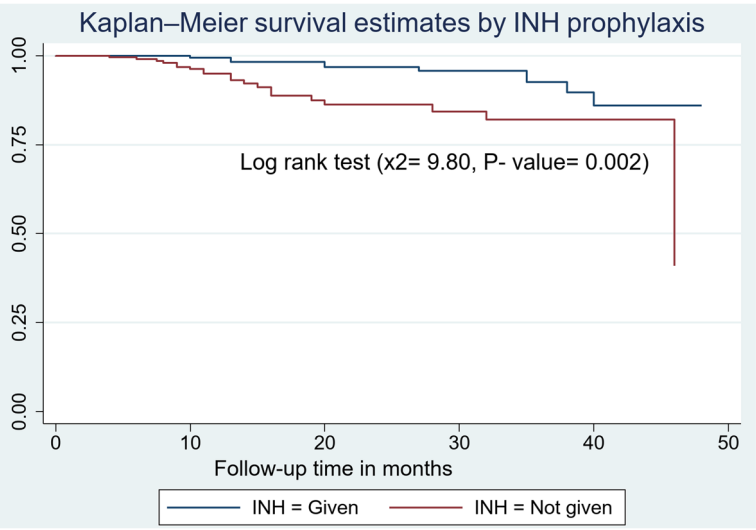



**Fig. 7** Kaplan–Meier survival curves to compare LTFU among HIV-infected under-five children receiving ART between INH prophylaxis takers and non-takers, Northwest Ethiopia, 2022

of LTFU [39]. Furthermore, fear of adverse reactions to ART is another common cause of LTFU.

Children who did not receive CPT had an almost four-fold greater risk of LTFU than children who received CPT. Ethiopian reports have shown comparable outcomes [40, 41]. CPT can reduce or prevent the occurrence of OIs and other complications. A study carried out in Ethiopia suggested that it is crucial to increase children's immune systems to reduce viral replication, which increases their survival rate by preventing and treating OIs [26]. Since CPT prophylaxis is a simple and effective means to decrease the rate of LTFU use in ART services, improve quality of life, lower morbidity and mortality, and reduce OIs, it has been suggested to benefit HIV/AIDS-infected patients [42].

The INH prophylaxis status of children under the age of five was one of the significant determinants of LTFU. Children with no history of INH prophylaxis were at increased risk with LTFU. This finding was consistent with findings in a study performed in Ethiopia [43, 44]. Since INH prophylaxis therapy controls one of the most common life-threatening comorbidity and mortality

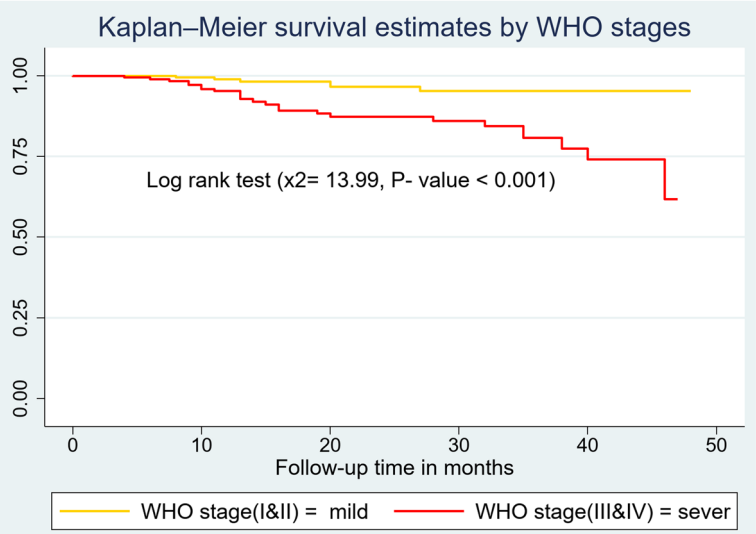



**Fig. 8** Kaplan–Meier survival curves to compare LTFU among HIV-infected under-five children receiving ART between mild and severe WHO clinical stages, Northwest Ethiopia, 2022

threats (i.e., tuberculosis co-infection among HIV-positive individuals), it may have a direct impact on reducing LTFU by strengthening the retention of HIV patients on ART services [45]. This existing intervention to improve the health of patients may encourage patients' retention of ART care. The higher rate of LTFU in these under-five children who did not receive INH prophylaxis during ART enrollment may also be related to the presence of several OIs, including recurring diarrheal illnesses, toxoplasmosis, tuberculosis, and pneumocystis pneumonia. INH prophylaxis could not be given if the child had any OIs.

Additionally, this study revealed that children who had a baseline advanced WHO clinical stage (III and IV) had a nearly fivefold greater risk of developing LTFU than did children who had mild WHO clinical stages (stages I and II). Similar findings have been reported in Ethiopia [40, 46], Sub-Saharan Africa, a systematic review in resource-limited settings, and Myanmar [47, 48]. One explanation for this could be that children who start ART at an advanced stage are more likely to develop OIs, which increases the risk of morbidity and mortality. In addition, children in advanced stages may experience adverse drug reactions, particularly during the first six months, which could further complicate the course of the illness [49]. The other possible explanation might be advanced WHO clinical staging, which can weaken immunity and lead to severe sickness as a result of viral replication, CD4 count depletion, and the rising prevalence of chronic illnesses, which makes treatment outcomes even more challenging. On the other hand, the results of this study were inconsistent with those of studies conducted in Kenya [50], Mozambique [51] and South Africa [52]. This may be explained by the fact that caregivers believe that children with early-stage HIV are not sick and therefore do not adhere to clinic appointments [50]. The other possible explanation might be that patients with stages I and II disease do not feel sick enough to accept restrictive medical care [53]. Furthermore, children in the mild stage of the disease in South Africa lacked symptoms, and health care professionals did not give them any more attention than those with more advanced disease [52].

### Implications of the study

This study will be important for policymakers, clinicians and subsequent researchers to reduce HIV-related morbidity and mortality associated with LTFU and to achieve the ambitious plan by the year 2030 of ending the HIV pandemic. The high level of LTFU underscores the necessity for focused efforts to develop and implement comprehensive interventions, including patient-centered services, social support, home visits, and community assistance aimed at attaining viral suppression. Moreover, our finding could have major policy implications because it implies that by boosting adherence counseling and diminishing drug resistance, Ethiopia could ameliorate the impact of HIV-related morbidity and mortality among children associated with LTFU.

### Limitations of the study

Due to the secondary nature of the data, this study did not include variables such as viral load, income, and the

**Table 6** Predictors of LTFU among HIV-positive under-five children receiving ART in West Amhara Comprehensive Specialized Referral Hospitals, Northwest Ethiopia, 2022

| Variables | Category of variables | Outcome status | | CHR [95% CI] | AHR[95% CI] | *P*-value |
|---|---|---|---|---|---|---|
| | | LTFU | Censored | | | |
| Age of the child | < 12 months | 6 | 50 | 2.03(0.83, 4.96) | 1.54(0.44, 5.39) | 0.501 |
| | 12 -59 months | 24 | 340 | 1 | 1 | |
| Age of caregiver | 18–30 years | 12 | 178 | 1 | 1 | |
| | 31–40 years | 10 | 150 | 0.91(0.39, 0.23) | 0.41(0.13, 1.24) | 0.113 |
| | 41–50 years | 5 | 41 | 2.4(0.84, 6.86) | 1.10(0.27, 4.47) | 0.891 |
| | > 50 years | 3 | 21 | 5.38(1.47,19.69)* | 0.82(0.13, 5.04) | 0.826 |
| Sex of the child | Male | 11 | 196 | 1 | | |
| | Female | 19 | 194 | 1.58(0.75, 3.33) | 1.86(0.77, 4.51) | 0.167 |
| Sex of caregiver | Male | 10 | 88 | 1 | | |
| | Female | 20 | 302 | 0.49(0.23, 1.07) | 0.50(0.18, 1.36) | 0.174 |
| Status of parents | Both alive | 20 | 304 | 1 | 1 | |
| | mother alive but father dead | 3 | 30 | 1.56(0.46, 5.26) | 1.18(0.26, 5.46) | 0.832 |
| | Mother dead, but father alive | 3 | 16 | 3.0(0.89, 10.14) | 0.74(0.15, 3.56) | 0.706 |
| | Both dead | 4 | 40 | 2.9(0.98, 8.6) | 1.04(0.26, 4.09) | 0.995 |
| Residence | Urban | 13 | 266 | 1 | 1 | |
| | Rural | 17 | 124 | 3.63(1.73, 7.59)* | **3.64(1.41, 9.37)** | **0.007**** |
| OI at baseline | Yes | 23 | 242 | 0.50 (0.22, 1.17) | 0.42(0.11, 1.64) | 0.212 |
| | No | 7 | 148 | 1 | 1 | |
| CD4 count | Above the threshold | 8 | 178 | 1 | 1 | |
| | Below the threshold | 22 | 212 | 1.97(0.88, 4.44) | 1.09(0.43, 2.77) | 0.849 |
| ART adherence status | Good | 14 | 308 | 1 | 1 | |
| | Fair | 6 | 51 | 2.38(0.91, 6.18) | 2.12(0.71, 6.37) | 0.179 |
| | Poor | 10 | 31 | 5.83(2.57, 13.26)* | **4.37(1.59,12.02)** | **0.004**** |
| Underweight | Normal | 15 | 237 | 1 | 1 | |
| | Moderate(WAZ < − 2) | 6 | 79 | 1.1(0.43, 2.84) | 1.72(0.48, 6.19) | 0.403 |
| | Severe (WAZ < − 3) | 9 | 74 | 2.85(0.73, 3.84) | 1.58(0.43, 5.78) | 0.494 |
| Wasting | Normal | 17 | 251 | 1 | 1 | |
| | Moderate(WHZ < − 2) | 6 | 65 | 1.35(0.53, 3.44) | 0.51(0.15, 1.75) | 0.282 |
| | Severe (WHZ < − 3) | 7 | 74 | 1.91(0.79, 4.63) | 0.72(0.21, 2.43) | 0.607 |
| Stunting | Normal | 13 | 262 | 1 | 1 | |
| | Moderate(HAZ < − 2) | 7 | 52 | 1.78(0.68, 4.63) | 1.36(0.42, 4.43) | 0.606 |
| | Severe (HAZ < − 3) | 10 | 76 | 1.68(0.74, 3.80) | 0.88(0.29, 2.59) | 0.813 |
| CPT | Yes | 22 | 350 | 1 | 1 | |
| | No | 8 | 40 | 6.6(2.89, 15.07)* | **3.75(1.39,10.08)** | **0.009**** |
| INH prophylaxis | Yes | 10 | 184 | 1 | 1 | |
| | No | 20 | 206 | 3.21(1.49, 6.94)* | **3.40(1.29, 9.01)** | **0.014**** |
| OI's during follow-up | Yes | 23 | 225 | 0.63(0.29, 1.37) | 0.42(0.11, 1.64) | 0.212 |
| | No | 7 | 165 | 1 | 1 | |
| Baseline Hgb | Anemic(< 10 g/dl) | 8 | 39 | 3.21(1.42, 7.25)* | 1.40(0.54, 3.67) | 0.488 |
| | Nonanemic(≥ 10 g/dl) | 22 | 351 | 1 | 1 | |
| WHO Clinical Stages | Mild (stage I & II) | 6 | 214 | 1 | 1 | |
| | Advanced (stage III&IV) | 24 | 176 | 4.67(1.91,11.50)* | **5.43(1.38,11.43)** | **0.016**** |

*OI* Opportunistic infections, *LTFU* Loss to follow-up, *ART* Antiretroviral therapy, *Hgb* Hemoglobin, *CPT* Cotrimoxazole Preventive Therapy, *INH* Isoniazid, *CD4* Cluster of Differentiation 4, *WAZ* Weight for Age Z-score, *WHZ* Weight for Height Z-score, *HAZ* Height for Age Z-score, *WHO* World Health Organization, *CI* confidence interval

1- Reference category

* Statistically significant at bi-variable with 5% level of significance

** Statistically significant at multivariable with 5% level of significance

children's vaccination status, micronutrient deficit, and the caregiver's educational status. This study was also unable to ascertain the reasons for and outcomes of LTFU due to incomplete documentation. Additionally, because children with ART follow-ups less than three months were not included in the study, the risk of early LTFU may have been underestimated.

## Conclusion and recommendations

The incidence rate of LTFU was high, especially in the first two years after ART initiation. The risk of LTFU increased if the child's residence was in a rural area, had poor ART adherence, presented with WHO clinical stages III and IV, and lacked CPT and INH prophylaxis. Therefore, particular emphasis and close follow-up should be given within the first two years of ART initiation. Moreover, special consideration and close monitoring of the higher-risk groups for LTFU highlighted in this study could decrease the rate of LTFU. Furthermore, tracing mechanisms should be strengthened for children from rural areas. Researchers should conduct qualitative studies to explore the influencing factors of LTFU who travel long distances from rural areas. Additionally, providing participatory advice and allowing patients to decide rather than enforcing them to start ART immediately after HIV confirmation and strengthening collaborative work with adherence counselors and frequent follow-up schedules are highly appreciated. Finally, further prospective follow-up studies should be performed by considering viral load, child immunization, and micronutrient deficiencies.

### Abbreviations

| | |
|---|---|
| AHR | Adjusted Hazard Ratio |
| AIDS | Acquired Immune Deficiency Syndrome |
| ART | Antiretroviral Therapy |
| CD4 | Cluster of Differentiation 4 |
| CI | Confidence Interval |
| CPT | Cotrimoxazole Preventive Therapy |
| HIV | Human Immunodeficiency Virus |
| INH | Iso Nicotinyl Hydrazide |
| IPT | Isoniazid Preventive Therapy |
| LTFU | Loss to Follow-Up |
| MTCT | Mother to Child Transmission |
| OIs | Opportunistic Infections |
| PYO | Person Years Observation |
| SSA | Sub-Saharan Africa |
| TB | Tuberculosis |
| WHO | World Health Organization |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-024-05086-2.

Supplementary Material 1.

Supplementary Material 2.

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### Authors' contributions

G.G., T.K., H.W., and B.M. were involved in conceptualization, methodology, execution, analysis, and interpretation. G.G, G.A., G.T., M.M., and M.A. participated in drafting and reviewing the article, writing the manuscript, and preparing all the components of the manuscript. All authors reviewed the final draft of the manuscript, gave final approval of the version to be published, agreed on the journal to which the article has been submitted.

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### Availability of data and materials

All study-related data are included in the manuscript or its supplemental material. The corresponding author can provide the data set utilized and analyzed for this work upon reasonable request.

## Declarations

### Ethics approval and consent to participate

The study was conducted in accordance with the 1964 Declaration of Helsinki and following amendments. An ethical clearance was obtained from Bahir Dar University's Institutional Review Board (IRB). Permission was obtained from each of the four hospital administrations of the four participating entities. As the data gathered were secondary (based on the patients' medical cards), informed consent from parents (legal guardians) was not needed. In addition, the study was waived by the IRB of Bahir Dar University. All collected data were coded and locked in a separate room, and computer data were secured by a personal password to maintain privacy. Finally, names and unique ART numbers were not included in the data collection format, and the data were not disclosed to anyone other than the principal investigator. Throughout the whole investigation, the information's confidentially was upheld.

### Consent to publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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## Publisher's Note