COLLEGE OF HEALTH SCIENCES

SCHOOL OF NURSING AND MIDWIFERY

INCIDENCE AND PREDICTORS OF ATTRITION AMONG CHILDREN ON ANTI-RETROVIRAL THERAPY AT GEDEO ZONE SELECTED PUBLIC HOSPITALS, SNNPR, 2020

BY: KIRUBEL BIMER

A RESEARCH THESIS SUBMITTEDTO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF NURSING AND MIDWIFERY, DEPARTMENT OF NURSING FOR PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF SCIENCE IN PEDIATRIC AND CHILD HEALTH NURSING.

SEPTEMBER, 2020

ADDIS ABEBA, ETHIOPIA

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Statement of declaration

By my signature below, I declare and affirm that this thesis is my own work. I have followed all ethical principles of research in the preparation, data collection, data analysis and compilation of this thesis. Any scholarly matter that is included in the thesis has been given recognition through citation.

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List of abbreviation and Acronyms

AHR	Adjusted Hazard Ratio
AIDS	Acquired Immune Deficiency Syndrome
ART	Anti-retroviral Therapy
ARV	Antiretroviral
BPH	Bule Primary Hospital
CD4	Cluster of differentiation 4 cells, type of T lymphocytes
CD4%	Percentage of Acluster of Differentiation 4 Cells
CI	Confidence Interval
CPT	Cotrimoxazole Prophylaxis Therapy
DRH	Dilla Referral Hospital
EFV	Efavirenz
EDHS	Ethiopian Demographic and Health Survey
HAART	Highly Active Antiretroviral Therapy
HFA	Height for Age
HIV	Human Immunodeficiency Virus
HR	Hazard Ratio
IRB	Institutional Review Board
LTFU	Lost to Follow up
OI	Opportunistic Infections
NVP	Nevirapine
PHC	Primary Health Center
PMO	Person Month Observation
PYO	Person Years Observation
SNNPR	South Nation Nationalities and People Region

TB	Tuberculosis
UNAIDS	United Nations Programs on HIV/AIDS
VIF	Variance Inflation Factor
WFA	Weight for Age
WHO	World Health Organization
YCH	Yirgachefe Primary Hospital

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Abstract

Background: Human immune deficiency virus (HIV) is one of the world's most serious public health challenges. However, the expanded access to antiretroviral therapy has led to an intense reduction in HIV related morbidity and mortality among children. Despite this remarkable achievement, the attrition of children from ART care has remain challenging.

Objective of the study: To assess the incidence and predictors of attrition among children on antiretroviral therapy in Gedeo zone public hospitals, Southern Ethiopia, 2020.

Method: Retrospective follows up study was employed among 254 systematicaly selected children <15 years who were receiving ART in Gedeo zone public hospitals. The total sample size was calculated using Epi Info version 7. Data were collected using data extraction tool. Data were cleaned and edited before analysis and then entered into epidata manager version 4.6 and exported to Stata version 14 for analysis. Data were described using Kaplan-Meier curve, log rank test, life table and crude hazard ratios. Predictors of attrition assessed using Cox proportional hazards model. Covariates with p-values (<0.25) in the bivariable analysis were included to multivariate analysis. Finally, a statistical significance was declared at p-value <0.05. Data were presented using tables, figures, and texts.

Results: The incidence rate of attrition was 11.3 per1000 person-months observation (95%CI: 9.20 -13.85) with a total of 8145.33 child-months observation. The median survival time was 68.73 months. Children with low hemoglobin levels (AHR = 3.5, 95% CI:1.6-7.4), low CD4 count (AHR=3.7, 95%CI:1.4- 9.7), delayed developmental stage (AHR=3.76, 95%CI:1.2-11), underweight (AHR=5, 95%CI:1.5-17.25) and poor/fair ART adherence levels (AHR=3.2, 95% CI:1.3-7.8) were at higher hazards of experiencing attrition.

Conclusion and recommendation: The incidence rate of attrition was 11.3 per1000 person-months observation. Low Hgb level (Hgb<10mg/dl), low CD4+count, underweight (WFAz < -2), delayed developmental stage and poor/fair ART adherence level were predictors of child attrition. So, early detection, close follow up, monitoring and management has to be strengthened particularly for patients with low CD4+ count, underweight and low haemoglobin level to reduce attrition from ART care. Improving adherence counseling and strengthen nurtritional support also crucial.

Keywords: ART, Children, HIV/ADIS, Attrition, Incidence, Ethiopia

1. Introduction

1.1. Background

Human immunodeficiency virus (HIV) is the virus that causes acquired immunodeficiency syndrome (AIDS). Human immunodeficiency virus (HIV) infection is the leading cause of morbidity and mortality throughout the world. According to the United Nations Programs on HIV/AIDS (UNAIDS) report by the end of 2018, 37.9 million people were living with human immune deficiency virus (PLHIV) globally. Of which 1.7 million were children less than 15 years with 64.7% residing in East and Southern Africa. In the same year, an estimated 160,000 children were newly infected with HIV and 770 000 people died from it. New HIV infections and death among children have declined by 41% and 33% respectively from 2010 to 2018. Of all 54 % of children living with HIV were having access to treatment in 2018 worldwide (1).

Due to this reason in 2014, the Joint United Nations Programs on HIV/AIDS (UNAIDS) outlined ambitious targets to end the HIV epidemic by ensuring that 90% of people living with HIV know their diagnosis, 90% of those diagnosed receive sustained antiretroviral therapy (ART), and 90% on ART achieve viral suppression by 2020. To achieve 90-90-90 targets for children, HIV-infected children must be identified, linked to care, initiated on ART, retained in care, and finally achieve sustained virologic suppression is needed. This target is focused not just on expanding access to diagnosis and treatment but also on the quality of care in terms of retention and suppression, which are key to optimal HIV outcomes(2–4).

According to the UNADS report in Ethiopia by 2018, 690 000 people were living with HIV, 23 000 people were newly infected with HIV and 11 000 people died from AIDS-related illnesses. Despite this between 2010 and 2018, the number of new HIV infections and AIDS related illnesses has been decreased by 79% and 55% respectively(5).

According to the Ethiopian Demographic and Health Survey 2016 (EDHS 2016), the national HIV prevalence was 0.9%. HIV prevalence varies from region to region ranging from less

than 0.1% in Ethiopia Somali to 4.8% in Gambella(6) The introduction of highly active antiretroviral treatment (HAART) improved the survival of children infected with the virus and contributed to preventing new infections(7). Antiretroviral therapy (ART) slows the disease progression by preventing virus replication and therefore decreasing the amount of virus in an infected person's blood called the 'viral load' (8).

According to 2016 World Health Organization (WHO) guidelines immediate treatment of people diagnosed with HIV, known as 'test and treat' or 'treat all' principle is recommended (9). Two third of infants and children infected with HIV could be reduced from mortality and HIV progression through early administration of ART. To achieve this early diagnosis of HIV infection, linking and retaining in care is crucial(10).

Retention of HIV-infected children in care is important for the prevention of HIV-related morbidity and mortality by early ART initiation, monitoring and treatment ofdisease progression and treatment failure, and provision of medications and supportive care(10). However, retention in care of children with HIV continues to be a major challenge requiring innovation and creativity. Studies inAsia and Africa have shown that it is challenging to enroll and retain pediatric patients on ART care(11,12). Attrition is defined as patients who are recorded as death or loss to follow up (LTFU)(13). Some causes of attrition are poor socio-economic and inadequate educational levels, living away from the ART facility; negative providers' attitudes, long waiting times, drug side effects and delayed defaulter tracing systems, and poor level of social and adherence support(14).

1.2. Statement of the problem

Human immune deficiency virus (HIV) is one of the world's most serious public health challenges. However, the expanded access to Antiretroviral therapy has led to an intense reduction in HIV related morbidity and mortality among children. Globally by the end of 2018, 160, 000 children living with HIV were having access to ART and AIDS-related deaths have been declined by 33% between 2010 and 2018. Despite this remarkableachievement, the attrition of children from ART care has remained challenging (1,15).

The accessibility and rapid scaling up of ART programsin resource constraint countries have enabled HIV-infected infants and children to survive and grow into adolescents and adults(16). To take full advantage of ART, improving the commitment of HIV testing and counseling, linking people to care, early ART initiation, supporting adherence and retention in care is needed(15). However, the attrition of children on ART care is higher in resource constraint settings when compared to developed countries (17,18).

Studies in different countries showed that there were a significant number of attrition children from ART care. A systematic review of studies conducted in Asia and Africa among children on ART revealed that 36-month of retention on ART was 74% and 66% respectively(19). A study conducted in India revealed that the cumulative incidence of attrition after ART initiation was 24.9% (CI=95%, 18.7–32.7) at 5 years(20). A study done on pediatric West African Database to evaluate AIDS showed that the incidence rate of attrition in children was 35.8/100 child-years, (CI =95%,25.9-26.4). Yielding a mortality rate of 9.6 /100 child-years and LTFU rate of 26.2/100 child-years(21). Another study done on children enrolled in Côte d'Ivoire's National ART Program showed that among 2110 children at ART initiation, 664 children were lost through attrition. Of which 237 children were died and 427 became LTFU. Much of the attrition 286(43%) occurred within 3 month of ART(11). Moreover, study conducted in Ethiopia among HIV-infected children initiating ART showed that the cumulative incidence of total attrition at 6, 12, and 24 months after ART initiation was 10.9%, 15.5% and 20.6%, respectively(22). So, retention in the care of children is crucial to improve adherence to ART, slow progression to AIDS, and increased survival. Being younger age, shorter duration of time on ART, severe immunosuppression, rural residence, baseline Hgb in g/dl<10g/dl, underweight, higher WHO clinical stages were some of the predictors of attrition

(11,13,23). Multiple factors may also contribute to attrition, including distance to health facilities, lack of transport, or inability to cover travel expenses, stigma and disclosure-related issues, and lack of understanding of the need for lifelong care. Patient attrition following an HIV diagnosis is a global challenge and causes avoidable morbidity and mortality, suboptimal treatment outcomes, increased cost of care, and preventable HIV transmission and drug resistance(10). Susceptibility of attrition from ART service is higher in children than adults because caregivers are responsible for their children to get access to health care services(10,24). In a study conducted in Sub-Saharan Africa, some interventions have been discussed that might help to prevent attrition on HIV care programs. These are ensuring uninterrupted drug supplies, consideration of simple, non-toxic ART regimens, decentralization of ART care, and a reduction in indirect costs for patients(25).

Based on the Strategic plan 2015-2020 in an Investment Case Approach Ministry of Health of Ethiopia developed a strategic framework for improving adherence and retention in care. The strategies articulated in the framework were considered as interventions that will be implemented during the investment case period to make the ART effective. These include nutrition support, strengthen family role in care and treatment, strengthening the tracing mechanism, and improving the availability of opportunistic infection(OI) drugs and management of OI(6). Moreover, retaining patients receiving ART in care are critical determinants of successful ART outcomes(15).

Even though attrition remains a critical challenge for HIV positive children in ART programs, little is known about the incidence and predictors of attrition in ART services in Ethiopia. On the other hand, a study conducted in incidence mortality or LTFU separately might be under or overestimation of the case. Therefore, LTFU and mortality was grouped as one in this study to solve this problem. Furthermore, as my review, there is no similar published study conducted in the study area. So, a better understanding of predictors of attrition can help to design interventions to reduce the incidence of attrition and improve the clinical outcome of patients who initiate ART. Therefore, this study determines the incidence and predictors of attrition among children initiating ART at the Gedeo zone selected public Hospitals.

1.3. Significance of the study

Early detection of HIV infection, linking and retaining children on antiretroviral therapy (ART) is essential for reducing AIDS-related morbidity, and improving survival. To do these determining the incidence and predictors of attrition are very important. Even though the rapid expansion of antiretroviral treatment (ART) is one of the most remarkable achievements in public health history, attrition remains a critical challenge for the quality of care and success of the ART program. Patient retention in ART care is crucial to improve ART adherence level, slow progression to AIDS, and improved survival. Therefore, identifying the predictors of attrition is valuable. The finding of this study

- Help as baseline information for further studies.
- Provide information on the current status of attrition, the time when most attrition occurs, and factors that contribute to attrition in ART care in the study area.
- Used to design an interventional project towards improving retention in care of children on ART service in the study area.
- Used to increase existing knowledge and skill of the health professional about attrition from ART care in the study area.
- The study also valuable for mother and child in reducing preventable morbidity and mortality results from attrition in ART care.

2. Literature review

2.1. Incidence of attrition among children on ART

Studies have been conducted in different countries to determine the incidence of attrition among HIV positive children on ART. Statistical Analysis study conducted in Thailand showed that the incidence rate of attrition was 5 per 100 PYO. Of which mortality rate was 2.1 (95% CI, 1.9-2.3) per 100 person-years and lost to follow-up rate was 2.9 (95% CI, 2.7-3.2) per 100 person-years(26). Another study done in Myanmar showed that the incidence rate of attrition was 3.89 per 100-person years of follow-up (95% CI: 3.48–4.34)(13).

A cohort study from the Asia Pacific region showed that the incidence rate of attrition was 6.5 per 1000 person-years. Of which the incidence rate was 4.6 per 100 child-years (95% CI, 4.1-5.2) and the mortality rate was 1.9 per 100 child-years (95% CI,1.6-2.4)(27). Another retrospective cohort study conducted in Uganda showed that the incidence of attrition was 14.4 per 100 person-years. Of which incidence of death and LFU were 1.8 and 12.6 per 100 person-years respectively(28). Another retrospective study conducted fromhealth facilities in Kenya, Lesotho, Mozambique, Rwanda, and Tanzania showed that the incidence of attrition at a primary health facility was 15 per 100PYS. Of which LTFU and mortality rates for children on ART were 9.8/100 PYs and 5.2/100 PYs, respectively and the incidence of attrition at secondary/tertiary health facilities was 26.2 per 100PYS, of which LTFU and mortality rate were 20.2/100 PYs and 6.0/100 PYs, respectively(29). Moreover, in study conducted in pediatric West African Database to evaluate AIDS revealed that a total of 461 children were experiencing attrition with an incidence rate of 26.2 per 100 child-years(21). Another retrospective cohort study performed from a DREAM Cohort in Sub-Saharan Africa on predictors of Adverse Outcomes in HIV-1–infected Children revealed that the attrition rate was 11.7 per 100 person-years (PYO) (30). A prospective cohort study done in Addis Ababa showed that the attrition rate was 8.3per 100 PYO (95%CI: 5.4± 12.1). Among these LTFU and mortality rate was 6.26 per100-PYO and 2.1per100PYO (95%CI: 0.8±4.3)(23).

2.2. Predictors of attrition

Several predictors can lead to attrition from ART services in children, which are documented in many kinds of literature. The main predictors were socio-demographic variables, clinical baselines, and treatment-related characteristics.

2.3. Socio-demographic variables

A retrospective cohort study conducted in Kenya, Mozambique, Rwanda, and Tanzania, from 2005- 2011 showed that the attrition rate was higher in less than one year of age(12). Another study from Democratic republic Congo, children younger than 2 years and caregivers' religion were independently associated with attrition(31–33). Age≥12 years at ART initiationwere at greatest risk of attrition(26). Studies from Zimbabwe and Mozambique showed that being male was more likely to have a higher risk of attrition with (AHR: 1.24, 95% CI: 1.08–1.43;p=0.004) and (AHR: 1.15, 95% CI: 1.0-1.3)(34,35)**.** Another prospective cohort study that conducted in Addis Ababa showed that child age below three years with (AHR=5.3), caregivers of the children who were coming from rural areas(AHR=3.97) and children of both biological parents alive and close biological relation of the caregiver compared to their counterparts were predictors of child's attrition(23). Another study done in Ethiopia revealed Children<1 year had a higher risk of attrition(22).

2.4. Clinical and Treatment-related characteristics

According to a studies conducted in Myanmar reported that underweight children (<-2 Z-score) (AHR=1.9, 95%CI =1.3–2.8), those with severe anemia (AHR= 2.7, 95%CI=1.5–4.9), severe immune deficiency and WHO stage III or IV at baseline were predictors of attrition. Moreover, patients with TB also had associated with attrition during the ART period and the attrition rates during the initial few months of initiation of ART were highest(13).

Another retrospective study done in Bali showed that the highest risk for LTFU/death was children having anemia, with (AHR=4.62; 95%CI:2.42-8.82) and also a child with malnutrition had a 2.57 higher (AHR=2.57; 95%CI: 1.41-4.67) chance of LTFU/ death compared to a child with normal/good nutrition(36). Findings also reported that children who initiated ART within three months of entry into care and shorter duration of time on ART were at higher risk of attrition(11,20). A systematic review conducted in resource-limited

settings reported that severe immunosuppression, malnutrition, and anemia were found to be independent predictors of attrition(11).

Another studies were done in children in Asia and Africa showed compared to children with earlier stages of clinical AIDS or stage-4 disease and CD4% ≥20, children with clinical AIDS or stage-4 disease and CD4% <10% had increased risk of attrition from ART care(33). A pediatric cohort study in Sub-Saharan Africa showed, baseline severe immunodeficiency, severe anaemia, and severe clinical status (WFA<-3 and WHO stage ≥3 were independently associated with attrition(37). Another study done in Kenya, Uganda and Malawi showed that severe clinical disease (WHO-stage 4), underweight, and moderate and severe immunosuppression compared to their counterparts were significantly associated with attrition(38). Additionally, in Uganda, children with mild immunosuppression (HR: 4.66, 95%CI: 1.21–17.98, p= 0.026), and weight-for-age z-scores of <−2SD (HR: 0.31, 95%CI:0.15–0.65, P = 0.002 were significantly associated with attrition(39). Another study done in Mozambique showed that children with anaemia were significantly associated with attrition. In contrast to this, cotrimoxazole user children within 90 days of ART initiation was associated with improved outcomes(40).

The pediatric West African Database to Evaluate AIDS, 2000-2008, advanced clinical stage, CD4 percentage <15% statically association with attrition(21). In Democratic Republic Congo study showed that attrition was higher in children with a CD4 cell count <200/mL (AHR: 2.70, 95% CI: 1.40–5.21) and those with a CD4 cell count between >200– <350/µL (AHR: 2.87, 95% CI: 1.36–6.07) than in those with CD4 count ≥ 350/µL(31).

Children who had WFA ($Z \leq -2$) , AHR= 2.36, 95% CI: 1.61, 3.44 for mortality and AHR= 1.36, 95% CI: 1.07, 1.72 for LTFU), and hemoglobin <8 g/dl (AHR= 1.42, 95% CI: 1.02, 1.97 for death) and (AHR=1.30: 95% CI:1.00, 1.68 for LTFU), were associated with increased risk of attrition in a study done in Côte d'Ivoire's(41). Another study done in Rwanda, children with severe malnutrition versus not malnourished (AHR = 3.2, 95% CI: 1.3– 8.1), advanced WHO stage versus WHO stage I (AHR stage II = 3.6, 95% CI: 1.3–9.6; AHR stage III = 2.6, 95% CI: 0.96–6.8; AHR stage IV = 9.8, 95% CI: 3.5–27.4; and severe immunosuppression versus no evidence of immunosuppression (AHR = 2.3, 95% CI: 1.7–

3.3)(32). Another retrospective review study conducted in Zimbabwe showed that, baseline WHO stage IV (AHR1.73; p = 0.012) as compared with WHO stages I/II and patients those who did not receive a cotrimoxazole prescription (AHR:1.94; p= .007) were significantly increased risk of attrition. Additionally CD4 cell count<50 (AHR: 1.36, p= 0.05) was more likely to experience attrition than those with CD4 cell count >200 in univariate analysis. However, no association were observed between CD4 cell count and attrition in the multivariable survival model(34).

A study done in Ethiopia revealed that children who had poor adherence to ART and children with severe malnutrition were more likely to experience a high risk of mortality (AHR=3.0, 95% CI: 1.2–7.5) and (AHR =2.5, 95% CI: 1.1 6.1) than their counterparts respectively(42). Another prospective cohort study conducted in Addis Ababa showed that, baseline Hemoglobin <10g/dl [AHR] =5.68 (95%CI: 2.03±6.23) and WHO stage III or IV (AHR=12.25, 95%CI: 1.26± 119.05 were significantly associated with child's attrition. Moreover, Children who initiated ART treatment with Zidovudine containing regimen, worsen existing anemia and were vulnerable further to opportunistic infections and end up with death(23). Another study conducted in Ethiopia also showed children with WHO stage IV disease (advanced disease) were also found to be a significant association with attrition(22).

2.5. Conceptual framework

The following conceptual framework shows association between independent variables with a dependent variable which was developed after reviewing different kinds of literature in the area of ART including the consolidated WHO guideline, the ART follow up tool and several journals and articles(11–13,20,23,31,33,34,36,38,40–43). According to these literature Socio-demographic, ART and other medications, baseline nutritional status, and baseline clinical and laboratory variables affect attrition of children in the continuum of HIV care.

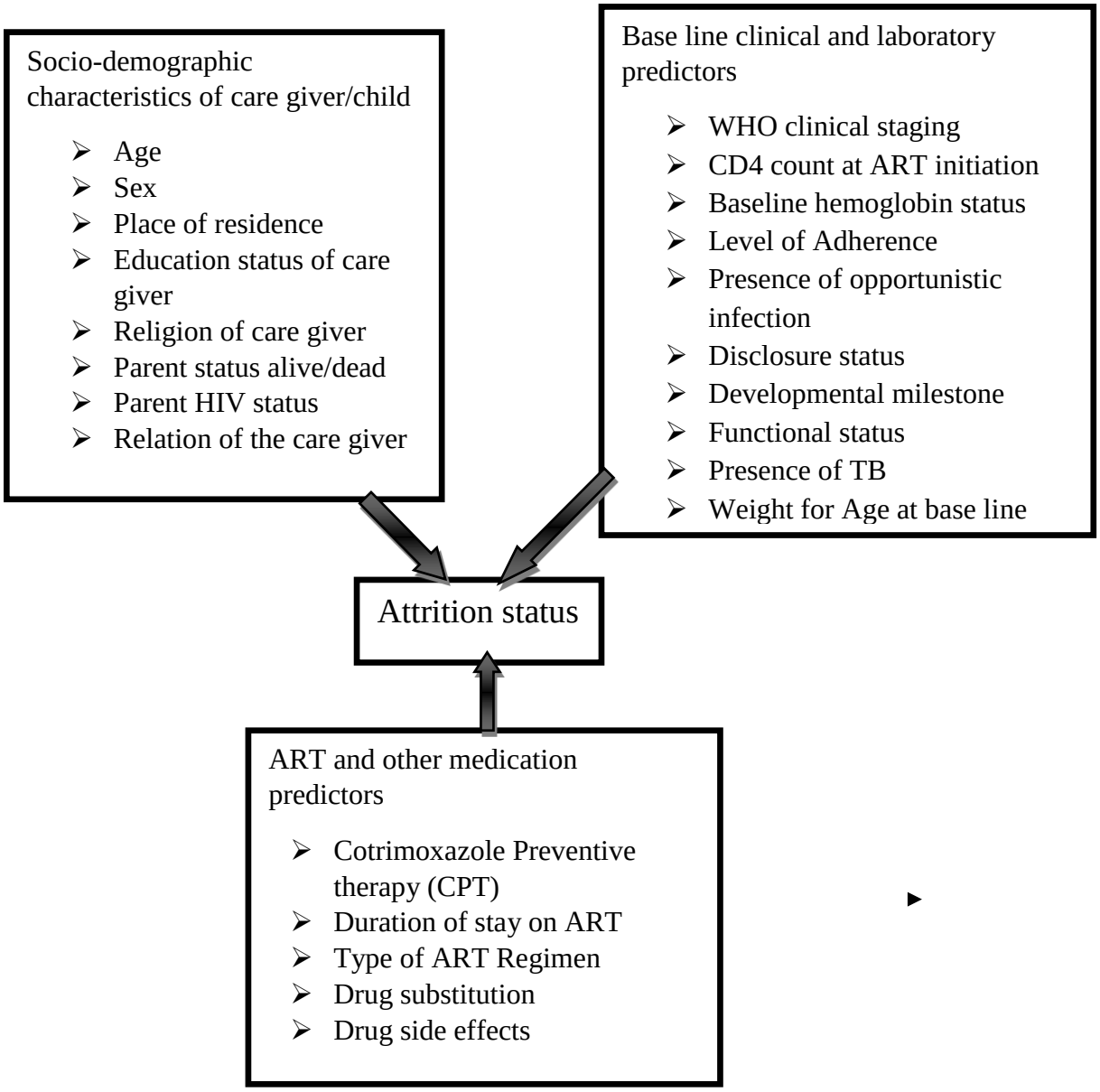


Figure 1**:** Conceptual framework for the incidence and predictors of attrition among children on antiretroviral therapy at Gedeo public Hospitals, Southern Regional State, 2020.

3. Objectives

3.1. General objective

To assess the incidence and predictors of attrition among children on antiretroviral therapy in Gedeo zone public hospitals, Southern Ethiopia, 2020.

3.2. Specific objectives

To determine the incidence of attrition among children on antiretroviral therapy in Gedeo zone public hospitals, Southern Ethiopia, 2020.

To identify predictors of attrition among children on antiretroviral therapy in Gedeo zone public hospitals, Southern Ethiopia, 2020.

4. Methods and materials

4.1. Study area and period

This study was conducted at ART clinics in public hospitals of Gedeo zone, namely Dilla Referral Hospital, Bule Primary Hospital, and Yirgachefe Primary Hospital. Gedeo zone is found in South Nation Nationalities and People Region (SNNPR) and the capital city is Dilla, which is found 394 Km away from Addis Ababa, which is the capital city of Ethiopia and 84km away from Hawassa. The altitude of Dilla is 1765m above sea level. Gedeo zone has a total of six woreda and two towns. In this Zone, there are one Referral Hospital, three district Hospitals, 36 Primary health centers (PHC), and 146 health posts. Bule and Yirgachefe primary hospitals are located 28.3 and 36 Kilometers far from Dilla respectively. Pediatric ART clinics existed in all hospitals. The study was conducted from April 15 to May 15, 2020, among records of children registered from 1st of January 2013 to December 31, 2019.

4.2. Study design

An institution-based retrospective follows up study was employed.

4.3. Populations

4.3.1. Source population

All HIV Positive children <15 years who were taking ART in Gedeo zone public Hospitals, Southern, Ethiopia.

4.3.2. Study population

All HIV Positive children <15 years who were taking ART at selected hospitals of Gedeo zone public Hospitals.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All children <15 years who were on ART and had a follow-up after ART initiation.

4.4.2. Exclusion criteria

Children's medical records containing incomplete data of the outcome variable(at least sociodemographic and baseline data) were excluded.

4.5. Sample size determination

The required sample size was determined using double population proportion formula calculating through EPi info version 7.0 by considering caregivers of children coming from a rural area and hemoglobin level as the major predictor variables based on a study done in Ethiopia(23). Moreover, caregivers of children coming from rural areas were considered as an independent predictor since it gives the maximum sample size (Table 1).

$$\frac{\left[\left[z\alpha/2\sqrt{(1+1/r)p(1-p)}\right]+\left[z\beta\sqrt{p(1-p1)+\frac{p2(1-p2)}{r}}\right]\right]^2}{(p1-p2)^2}$$

Table 1: Sample size calculation to determine the incidence and predictors of attrition among HIV positive children on antiretroviral therapy in Gedeo zone hospitals, Southern Ethiopia, 2020

Variables	**P1 and p2**	**Hazard ratio**	**Final sample size after adding 10% incomplete data**
Caregivers of children coming from a rural area	P1= 20% P2 = 6.8%	3.97	**262**(23)
Haemoglobin<10 g/dl	P1=24.4% P2=4.16%	3.3	123(23)

P1: is the percent of exposed with the outcome

P2: is the percent of non-exposed with the outcome

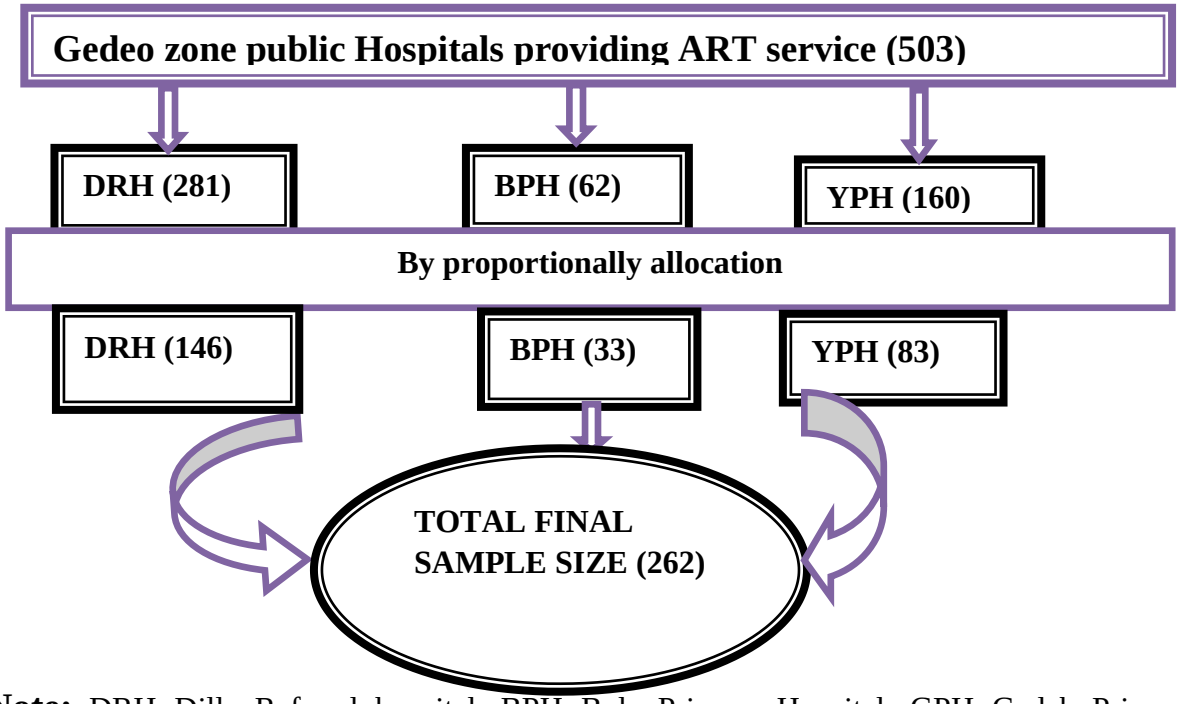
Z α/2: is taking CI 95%,

Z β:80% power and **r:**is the ratio of non-exposed to exposed 1:1

Then the largest sample size (N= 262) is selected as the final sample size for the study.

4.5.1. Sampling procedure

There are four public hospitals in Gedeo zone in which ART clinics existed. Out of these three were randomly selected and were included in the study, namely Dilla Referral Hospital, Bule Primary Hospital, and Yirgachefe Primary Hospital. The study was conducted at the Gedeo zone selected public hospitals. First, the sample size was proportionally allocated to select the study participants from each hospital. After that, medical records of children who started ART between January 1st, 2013 to December 31, 2019, were selected. From the selected medical charts in each hospital, a systematic random sampling technique was used to select the study participants. By using the formula N÷n to calculate K value; 503 ÷262 =2. So, the lottery method used to select the first study participant and considered as a starting point, and then every 2nd interval of medical records of children was taken to the required sample size. Finally, the selected medical charts were followed for seven years.



Note: DRH=Dilla Referral hospital, BPH=Bule Primary Hospital, GPH=Gedeb Primary Hospital, YPH=Yirachefe Primary Hospital

Figure 2**:** Schematic presentation of sampling procedure to assess the incidence of attrition and its predictors among children on antiretroviral therapy in Gedeo zone public hospitals, 2020.

4.6. Study variables

4.6.1. Dependent variable

Attrition status

4.6.2. Independent variables

- Socio-demographic characteristics of caregiver/child (age, sex, religion of the caregiver, place of residence, education status of the caregiver, parent status alive/dead, Parent HIV status, the relation of the caregiver)
- Baseline clinical and laboratory predictors (WHO clinical staging, CD4 count, or % at ART initiation, Baseline hemoglobin status, OIs, Disclosure status, Level of Adherence, Developmental milestones, Functional status, Baseline height for age and Baseline Weight for age).
- ART and other medication predictors (provision of cotrimoxazole prophylaxis therapy (CPT), duration of stay on ART treatment, type of ART regimen, drug substitution, drug side effects).

4.7. Operational definitions

Times to event or censor: Time to occurrence of attrition or other outcomes measured from the starting time of ART to date that the event or outcome occurred.

Attrition (event): Children who were dead or lost to follow-up recorded in children medical records in the follow up period (13,23)

Mortality: Recorded as "dead" on the children's medical card.

A loss to follow-up: Children who did not return to the facility for 90 days or more after their last scheduled appointment (36).

Censored: Individuals transferred out to other health institutions after the beginning of the study, those exceed 15 years during follow-up, individuals who were active on ART at the end of the study.

Retention: This is defined as the proportion of children alive and still on ART after ART initiation.

Time scale: The time to occurrence of an event or censored cases was measured in months.

CD4 count below the threshold for severe immunodeficiency: Is classified according to the child's age (for infants CD4 <1500/mm3, 12–35 months <750/mm3, 36–59 months < 350/mm3 and ≥5 years <200/mm3) (44).

Adherence to ART: Is classified into good, fair, or poor by the percentage of drug dosage calculated from the total monthly doses of ART drugs(44).

- Good adherence: equal to or greater than 95% or ≤ 3 doses missed per month.
- Fair adherence: 85-94% or 4-8 doses missed per month.
- Poor adherence: less than 85% or ≥ 9 doses missed per month.

Developmental milestones: Using the WHO window of achievement, for six gross motor milestones were assessed and classified as: delayed, if a child fails to attain milestone for age; regression, if a child loses what has been attained for age, otherwise normal(43).

4.8. Data collection tools and procedures

The data extraction checklist was adapted from the standardized ART entry and follow up form that is currently used by the ART clinics of the study health facility(43), ART registration booklet, ART monitoring multi-chart and reviewing related articles. The patient records were first observed and an appropriate data extraction format was prepared in English. Data were extracted from children's charts `in terms of socio-demographic, clinical, and treatment-related variables. The list of study participants were taken from the ART data clerk and MRN or unique ART number were used to find charts from the hospital card room. Three data collectors (BSc nurses) and one supervisor (ART trained BSc) were recruited.

4.9. Data quality control

Data about attrition were collected from the patients' charts. The data were collected by three experienced BSC nurses (one in each hospital) who were trained on comprehensive HIV care and involved in the patient follow up care. The pretest was done by the principal investigator on 5%(13) of randomly selected medical records to check the consistency and clarity of the abstraction tool at the yirgalem General hospital, which was not included in the actual study. The training was given for both data collectors and supervisors for one day on how to review the documents and extracting the needed data from medical records. Principal investigator and supervisors made spot-checking and reviewing the complete checklist by the data collectors to ensure completeness and consistency of the data that were filled. The filled formats were checked for completeness each day by the supervisor and investigator.

4.10. Data processing and analysis

The collected data were checked for its completeness and consistency. Data were cleaned and edited before analysis and then entered into epidata manager version 4.6 and exported to Stata version 14 for analysis. Exploratory data analysis was done to check the level of missing values, the presence of influential outliers, and normality. Then the data were described using

relative frequency and percent through the table and figures. Incidence of attrition was calculated in both per person-month and year of observation. A Kaplan Meier curve was used to estimate median survival time and the log rank test was used to compare the survival curves of children between different categories of predictor variables. The life table was used to estimate the cumulative probability of survival at different time intervals. Bivariable analysis was performed to identify the association between the dependent and each independent variable. Any variable significant at $p < 0.25$ level in the bivariable analysis were included in multivariate analysis to identify independent predictors of attrition. Multicollinearity was cheeked using the VIF command (mean VIF=1.39)(Annex IV). Cox proportional hazard model for its fitness to the data was cheeked using cox Snell residuals, in which the hazard function follows the 45-degree line except for the large values of the time(Annex V). Additionally, proportional hazard assumptions were checked using both Schoenfeld residual test (global test) with a value of p>x2=0.9982(Annex III), and Harrell's c(c=0.8359), which indicates that this study can correctly order survival times for pair of children 83.6% of the time based on observations of fitted variables in the model. Generally, it can conclude that the final model fits the data successfully. In multivariate analysis, any statistical test was considered significant at $p< 0.05$. Then, the association was summarized by using adjusted hazard ratio and statistical significances tested at 95%CI. Finally, the finding was presented using tables, graphs, and texts.

4.11. Ethical consideration

Ethical issues within the study were taken into consideration when carrying out this study. Ethical clearance was obtained from the institutional review board of Addis Ababa University, College of health sciences, school of nursing, and midwifery. After approved by IRB with the protocol number: 02/20/SNM, Official letter of co-operation was written to each selected hospital from school of nursing. The official letter was submitted to the medical director and permission was received to get full access of information from respective units like ART data clerks and the card rooms. Then, data were collected after getting permission from selected hospitals on the behalf of patients and respective units of each hospital since the study was conducted through review of medical records. Since this is a retrospective study using secondary data, informed consent from individual patients were not requested. Data

were coded and locked in the passward during data entry and analysis to maintain the confidentiality of the study participants. Names and children's unique ART numbers were not included during data collection.

4.12. Dissemination of the results

The findings of this study will be submitted to Addis Ababa University, School of Nursing, and Midwifery. Also, the result will be submitted to health facilities where the study was conducted. Further effort will be made to present it on workshops and conferences and to publish on peer review reputable journals.

5. Results

A total of 262 medical records of children who were on ART from 1st of January 2013 to December 31, 2019, were reviewed. Of which, 254 children medical charts were eligiable and included in this study with a response rate of 96.9%.

5.1. Socio-demographic characteristics of children on ART

The finding revealed that among 137(54%) male participants, 46(18.11%) were experienced attrition. One hundred thirty-three (52.4%) study participants were living in an urban area. Of which , 42(16.54%) were experienced attrition. Of one hundred twenty-one (47.6%) those who were living in rural area, 50 (19.68%) were having attrition. One hundred eighty- six (73.23%) of respondents were living with their parents. Of whom, 67(26.38%) were experienced attrition, while 51 (20.08%) children's parents were either mother or father died and 7.48% were experienced attrition. The finding also showed that about 171(67.32%) of children’s caregivers were married. Among those, 58 (22.83%) children were developed attrition (Table 2).

Table 2: Baseline socio-demographic characteristics of Children on ART at Gedeo Zone hospitals, Southern Ethiopia, 2020,(N=254).

Independent variables	Outcome variable: Attrition		censored		Total
	Frequency	Percent	Frequency	Percent	
Age(years)					
<3	24	9.45%	26	10.24%	50(19.7%)
4-8	46	18.11%	83	32.68%	129 (50.8%)
≥ 9	22	8.66%	53	20.87%	75 (29.5%)
Sex					
Male	46	18.11%	91	35.83%	137(54%)
Female	46	18.11%	71	27.95%	117(46%)
Religion of care giver					
Orthodox	31	12.2%	63	24.8%	94(37%)
Muslim	12	4.72%	30	11.8%	42(16.5%)
Protestant	46	18.11%	65	25.59%	111(43.7%)
Catholic	3	1.18%	4	1.57%	7(2.8 %)
Residence					
Rural	50	19.68%	71	27.95%	121(47.6 %)
Urban	42	16.54%	91	35.83%	133 (52.4%)
Marital status of care giver					
Single	10	3.94%	14	5.5%	24(9.44%)
Married	58	22.83%	113	44.5%	171(67.33%)
Divorced	8	3.15%	11	4.33%	19(7.48%)
Widowed	16	6.3%	24	9.45%	40(15.75%)
Age of the care giver					
18-24	8	3.15%	18	7%	26(10.15%)
25-34	47	18.5%	77	30.5%	124(49%)
35-44	28	11%	51	20%	79(31%)
>44	9	3.54%	16	6.4%	25(9.85%)
Parent status					
Both alive	67	26.38%	119	46.85%	186(73.23%)
Either dead	19	7.48%	32	12.59%	51(20.08%)
Both dead	2	0.79%	8	3.15%	10(3.94%)
Unknown	4	1.57%	3	1.18%	7(2.75%)
HIV status of care giver					
Reactive	53	20.87%	89	35%	142(55.9%)
Non- reactive	2	0.79 %	7	2.75%	9(3.5%)
Unknown	37	14.57%	66	25.98%	103(40.6%)
Relation of care giver					
Biological	90	35.43%	153	60.24%	243(95.67%)
Others	2	0.79%	9	3.54%	11(4.33%)
Occupation of care giver					
Governmental employee	3	1.18%	13	5.12%	16(6.3%)
House wife	46	18.11%	74	29.13%	120(47.24%)

Self-employee	41	16.14%	67	26.38%	108(42.52%)
Others	2	0.79%	8	3.15%	10(3.94%)
Educational status of the care giver					
Illiterate	45	17.72%	85	33.46%	130(51.2%)
Read and write	18	7%	26	10.24%	44(17.2%)
Grade 1-8	21	8.27%	27	10.63%	48(19%)
grade 9-12	3	1.18%	8	3.15%	11(4.3%)
College and above	5	1.97%	16	6.3%	21(8.3%)

The median age of the study participants was 6 years (Interquartile range (IQR):3-9) and 129 (50.79%) of them were found to be in the age group of 4-8 years. Children were followed for a minimum of 1 month and a maximum of 80 months with a median follow up of 26.4 months starting from 1stof January 2013 to December 31, 2019. The Median CD4+cell count at baseline was 606 cells/µL (IQR: 277-1066) (Table 3).

Table 3. Overall description of continuous variables using numeric measures among children on ART in Gedeo zone public hospitals, Southern Ethiopia, 2020 (n=254).

Descriptive measures		**Patient age (in years)**	**Care givers age (inyears)**	**Cd4+ count**	**Hgb level (mg/dl)**	**Duration of follow up (in months)**	**Wt. At Baseline (kg)**	**Ht at baseline (cm)**
Median		6	32	606	11.55	26.4	16	110
Skewness		0 .22	1.4	0.84	-0.16	0.55	0.9	-0.3
Kurtosis		2.04	5.7	3.7	2.76	2.15	3.6	2.45
Range		13.7	51	1826	11.1	83.1	45	130
Percentiles	1st (25%)	3	26	277	13.7	10.1	11	88
	2nd (50%)	6	32	606	11.55	26.4	16	110
	3rd (75%)	9	36	1066	12.8	50.6	23	125

Note: Wgt= weight, Hgt=Height

5.2. Clinical, laboratory and treatment-related characteristics of children on ART

Based on the finding, more than two-thirds of study participants 176 (69.29 %) had a baseline CD4 cell count greater than 350 cells/µL. Of which 45(17.72%) were experiencing attrition. On the other hand, 13.78% who had CD4+counts of </=200 cells/µL, 9% of them were

developed attrition. Among those children who started ART with advanced clinical stage (WHO III or IV), 15.35% were experienced attrition. Of seventy-four(29%) who had Hgb level below 10mg/dl at the initiation of ART, 51(20%) were having attrition. Among 102 study participants, 89 (87.25%) had appropriate in motor developmental status while the remaining 13(12.75%) had delayed developmental status at baseline. About 55 (21.65%) respondents had developed an opportunistic infection. Of whom 25(9.84%) had diarrhea and 12 (4.72%) had pneumonia. Thirty-two (12.60%) who were not taking cotrimoxazole preventive therapy, 17(6.69%) were developed attrition. Moreover, 78(30.7%) of respondents had developed a drug side effect and, 74 (29.13%) of children had changed their ART into another drug regimen (Table 4).

Table 4. Baseline clinical, laboratory and ART information of Children on ART at Gedeo Zone hospitals, Southern Ethiopia, 2020, (n=254).

	Outcome variable				
Independent Variable	**Attrition**		**Censored**		**Total**
	Frequency	**Percent**	**Frequency**	**Percent**	
Who clinical stage					
WHO stage I and II	53	20.87%	121	47.64%	174(68.5%)
WHO stage III and IV	39	15.35%	41	16.14%	80(31.5%)
ART adherence level					
Good	45	17.72%	150	59%	195(76.7%)
Poor/fair	47	18.5%	12	4.72%	59(23.3%)
Disclosure status					
Disclosed	26	10.24%	61	24%	87(34.3%)
Not disclosed	33	12.99%	57	22.44%	90(35.4%)
Unknown	33	12.99%	44	17.32%	77(30.3%)
Cd4+ count					
<200	23	9%	12	4.72%	35(13.7%)
>200-350	24	9.49%	19	7.48%	43(17%)
>350	45	17.72%	131	51.57%	176(69.3%)
Hemoglobin level					
<10mg/dl	51	20%	23	9%	74(29%)
≥10mg/dl	41	16.14%	139	54.72%	180(71%)
Baseline WfA					
Normal (z >-2)	72	28.35%	152	59.84%	224(88.2%)
Under weight (z <-2)	20	7.87%	10	3.94%	30(11.8%)
Baseline HfA					

Normal (z >-2)	75	29.53%	154	60.63%	229(90.16%)
Stunting (z <-2)	17	6.69%	8	3.15%	25(9.84%)
Baseline functional status for age ≥5 years					
Working	25	16.45%	59	38.8%	84(55.2%)
Ambulatory	18	11.84%	41	26.97%	59(38.8%)
Bedridden	7	4.6%	2	1.3%	9(6%)
Developmental status for age <5 years					
Appropriate	32	31.37%	57	55.88%	89(87.25%)
Delayed	10	9.8%	3	2.94%	13(12.75%)
Opportunistic infection					
Yes	26	10.24%	29	11.42%	55(21.66%)
No	66	25.98%	133	52.36%	199(78.34%)
Cotrimoxazole preventive therapy					
Given	75	29.53%	147	57.87%	222(87.4%)
Not given	17	6.69%	15	5.9%	32(12.6%)
Presence of Tb					
Yes	10	3.93%	11	4.33%	21(8.3%)
No	82	32.28%	151	59.39%	233(91.7%)
Regimens started					
4a= d4T- 3TC- NVP	14	5.5%	19	7.48%	33(12.9%)
4c=AZT-3TC-NVP	56	22%	95	37.4%	151(59.4%)
1e=TDF-3tc-EFV	3	1.18%	12	4.72%	15(6 %)
1g=ABC-3TC-EFV	2	0.79%	5	1.97%	7(2.8%)
4d=AZT-3TC-EFV	7	2.75%	10	3.93%	17(6.7%)
1h=ABC-3TC-NVP	7	2.75%	4	1.57%	11(4.3%)
Others	3	1.18%	17	6.69%	20(7.9 %)
Drug side effect					
Yes	44	17.32%	34	13.38%	78(30.7%)
No	48	18.89%	128	50.39%	176(69.3%)
Drug substitution					
Yes	22	8.66%	52	20.47%	76(29.13%)
No	70	27.56%	110	43.3%	180(70.87%)

Note: WHO = World health organization, ART = Antiretroviral therapy, WFA= Weight forage, HFA = Height for age, TB = Tuberculosis, d4T = Stavudine, AZT = Zidovudine, 3TC= lamivudine, TDF = Tenofovir, ABC=Abacavir, NVP = Nevirapine, EFV= Efavirenz, LPV/r = Lopinavir/ritonavir

During the follow-up period of the study, among the total of 254 children who were on ART, 162 (63.8%) were censored and 92(36.2%) were experiencing attrition. Of those, 127(50%) were actively on follow up, 35(13.8%) were transfer out to other health facilities, 70 (27.5%) were lost to follow up, and 22(8.7%) were mortality (Figure 3). Fifty-seven (48%) of attrition were occurred after 60 months of the following period.

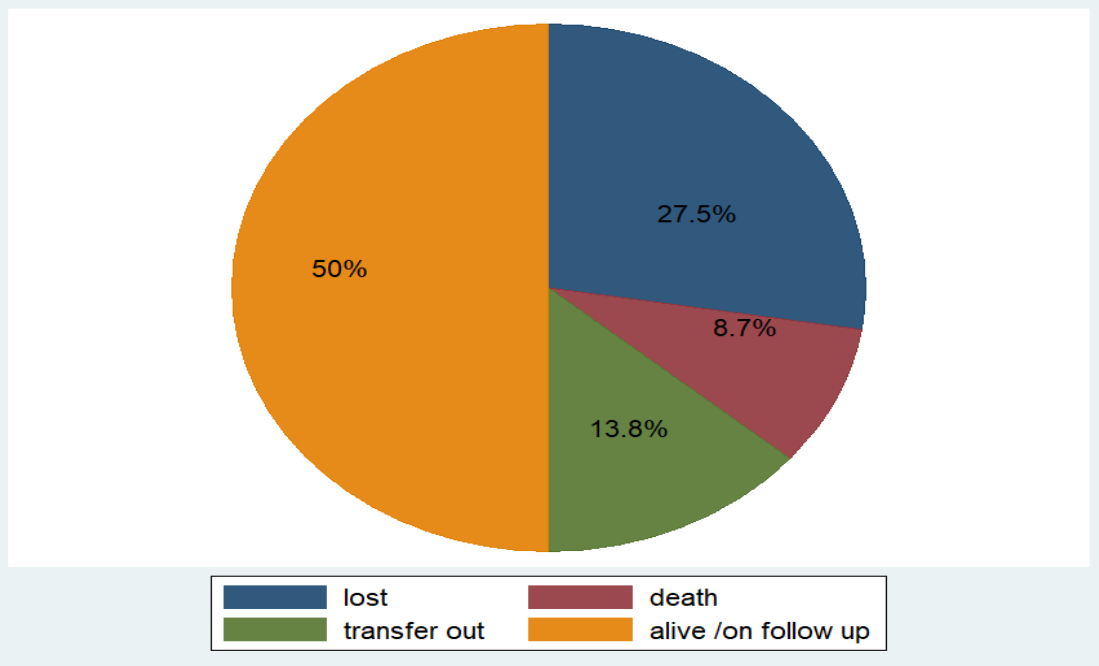


Figure 3: Diagrammatic presentation of type outcome status among HIV infected children on ART in public hospitals of Gedeo zone, Southern Ethiopia, 2020 (n=254).

5.3. Comparison of survival status using Kaplan Meier and Log-rank test

The Kaplan Meier failure curve increases stepwise and it crosses the failure function at failure probability of 0.5 (Figure 4).

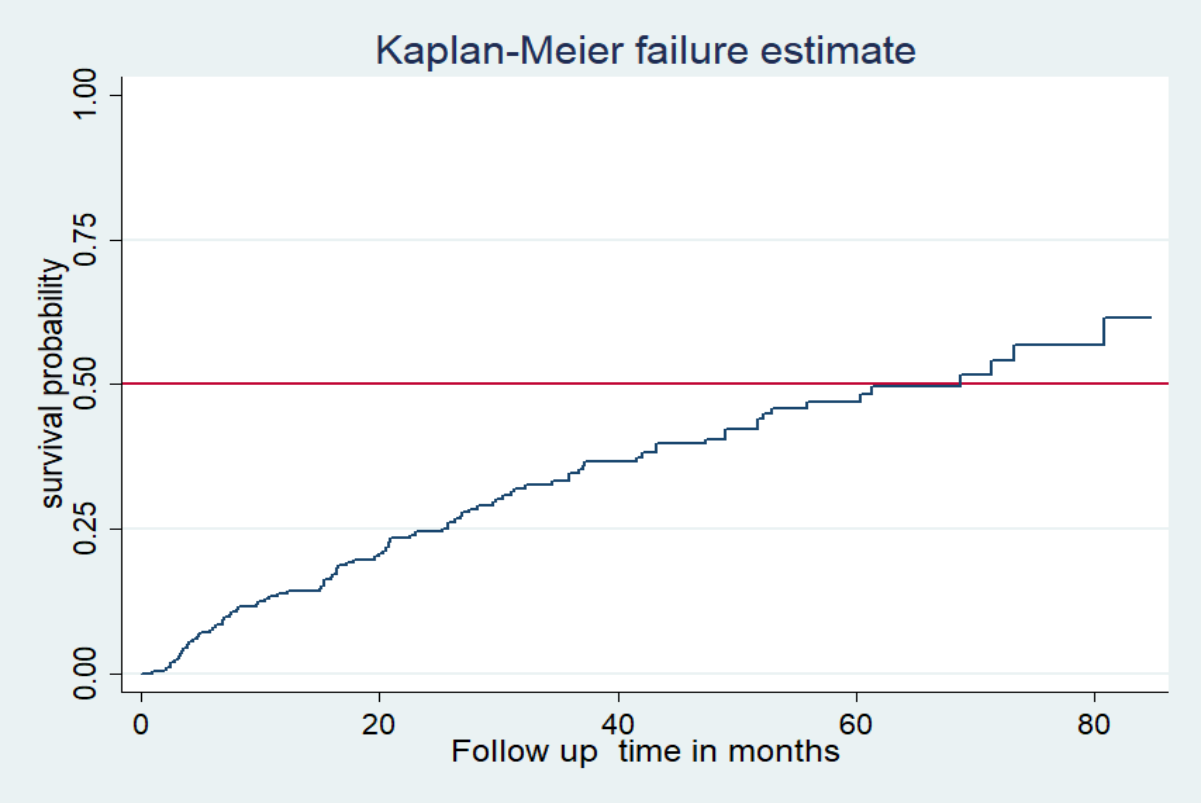


Figure 4. Overall Kaplan-Meier failure estimate among children on antiretroviral therapy at Gedeo Zone hospitals, Southern Ethiopia, 2020 (n=254)

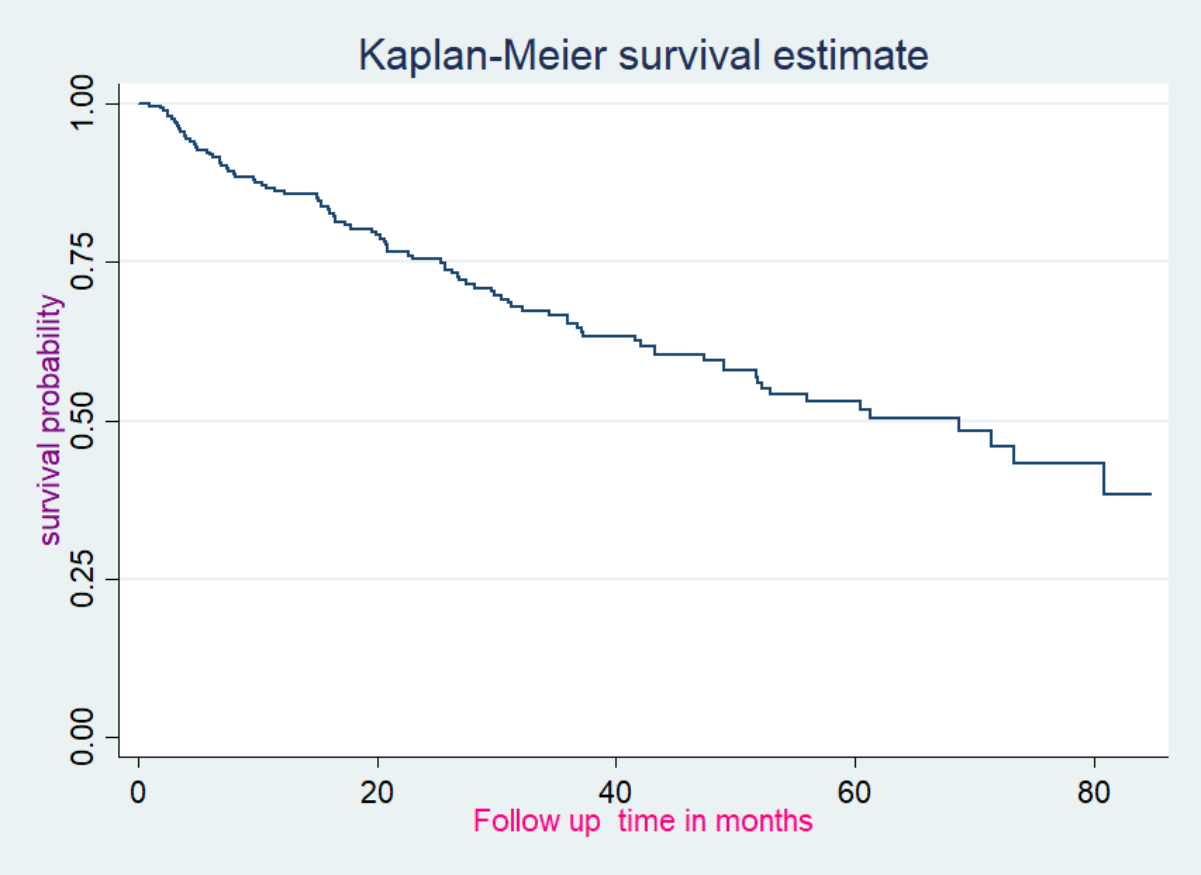


Figure 4: Overall Kaplan-Meier curve of Attrition-free survival probability among children on antiretroviral therapy at Gedeo Zone hospitals, Southern Ethiopia, 2020 (n=254)

The log-rank test statistics revealed that there is a significant difference in survival function for different categorical variables. These variables include patients with underweight, WHO clinical stage, hemoglobin level, ART adherence at baseline, developmental stage at baseline, side effect, and patients who didn't take co-trimoxazole therapy.

In this follow-up study those study participants who were underweight (z score <-2) have lower survival time as compared to those who were not underweight (z score >-2). The survival time difference between the groups was showed statically significant with P-value = 0000 (Figure 5)

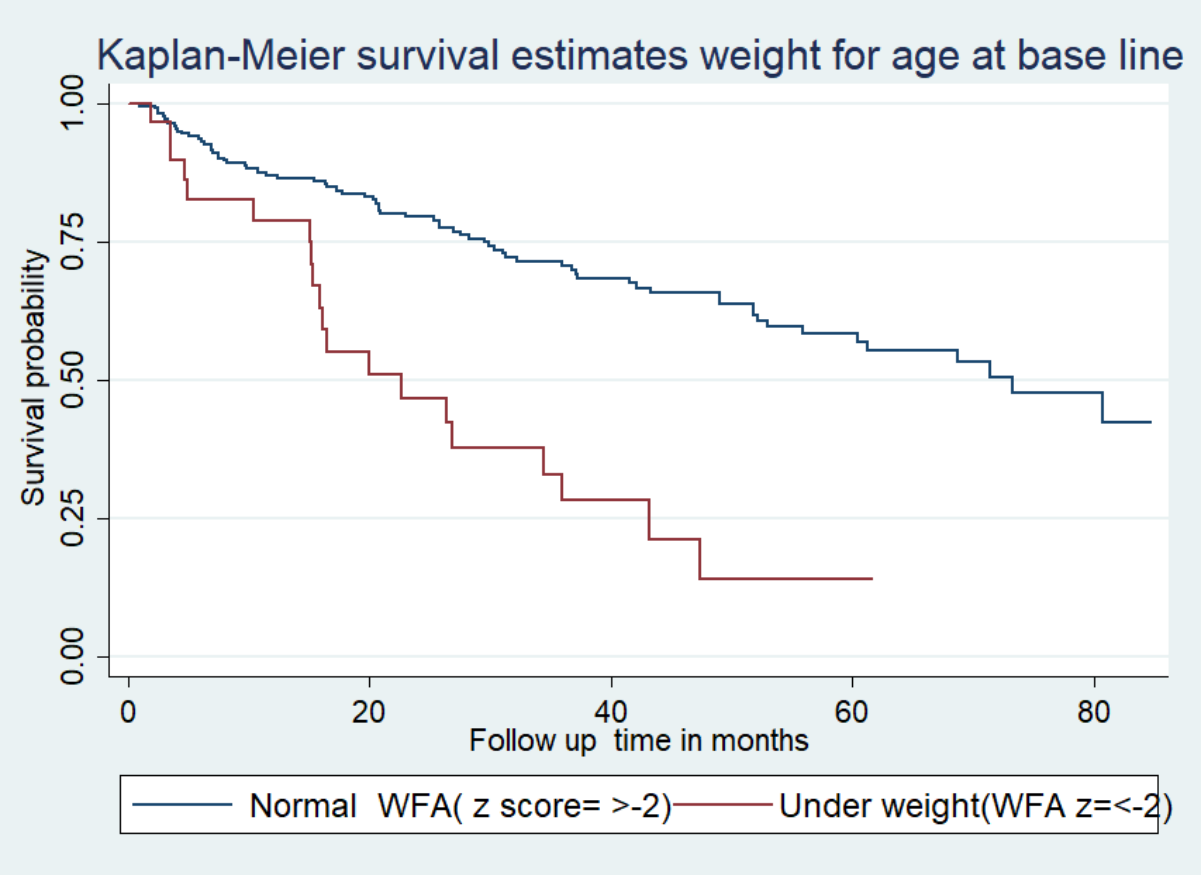


Figure 5:Sample Kaplan-Meier of attrition-free survival probability plots showing survival differences by weight for age among children on antiretroviral therapy at Gedeo zone hospitals, Southern Ethiopia,2020(n=254)

Another variable that showed the survival time difference between the groups was the developmental stage at baseline. Those children with HIV who had delayed developmental stages at baseline have lower survival time than that of children who had a normal developmental stage. The survival time difference between the groups was showed statically significant with P-value=0.0010 (Figure6).

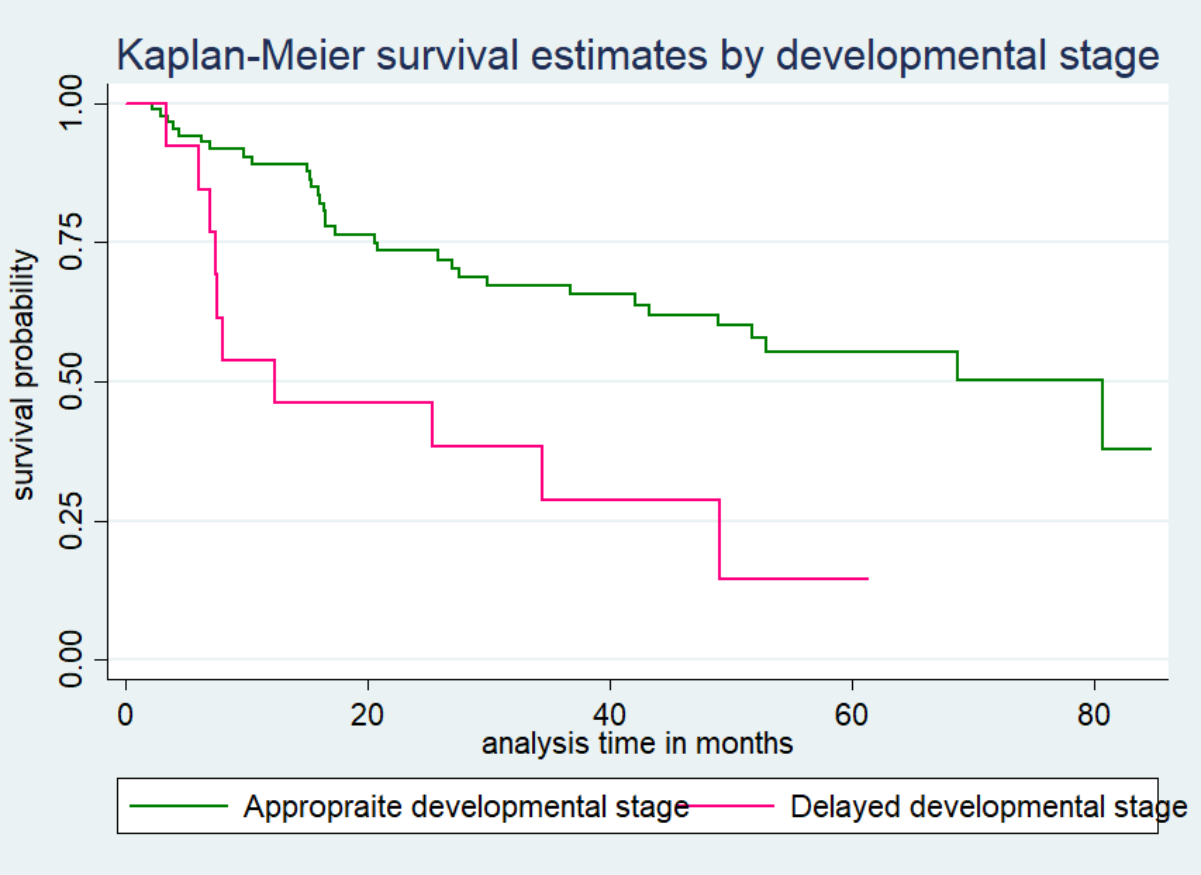


Figure 6: Sample Kaplan-Meier of attrition-free survival probability plots showing survival differences by developmental stage at base line among children on antiretroviral therapy at Gedeo zone hospitals, Southern Ethiopia, 2020 (n=254)

Similarly, this study also revealed that study participants who had lower hemoglobin level (Hgb <10mg/dl) have lower survival time as compared to their counterparts. The survival time difference between the groups was statically significant with P-value=0.0000 (Figure7).

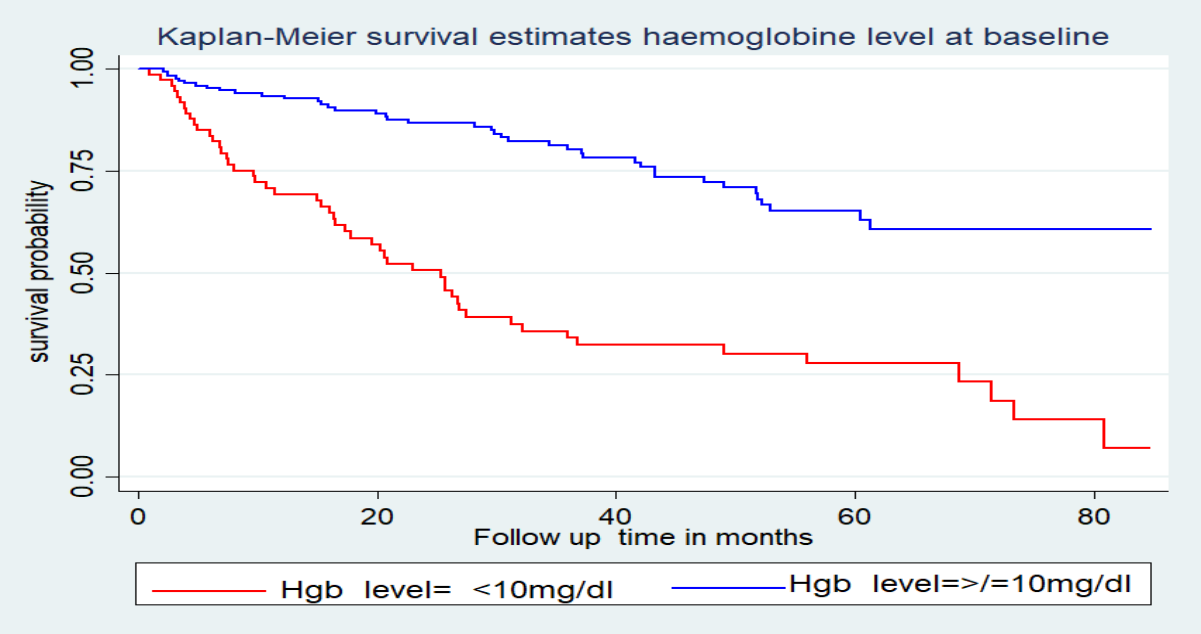


Figure 7: Sample Kaplan-Meier of attrition-free survival probability plots showing survival differences by haemoblobin level among children on antiretroviral therapy at Gedeo zone hospitals, Southern Ethiopia, 2020 (n= 254)

The figure plotted below showed that the Kaplan Maier survival function for sex of children cross each other which indicate that as there is no survival difference between male and female (Figure 8).

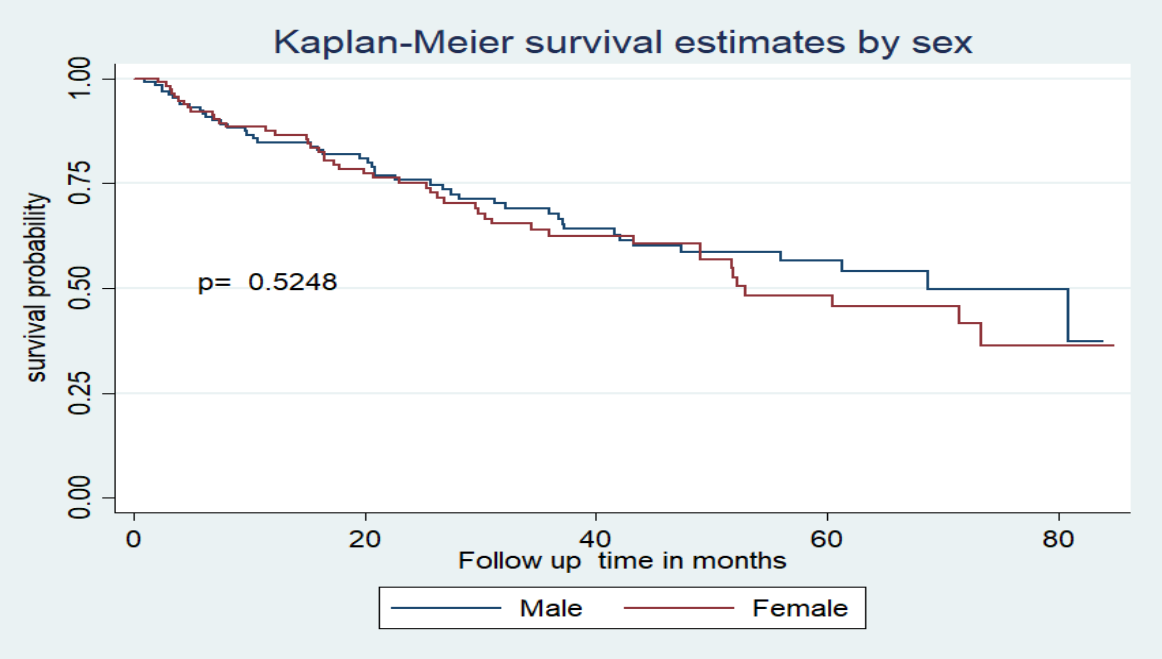


Figure 8: Sample Kaplan-Meier of attrition-free survival probability plots with no survival differences by sex among children on antiretroviral therapy at Gedeo zone hospitals, Southern Ethiopia, 2020(n=254).

The log-rank test revealed that WHO clinical stage at baseline, ART adherence level at baseline, developmental stage at baseline, functional status at baseline, Cd4+ count at baseline, Hgb level at baseline, weight for age at baseline, Height for age at baseline, presence of OI during follow up, presence TB, drug side effect, drug substitution during follow up, cotrimoxazole preventive therapy, had statistically significant difference among survival curves of observed groups with p-value <0.05 (Table 5).

Table 5: Log rank test for equality of survivor functions between groups among children on ART, in Gedeo zone public hospitals, Southern Ethiopia, 2020(n=254).

		Log-rank test	
No,	Variables	x2	p>x2
1	Patient age	4.3	0.1137
2	Sex	0.4	0.5248
3	The religion of the caregiver	4.34	0.2273
4	Residence	2.94	0.0866
5	Marital status of the caregiver	2.52	0.4722
6	Care giver age	0.44	0.9311
7	Parent status	3.11	0.3745
8	HIV status of Care giver	0.08	0.9623
9	Caregiver relationship	0.36	0.5489
10	Occupation of the caregiver	2.11	0.5502
11	Educational status of the care	2.07	0.7231
12	WHO clinical stage	6.06	**0.0138**
13	Disclosure status	0.24	0.8886
14	CD4 count	26.49	**0.0000**
15	Haemoglobin level	47.95	**0.0000**
16	WFA	23.43	**0.0000**
17	HFA	16.75	**0.0000**
18	Functional status	32.63	**0.0000**
19	Developmental status	10.78	**0.0010**
20	OI	35.59	**0.0000**
21	Cotrimoxazole preventive therapy	5.6	**0.0175**
22	Presence TB	8.90	**0.0117**
23	ART adherence level	79.88	**0.0000**
24	Drug side effect	7.52	**0.0233**
25	Drug substitution	4.33	0.6326

5.4. Survival function and Incidence of attrition during the follow-up period

Two hundred fifty-four study participants were followed for different periods for a maximum of seven years and gives a total of 8145.33 child -months (678.775 child-years) observation. The median follows up time was 26.4 (IQR,10-51) months. At the end of follow-up, 162

(63.8%) were censored and 92(36.2%) were experiencing attrition. Out of censored, 127 (50%) of the children were under active follow-up, 35(13.8%) were transferred out to other health facilities. The incidence rate of attrition was 11.3 per1000 person-months observation (95%CI: 9.20-13.85) or 13.5 per100 person-years observation (95%CI: 11-16.6). The rate of lost to follow-up and mortality was 8.6 and 2.7 per 1000 PMO respectively. The cumulative probabilities of survival at the end of 12, 24, 36, 48, and 60 months of after ART initiation were 86.1%, 75.5%, 65.35%, 59.5%, and 52.96% respectively. The median survival time was found to be 68.73 months. Therefore, 50% of participants retained on their treatment utill 68.73 months (Table 6).

Table 6: Life table of HIV infected children who were on ART at Gedeo zone public hospitals, Southern Ethiopia, 2020(n=254).

Time interval (months)	Beginning (total)	Attrition	Lost	Cumulative Failure probability	Std.error	(95% CI)
[0 - 12]	254	33	37	0.1401	0.0226	0.10, 0.19
[12-24]	184	21	27	0.246	0.0294	0.19, 0.309
[24-36]	136	17	20	0.3478	0.0342	0.285, 0.419
[36- 48]	99	8	17	0.4054	0.0368	0.337, 0.48
[48-60]	74	7	24	0.4725	0.0404	0.397, 0.555
[60-72]	43	4	21	0.5375	0.0467	0.449, 0.63
[72-84]	18	2	14	0.6216	0.0660	0.495, 0.749

5.5. Predictors of attrition among children who were on ART

In the bivariable analysis variables like age of the patient, residence, religion of the caregiver, ART adherence level, baseline WHO clinical stage, baseline hemoglobin, baseline underweight, stunting, functional status, developmental stage, cotrimoxazole preventive therapy nonusers, opportunistic infection, TB status, side effect, and drug substitution were found to have a p-value less than 0.25 and included in the multivariate analysis. However, some variables were not included in multivariate analysis because they violated the proportional hazard assumption with a p-value of less than 0.05 during the global test. Those variables were the religion of the caregiver, presence TB, baseline functional status, and cotrimoxazole non-users. Finally, Cox proportional hazard model (multivariate analysis) showed that low haemoglobin level, low CD4 count, underweight, poor/fair ART adherence level and delayed developmental stage at baseline were found to be significant predictors of attrition at 5% significance level (p-value <0.05). (Table 7)

Those children having low hemoglobin levels (Hgb=<10mg/dl) were three and half times (AHR = 3.5, 95 CI%: 1.6- 7.4) at higher hazard of attrition than those children who have a haemoglobin level of >/=10mg/dl. Children who had delayed developmental milestones at the

initiation of ART were observed to have a higher hazard of attrition (AHR=3.76, 95 %CI:1.2-11.8) as compared to those with appropriate developmental milestones at baseline. Patients who had underweight at baseline (WFA z score <-2) were also 5 times at the higher hazard of developing attrition than those patients with normal nutrition status (WFA z score= >-2), (AHR=5, 95%CI:1.5-17.25). In addition to this, children who had CD4 level </=200 at the start of ART were 3.7(AHR=3.7, 95%CI: 1.4- 9.7) times higher at the hazard of attrition than their counterparts. Moreover, patients who had poor/fair ART adherence levels at baseline were 3.2 times more likely to have attrition as compared to those who had a good adherence level at baseline (AHR=3.2, 95%CI: (1.3-7.8).

Table 7: Bivariable and Multivariate analysis using Cox regression model for predictors of attrition among children on ART at Gedeo zone hospitals, Southern Ethiopia from January 2013- December 2020) (n=254)

	SURVIVAL STATUS					
Variables	**Censored (N=162(63.8%)**	**Attrition N=92(36.2%)**	**CHR (95%CI)**	**P-value**	**AHR (95%CI)**	**P-value**
Age (yrs)						
<3	26 (10.24%)	24 (9.45%)	1.6(0.9-2.9)	0.093	1.4(0.2,12.5)	0.745
4-8	83(32.68%)	46 (18.11%)	1(0.6, 1.7)	0.967	0.7(0.09, 5.8)	0.765
>/=9	53 (20.87%)	22 (8.66%)	Reference	---	--	--
Residence						
Rural	71(27.95%)	50(19.68%)	1.4(0.9,2.15)	0.088	1.4(0.6,3.4)	0.423
Urban	91(35.83%)	42(16.54%)	Reference	---	--	--
WHO stage						
Stage I or II	121(47.64%)	53(20.87%)	Reference	---	---	---
Stage III or IV	41(16.14%)	39(15.35%)	0.6(0.4, 0.9)	0.015	2(0.9, 4.4)	0.093
ART adherence						
Good	150(59%)	45(17.72%)	Reference	----	**----**	----
Poor/fair	12(4.72%)	47(18.5%)	5.6(3.6,8.5)	0.000	**3.2(1.3, 7.8)**	**0.012**
Developmental stage <5years						
Appropriate	57(55.88%)	32(31.37 %)	Reference	---	--	--
Delayed	3 (2.94%)	10(9.8 %)	3.15(1.5,6.5)	0.002	**3.76(1.2,11.8)**	**0.023**
Haemoglobin level						
<10mg/dl	23(9%)	51(20%)	3.9(2.6,5.8)	0.000	**3.5(1.6, 7.4)**	**0.001**
>/=10mg/dl	139(54.72%)	41(16.14%)	Reference	----	----	----
CD4+ count						
</=200	12(4.72%)	23(9%)	3.2(2, 5.3)	0.000	**3.7(1.4,9.7)**	**0.008**
>200-350	19(7.48%)	24(9.49%)	2.4(1.5, 4)	0.001	1.3(0.5 ,3.8)	0.570
>350	131(51.57%)	45(17.72%)	Reference	----	----	----

Opportunistic infection						
Yes	29(11.42%)	26(10.24%)	1.4(0.9,2.2)	0.144	1.8(0.8, 4.2)	0.179
No	133(52.36%)	66(26.18%)	Reference	--	--	--
Cotrimoxazole preventive therapy						
Given	147(68.89%)	75(29.53%)	Reference	----	----	----
Not given	15(5.9%)	17(6.69%)	1.9(1.1, 3.2)	0.019		
Presence of tb						
Yes	150(59%)	81(31.89%)	1.6(0.9, 3.2)	0.137	--	--
No	12(4.72%)	11(4.32%)	Reference	----	--	--
Drug side effect						
Yes	34(13.38%)	44(17.32%)	1.7(1.14, 2.6)	0.010	0.6(0.3, 1.4)	0.257
No	128(58.39%)	48(18.89%)	Reference	----	--	--
Drug substitution						
Yes	52(20.47%)	22(8.66%)	Reference	----		
No	110(43.3%)	70(27.56%)	2(1.2, 3.2)	0.007	1.9(0.8, 4.6)	0.129
Weight for age (underweight)						
Z score = >-2	152(59.84%)	72(28.35%)	Reference	----		
Z score = <-2	10(3.94%)	20(7.87%)	3.3(2.0, 5.4)	0.000	**5(1.5,17.25)**	**0.010**
Height for age (stunting)						
Z Score = >-2	154(60.63%)	75(29.53%)	Reference	----	--	--
Z Score = <-2	8(3.15%)	17(6.69%)	2.9(1.7, 4.9)	0.000	0.5(0.1,2.2)	0.348

Those bold numbers above showed significantly associated predictors of attrition.

CHR: Crude Hazard Ratio; **AHR**: Adjusted Hazard Ratio; **CI**: Confidence Interval

P-value: is from Cox-regression model adjusted for all predictors in the final model

6. Discussion

This study aimed to determine the incidence and predictors of attrition among children on ART at Gedeo zone public hospitals, from 1st of January 2013 to 31 December 2019. According to this finding, at the end of follow-up, 162(64.8%) were censored and 92(36.2%) were experiencing attrition. Of those, 127 (50%) were actively on follow up, 35(13.8%) were transfered out to other health facilities, 70 (27.5 %) were lost to follow up, and 22 (8.7%) were mortality. This study revealed that the overall incidence rate of attrition was 11.3 per1000 person-months observation (95%CI: 9.20-13.85) or 13.5 per 100-person years observation (95%CI: 11- 16.6). The median survival time of follow up was found to be 68.73 months. The cumulative probabilities of survival at 12, 24, 36, 48 and 60 months of after ART initiation were 86.1%, 75.5%, 65.35%, 59.5% and 52.96% respectively. Moreover, baseline haemoglobin level, baseline CD4 level, poor/fair ART adherence level, delayed developmental stage at baseline, and underweight were found to predict children's attrition.

In this study, the overall incidence of attrition for children was 13.5 per 100-person years of observation (95%CI: 11-16.6). This finding was consistent with the study conducted in Uganda (28), In the primary health care of Kenya, Lesotho, Mozambique, Rwanda, and Tanzania(29), Sub-Saharan Africa (30) with the incidence rate of attrition 14.4, 15, and 11.7 per 100 PYO respectively. However, this study was much lower when compared to the study conducted at secondary/tertiary health facilities of Kenya, Lesotho, Mozambique, Rwanda, and Tanzania (29), which was 26.2 PYO and West Africa(21) that was 26.2 PYO. This difference may be explained in different ways. The first reason for the lower attrition rate in this study might be a difference in study participants included in the study. For example, A study conducted in Secondary/Tertiary health facilities of Kenya, Lesotho, Mozambique, Rwanda, and Tanzania (29), the attrition rate was determined in patients who were in both pre-ART and ART period while this study was considering only for patients who were on ART. The second reason could be, in this study lower attrition rate might result from the current rapid expansion and availability of potent antiretroviral treatment (ART). The other possible reason may be the difference in sample size as study shown at Secondary/Tertiary

health facilities of Kenya, Lesotho, Mozambique, Rwanda, and Tanzania (29), (N= 17,155) and West African countries (21), (N=2170).

On the contrary, this study revealed a higher incidence rate as compared to a previously conducted study in Thailand(26), 5 per 100 PYO, Myanmar (13), 3.89 per100 PYO, Asia Pacific region (27), 6.5 per 100 person-years, and Ethiopia(23), 8.3per 100 PYO. This gap could be explained by the difference in study design like study was done previously in Ethiopia(23) employed prospective study design and had regular reminders to the caregivers through ART providers and data clerks and the length of the study also have its contribution for the difference in incidence rate because study done previously in Ethiopia had 2 years follow up time. The difference in the quality of care also a possible explanation for the higher attrition rate for this study than those findings reported in Thailand (26), Asia Pacific region (27) , and Myanmar (13).

This study showed that children with low hemoglobin levels (Hgb level =<10mg/dl) at ART initiation were independently associated with attrition (AHR=3.5, 95CI%:1.6-7.4). The previous studies conducted in Systematic review in a limited-resource setting (11), Myanmar (13), Bali (36), Sub-Saharan Africa(38), Mozambique(40), Côte d'Ivoire's(41), and Ethiopia(23) were in line with this study. The rationale for this may be, the existing anemia could worsen in HIV-infected children who initiated their ART regimen containing Zidovudine (AZT), lead them to develop further opportunistic infections and eventual loss to follow up or death(23). Another explanation could be the issue of decreased ART tolerance because of decreased absorption and the effect of immune defense from anemia. As can be noted from this study, almost two-thirds of 168 (66.1%) of children have started ART regimen containing Zidovudine (AZT). Of these, 64 (24.75%) children had experienced attrition.

This study also showed hazards of attrition was higher in patients with low cd4+ level (cd4+ count </=200) as compared to patients with cd4+ level of >200 (AHR=3.7, 95%CI: 1.4- 9.7). This finding was supported by a study conducted in Myanmar, Asia, and Africa, Democratic Republic of Congo, Systemic review in resource-limited settings, West Africa, Sub Saharan Africa, Rwanda, and combined study in Kenya, Uganda, and Malawi (11,13,21,31–33,37,38).

This could be due to low level of CD4+T cells is associated with the progression of HIV disease and increased the presence of opportunistic infections and other clinical conditions. So, the above-mentioned mechanisms will lead to exhaustion and non-compliance to ART follow-up leading to missed follow-up.

Another important independent predictor of attrition was poor or fair ART adherence level at baseline. Patients who had poor/fair ART adherence levels at baseline were 3.2 times more likely to experience attrition than those who had a good adherence level at baseline (AHR=3.2, 95%CI:1.3-7.8). This could occur because poor or fair adherence from ART contributes to increasing viral replication, poor immunological, and clinical outcomes as well as increase the risk of developing ARV drug resistance. This in turn increases the number of lost to follow-up patients from ART care or mortality. On the contrary to this, good adherence to ART plays an important role in sustaining viral suppression, preventing the progression of disease, and motivates retention of care, and decreases the mortality rate(43).

Children who had underweight at baseline (WFA z score <-2) also have five times at higher hazards of developing attrition than those patients with normal nutrition status (WFA z score= >-2), (AHR=5, 95%CI:1.5- 17.25). This was in line with the study done in Myanmar (13), Bali (36), Systematic Review in resource-limited settings (11), Côte d'Ivoire's(41), Uganda (39), a combined study in Kenya, Uganda, and Malawi (38). This may be explained in different ways. The main reason could be, malnutrition in patients living with HIV results in compromised immunity, which in turn predisposes them to opportunistic infections and further progression of diseases so that patients may end up with attrition from ART care (45). Poor nutrition status also decreases the effectiveness and response to ART and then results in early mortality(43).

Another predictor of attrition in this study was a delayed developmental milestone. Children who had delayed developmental milestones at the initiation of ART were observed to have a higher hazard of attrition (AHR=3.76, 95CI%:1.2-11.8) as compared to those with appropriate developmental milestones at baseline. Developmental delay at ART initiation associated with the dependents of children on their caregivers for ART care may further complicate the immunological and clinical recovery and also affects retention of care.

7. Limitation and Strength of the study

Limitation

Since the study was conducted using secondary data (chart review), some variables which might be possible predictors of attrition such as clinical and laboratory baseline data were excluded due to missed value so that it may affect the finding. Medical records that were not available during the data collection period were also excluded from the study and may underestimate or overestimate the results of the study. Another limitation of the study was variable like, child viral load was not considered as a predictor variable.

Strength

One strength of the study was the consideration of censored observations. Since it provides more accurate estimates since it follows those cases like transfer out to other health facilities. as far as they were on follow up.

8. Conclusion

The incidence rate of attrition is found to be 11.3 per 1000 person month observation. Children who had low Hgb level (Hgb <10mg/dl), low CD4+count, delayed developmental stage , poor/ fair ART adherence level, and children who were underweight (WFA z <-2) had higher hazards of attrition among children on ART in Gedeo zone public hospitals, Southern Ethiopia, 2020.

9. Recommendation

Even though high access to ART and decentralized care has been available nowadays, still attrition from ART care is a concerning issue. Attrition from ART care has to be reduced to achieve long term success for the ART program. According to the finding, the following recommendation was forwarded.

For policymakers:

The impact of low hemoglobin level, low CD4 levels, and underweight at the initiation of ART on attrition suggests strategies should be strengthened on early detection, close follow-up, and monitoring as well as management for patients experiencing the above-mentioned cases.

For Gedeo Zone public hospitals

To give attention on early detection and management for patients with poor clinical and laboratory baseline data.

To health care professional who is working at ART clinic of DRH,YCPH, AND BPH

- For a patient with a low CD4+ count, the health care provider needs to strengthen ART adherence and consideration should be given to continue prophylaxis for opportunistic infections such as co-trimoxazole preventive therapy till patients recover immunologically.
- The study suggests the need for improving adherence counseling, early tracking of missed appointments, and increase the frequency of follow up to minimized attrition patients from a care.
- The health worker shall provide continuous nutrition assessment, care, and support to reduce patient attrition from ART care.
- Special priority during follow up time also shall be given for patients with delayed developmental milestones.

To researchers

Next researcher shall conduct a longitudinal prospective study to address those medical records that were not available during the data collection period and also incorporate variables like a viral load to know its effect on attrition.

Reference

1. UNAIDS. 2017 Global HIV Statistics. End AIDS Epidemic. 2018;1–6.

2. Davies MA, Pinto J. Targeting 90-90-90 - Don't leave children and adolescents behind. J Int AIDS Soc. 2015;18(Suppl 6):1–6.

3. Joint United Nations Programme on HIV/AIDS, UNAIDS 2017. Ending Aids: Progress Towards the 90-90-90 Targets. Glob Aids Updat. 2017;198.

4. Ragna.S, Sonia. B, Anton. P, Job.c, Silva. B T f etal. Suboptimal viral suppression rates among HIV-infected children in low- and middle-income countries: a meta-analysis. 2015;1–24.

5. UNAIDS. Ethiopia | UNAIDS [Internet]. 2013. Available from: http://www.unaids.org/en/regionscountries/countries/ethiopia

6. EDHS. Ethiopia Demographic and Health Survey HIV Prevalence Report. Ethiopians Water Sector Development Program. 2016. 11 p.

7. Ababa A. Determinants of Survival among HIV Positive Children on Antiretroviral Therapy in Public. 2017;25:235–41.

8. World Health Organization. Guideline on When To Start Antiretroviral Therapy and on Pre-Exposure Prophylaxis for HIV. 2015;(September):1–76.

9. WHO SUPPORT FOR COUNTRY IMPACT. PREVENT HIV, TEST AND TREAT ALL PROGRESS REPORT: 2016. 2016;

10. FMOH. National Consolidated Guidelines for Comprehensive Hiv Prevention, Care and Treatment. Fmoh. 2018;

11. Abuogi LL, Smith C, McFarland EJ. Retention of HIV-infected children in the first 12 months of anti-retroviral therapy and predictors of attrition in resource limited settings: A systematic review. PLoS One. 2016;11(6):1–17.

12. Mcnairy ML, Lamb MR, Carter RJ, Fayorsey R, Mph M, Tene G, et al. Retention of HIV-infected children on antiretroviral treatment in HIV care and treatment programs in Kenya, Mozambique, Rwanda and Tanzania Margaret. J Acquir Immune Defic Syndr Author manuscript; available PMC 2016 Novemb 03. 2016;62(3).

13. Minn AC, Kyaw NTT, Aung TK, Mon OM, Htun T, Oo MM, et al. Attrition among HIV positive children enrolled under integrated HIV care programme in Myanmar: 12 years cohort analysis. Glob Health Action. 2018;11(1).

14. Lafort Y, Couto A, Sunderbrink U, Hoek R, Shargie E, Zhao J, et al. Validity of reported retention in antiretroviral therapy after roll-out to peripheral facilities in Mozambique: Results of a retrospective national cohort analysis. PLoS One. 2018;13(6):1–14.

15. WHO - UNICEF. Global Update on Hiv Treatment 2013 : Glob Updat HIV Treat 2013 results, impact Oppor. 2013;(June):7.

16. Edmonds A, Yotebieng M, Lusiama J, Matumona Y, Kitetele F, Cole SR, et al. The Effect of Highly Active Antiretroviral Therapy on the Survival of HIV-Infected Children in a Resource-Deprived Setting : A Cohort Study. 2011;8(6).

17. Peacock-villada AE, Barbra A. Post-HAART Outcomes in Pediatric Populations : Comparison of Resource-Limited and Developed Countries. 2011;127(2).

18. Organization WH. Retention in hiv programmes--Defining the challenges and identifying solutions. 2011;(September).

19. Fox MP, Rosen S. Systematic review of retention of pediatric patients on HIV treatment in low and middle-income countries 2008-2013. Aids. 2015;29(4):493–502.

20. Alvarez-Uria G. Description of the cascade of care and factors associated with attrition before and after initiating antiretroviral therapy of HIV infected children in a cohort study in India. PeerJ. 2014;2014(1).

21. Ekouevi DK, Azondekon A, Dicko F, Malateste K, Touré P, Eboua FT, et al. 12-month

mortality and loss-to-program in antiretroviral-treated children : The IeDEA pediatric West African Database to evaluate AIDS (pWADA), 2000-2008. BMC Public Health. 2011;11(1):519.

22. Melaku Z, Lulseged S, Wang C, Lamb MR, Gutema Y, Teasdale CA, et al. Outcomes among HIV-infected children initiating HIV care and antiretroviral treatment in Ethiopia. Trop Med Int Heal. 2017;22(4):474–84.

23. Biru M, Hallström I, Lundqvist P, Jerene D. Rates and predictors of attrition among children on antiretroviral therapy in Ethiopia: A prospective cohort study. PLoS One. 2018;13(2):1–13.

24. Andrew .F, Moise .Z , Kunomboa. A, Ray.W, Fayama. M, Joseph. S E. Mortality among pediatric patients on HIV treatment in sub-Saharan African countries : a systematic review and meta-analysis. 2019;1–13.

25. Harries AD, Zachariah R, Lawn SD, Rosen S. Strategies to improve patient retention on antiretroviral therapy in sub-Saharan Africa. Trop Med Int Heal. 2010;15(SUPPL. 1):70–5.

26. Teeraananchai S, Kerr SJ, Puthanakit T, Bunupuradah T, Ruxrungtham K, Chaivooth S, et al. Attrition and Mortality of Children Receiving Antiretroviral Treatment through the Universal Coverage Health Program in Thailand. J Pediatr. 2017;188:210-216.

27. Pagakrong.L, Azar.k, Linda.A, Rawiwan. H, Thanyawee.P, Nia.k E. Survival of HIV-infected children: A cohort study from the Asia- Pacific region. J Acquir Immune Defic Syndr. 2012;56(4):365–71.

28. William M. Attrition and Loss to Follow-up Among Children and Adolescents in a Community Home-Based Care HIV Programme in Uganda. Pediatr Ther. 2013;03(05).

29. Leroy V, Malateste K, Rabie H, Lumbiganon P, Ayaya S, Dicko F et al. Outcomes of antiretroviral therapy in children in Asia and Africa: a comparative analysis of the IeDEA pediatric multiregional collaboration. J Acquir Immune Defic Syndr. J Acquir Immune Defic Syndr. 2017;176(1):139–48.

30. Marazzi MC, Luca S De, Palombi L, Scarcella P. Predictors of Adverse Outcomes in HIV-1 – infected Children Receiving Combination Antiretroviral Treatment. 2014;33(3):295–300.

31. Ditekemena J, Luhata C, Bonane W, Kiumbu M. Antiretroviral Treatment Program Retention among HIV-Infected Children in the Democratic Republic of Congo. 2014;1–16.

32. Tene G, Lahuerta M, Teasdale C, Kayonde L, Muhayimpundu R, Pierre J, et al. High Retention Among HIV-infected Children in Rwanda During Scale-up and Decentralization of HIV Care and Treatment Programs, 2004 to 2010. 2016;32(8):1–16.

33. Dicko F, Davies M, Kariminia A, Wools-kaloustian K. Outcomes of antiretroviral therapy in children in Asia and Africa: a comparative analysis of the IeDEA pediatric multiregional collaboration Valeriane. 2014;62(2):208–19.

34. Mutasa-apollo T, Shiraishi RW, Takarinda KC, Dzangare J, Mugurungi O, Murungu J, et al. Patient Retention , Clinical Outcomes and Attrition- Associated Factors of HIV-Infected Patients Enrolled in Zimbabwe ' s National Antiretroviral Therapy Programme , 2007 – 2010. 2014;9(1):2007–10.

35. Molfino L, Kumar AM V, Isaakidis P, Bergh R Van Den, Khogali M, Hinderaker SG, et al. High attrition among HIV-infected patients with advanced disease treated in an intermediary referral center in Maputo, Mozambique. 2014;1:1–8.

36. Juergens S, Agung A, Sawitri S, Dewi K, Wati K, Gede IW, et al. Predictors of Loss To Follow Up and Mortality Among Children ≤ 12 Years Receiving Anti Retroviral Therapy during the First Year at a Referral Hospital in Bali Prediktor Lost To Follow Up dan Kematian pada Anak-anak ≤ 12 Tahun , yang Menerima Terapi Anti-R. 4(2):101–6.

37. Dabis F, Mbori-Ngacha D, Arrive E, Kyabayinze D, Marquis B, Namale L, et al. Low risk of death, but substantial program attrition, in pediatric HIV treatment cohorts in

sub-saharan Africa. J Acquir Immune Defic Syndr. 2008;49(5):523–31.

38. Ben-farhat J, Schramm B, Nicolay N, Wanjala S, Szumilin E, Balkan S, et al. Mortality and clinical outcomes in children treated with antiretroviral therapy in four African vertical programmes during the first decade of paediatric HIV care , 2001 – 2010. 2017;22(3):340–50.

39. Massavon W, Mugenyi L, Mcfarland W, Gray G, Lundin R, Costenaro P, et al. Factors Determining Survival and Retention among HIV-Infected Children and Adolescents in a Community Home-Based Care and a Facility-Based Family-Centred Approach in Kampala , Uganda : A Cohort Study. 2014;2014.

40. Moiane L, Vermund SH, Blevins M, Moon TD, Jose E, Tique A, et al. Poor Clinical Outcomes for HIV Infected Children on Antiretroviral Therapy in Rural Mozambique : Need for Program Quality Improvement and Community Engagement. 2014;9(10).

41. Andrew. F, Moise Z, Kunomboa .A E, Ray .W, Shiraishi E. Temporal Trends in Mortality and Loss to Follow-up Among Children Enrolled in Côte d'Ivoire's National Antiretroviral Therapy Program. 2014. p. 1134–40.

42. Arage G, Assefa M, Worku T, Semahegn A. Survival rate of HIV-infected children after initiation of the antiretroviral therapy and its predictors in Ethiopia : A facility-based retrospective cohort. 2019;

43. Minstry F, Health OF. NATIONAL GUIDELINES FOR COMPREHENSIVE HIV PREVENTION , CARE AND TREATMENT. 2017;

44. Koye DN, Ayele TA, Zeleke BM. Predictors of mortality among children on Antiretroviral Therapy at a referral hospital, Northwest Ethiopia: A retrospective follow up study. BMC Pediatr. 2012;12.

45. Takarinda KC, Harries AD, Shiraishi RW, Mutasa- T, Abdul-quader A, Mugurungi O, et al. Gender-related differences in outcomes and attrition on antiretroviral treatment among an HIV-infected patient cohort in Zimbabwe: 2007–2010 Kudakwashe. Int J Infect Dis. 2016;98–105.

Appendices

Annex I: Information sheet

Title of the Research Project: Incidence and predictors of attrition among children on antiretroviral therapy at Gedeo zone selected public hospitals, SNNPR, 2020.

Name of Investigator: Kirubel Bimer (Bsc)

Name of the Organization: Addis Ababa University College of health science, school of nursing and midwifery, department of pediatrics and child health nursing.

Name of the Sponsor: Addis Ababa University.

Introduction: This information sheet is prepared for Dilla Referal Hospital,Yirgachefe Primary Hospital and Bule Primary Hospital administrators and ART coordinating office. The aim of the form is to make the above-concerned office clear about the purpose of research, data collection procedures and get permission to conduct the research.

Purpose of the Research Project: To assess the incidence and predictors of attrition among children on antiretroviral therapy in Gedeo zone public hospitals, Southern Ethiopia, 2020.

Procedure: In order to achieve the above objective, information, which is necessary for the study, will be taken from children ART medical charts.

Risk and /or Discomfort: Participating in this research is not anticipated to cause any disadvantages or discomfort, since the study will conducted by taking appropriate information from medical charts.

Benefits: The research have no direct benefit for one whose document/ chart is included in this research. However, the collected information from the study will help to improve patient retention in ART care, this inturn enhance ART adherence level, slow progression to AIDS, and improved survival.

Confidentiality: All information which is collected during the course of the research will be kept strictly confidential, and any collected information will be reported in group, and name and address of participants will not be specified so that cannot be recognized.

Person to contact: This research project will be reviewed and approved by the institutional review board of College of Health Science, school of nursing and midwifery, Addis Ababa University. If you have any question you can contact any of the following individuals (Investigator and Advisors) and you may ask at any time you want.

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Annex-I: Data Extraction Tool

This tool was prepared for the collection of socio-demographic, clinical, laboratory, treatment-related information that are important for the assessment of Incidence and predictors of Attrition among Children who were on Antiretroviral Therapy in selected Gedeo zone Hospitals, Southern, Ethiopia from 2013 to 2019. All this information was retrieved from the client's ART registration book and individual patient card without mentioning the name of clients. This information was collected by health care providers (BSc Nurses) who were trained on comprehensive ART care in each selected hospital.

Data collection date----------month----------Year----------

Name of the Hospital ----------

Name of data collector----------signature----------

Name of supervisor----------signature----------

Code no----------

NO,	Part I: Sociodemographic Characteristics of care child and caregiver	Possible answer	Skip to
101	Age of the child	(---------) year or (--------) month	
102	Sex of the child	1. Male 2. Female	
103	The religion of the caregiver	1. Orthodox 2. Muslim 3. Protestant 4. Catholic 5. Others----------	
104	Residence	1. Rural 2. Urban	
105	Marital status of the caregiver	1. Single 2. Married 3. Divorced 4. Widowed	
106	Age of the caregiver	----------year	
107	Status of the parent	1. Both alive 2. Either dead 3. Both dead 4. unknown	
108	HIV status of Caregiver	1. Reactive 2. Non-reactive 3. Not known	
109	caregiver-child relationship	1. Biological family 2. Others	
110	Occupation of the caregiver	1. Governmental employee 3. Self-employee	

		2. Housewife 4. Other (specify)-------	
111	Educational status of the caregiver	1. Illiterate 2. Read and write 3. Grade 1-8 4. Grade 9-12 5. College and above	

Part II: clinical, laboratory and treatment-related characteristics

201	WHO clinical stage at baseline	1. Stage I 2. Stage II 3. Stage III 4. Stage IV	
102	Disclosure status	1. Disclosed 2. Not disclosed 3. Unknown	
203	CD4 count (CD4%) at base line	1. ---------or (-------- %) 2. Unknown	
204	Hemoglobin level at baseline	1. ----------gm/dl 2. Unknown	
205	Weight at baseline	(----------) Kg	
206	Height/length at baseline	(----------) Cm	
207	Nutritional status	1. Normal 2. Undernutrition(specify)----------	
208	Functional status at baseline for age>/= years	1. Working 2. Ambulatory 3. Bedridden	
209	Developmental status at baseline for age <5 yrs.	1. Appropriate 2. Delayed 3. Regressed	
210	Opportunistic infection during the follow-up	1. Yes 2. No 3. unknown	213
211	If yes, please specify	----------	
212	Cotrimoxazole preventive therapy	1. Given 2. Not given 3. Unknown	
213	TB diagnosed previously	1. Yes 2. No 3. Unknown	215
214	If yes, was the child treated for TB?	1. 2SRHZ/4RH 2. 2HRZE/4RH 3. Others (specify)_____	
215	Opportunistic infection prophylaxis was given	1. Cotrimoxazole 2. INH 3. Not given 4. Others specify----------	

PART III: Patient follow up information

301	Date confirmed HIV positive	(----------/----------/----------)	
302	The date at ART initiated	date----------/month----------/year----------	
303	Duration since initiation of ART	(----------) months	

304	Regimens started at baseline	1. 4a=d4t-3TC-NVP 5. 4b=d4t-3TC-EFV 2. 4c=AZT-3TC-NVP 6. 4d=AZT-3TC-EFV 3. 1e=TDF-3TC-EFV 7. 1h=ABC-3TC-NVP 4. 1g=ABC-3TC-EFV 8. 2nd line regimens 9. Others specify (----------)	
305	ART adherence level	1. Good 2. Fair 3. Poor 4. Unknown	
306	Reason for fair/poor adherence	1. Toxicity/SE 2. Share with others 3. Forgot 4. Felt better 5. Too ill 6. Stigma 7. Drug stokes out 8. Traveling problem 9. Depression 10. Others specify----------	
307	Drug side effect	1. Yes 2. No 3. unknown	
308	If yes, which drug side effect developed?	1. Nausea / Diarrhea 2. Fatigue 3. Headache 4. Numbness 5. Rash 6. Anemia 7. Fat chance 8. Nightmare 9. Dizziness 10. Others(specify)----------	
309	Any drug substitution	1. Yes,2. No 3. Unknown	412
310	When was it changed?	--------/……/……. (DD/MM/YY)/	
311	Reason for drug substitution	1. Toxicity/Side effect 2. New drug available 3. Dugout of stock 4. Treatment failure 5. Other (specify)----------	
312	What was the last outcome during the follow-up period?	1. Lost 2. Death 3. Transfer out 4. On follow up (retained)/Alive	
313	When the outcome occurred?	---/-----/---DD/MM/YY	

Annex III: Test of proportional-hazards assumption (estat, phtest) for HIV/ADIS infected children who were on ART in Gedeo zone public hospitals, Southern Ethiopia, 2020 (n=254).

	X2	DF	PROB> X2
Age of patient(years)			
<3	0.24	1	0.6263
4-8	0.17	1	0.6795
Adherence level at baseline			
Poor/fair adherence level	0.26	1	0.6092
Residence			
Rural	0.01	1	0.9038
Weight for age			
Under weight (z score <-2)	0.01	1	0.9245
Height for age			
Stunting (z score <-2)	0.36	1	0.5503
Developmental stage			
Delayed developmental stage	0.22	1	0.6372
Opportunistic infection on follow up			
Yes	1.08	1	0.2980
Drug side effect			
Yes	0.00	1	0.9725
Unknown	0.00	1	1.0000
Drug substitution			
No	0.45	1	0.5038
Hemoglobin level			
>/= 10mg/dl	0.08	1	0.7792
Cd4+ level at baseline			
<200	0.15	1	0.6979
200-350	0.02	1	0.8910
Who clinical stage			
Stage III and IV	0.00	1	0.9618
GLOBAL TEST(OVERALL)	**3.85**	**15**	**0.9982**

Annex IV: Multi- collinearity check for HIV/ADIS infected children who were on ART in Gedeo zone public hospitals, Southern Ethiopia, 2020 (n=254)

Variable	**VIF**	**1/VIF**
Age of patient(years)	1.20	0.832901
Religion of care giver	1.18	0.844929
Residence	1.25	0.799484
Weight for age	2.05	0.487195
Height for age	2.01	0.497277
Haemoglobine level	1.32	0.757015
CD4+ level at base line	1.31	0.760843
Adherence level at baseline	1.70	0.589321
WHO clinical stage	1.33	0.752593
Presence of TB	1.21	0.824198
Opportunistic infection follows up	1.24	0.806917
Cotrimoxazole preventive therapy	1.22	0.820057
Drug side effect	1.41	0.709662
Drug substitution	1.13	0.881809
Mean VIF	**1.39**	

Annex V: Cox-Snell residual cumulative hazard graph for HIV/AIDS infected children who were on ART in Gedeo zone public hospitals, Southern Ethiopia, 2020 (n=254)