Original article

# Survival time and its predictors among HIV-infected children after antiretroviral therapy in public health facilities of Arba Minch town, Gamo Gofa Zone, Southern Ethiopia

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**Abstract**

**Background:** Antiretroviral therapy is a drug treatment that plays a great role in reduction of mortality among children infected with human immunodeficiency virus. Studies in Africa have shown that there is short survival time among children receiving antiretroviral therapy. Factors that contribute to low survival probability have been poorly described in sub-Saharan Africa, particularly in Ethiopia.

**Objective:** The study was conducted to estimate the survival time and identify associated factors among HIV-infected children after initiation of antiretroviral therapy.

**Methods:** Institution-based retrospective cohort study was conducted among 421 children enrolled on antiretroviral therapy from January 2009 to December 2016 in public health facilities in Arba Minch town, Gamo Gofa zone, Southern Ethiopia. Cox proportional-hazard regression model was used to determine independent predictors of survival time.

**Results:** Two hundred and sixty one (62%) children were alive; 43 (10.2%) were lost to follow-up; 52 (12.4%) were transferred out to other facilities and 65 (15.4%) were reported to have died. The probability of survival of children on antiretroviral therapy was 73.9% after 96 months and overall mean survival time was 82.3 (95% CI= 79.48 - 85.14) months. Multivariate analysis showed that low hemoglobin level (AHR =3.3, 95% CI=1.83-6.04), absolute CD4 count below threshold (AHR=2.1, 95% CI=1.15-3.77), fair and poor adherence to antiretroviral therapy (AHR=2.17, 95% CI=1.12-4.79), (AHR=2.1, 95% CI=1.02-4.13), Isoniazid prophylaxis (AHR=0.4, 95%, CI=0.22 -0.68) and Cotrimoxazole prophylactic therapy (AHR=0.3, 95% CI=0.15-0.46) were independent predictors of the survival time.

**Conclusions:** Survival time was very low among children below 1 year and 5-14 years olds as compared to those aged between 1-4 years. The main predictors for this variation were nutritional status, poor adherence to antiretroviral therapy, absolute CD4 below threshold, and absence of Isoniazid and Cotrimoxazole prophylaxes. Therefore, children living with HIV should be encouraged to adhere to the antiretroviral therapy, take Cotrimoxazole and isoniazid preventive therapies. [*Ethiop. J. Health Dev.* 2018; 32(2):88-96]

**Key Words**: Antiretroviral therapy, Co-trimoxazole preventive therapy, isoniazied preventive therapy, children, Ethiopia

## Introduction

Acquired Immune Deficiency Syndrome (AIDS) is a disease caused by a retrovirus known as human immunodeficiency virus (HIV)(1). HIV/AIDS remains one of the world's most significant public health challenges, particularly in low-and middle-income countries (2). Children constitute a segment of the population affected by the virus. HIV contributes to illness and death of children and is the commonest cause for pediatric hospital admission (3).

Of the total 1.8 million children living with HIV, an estimated 110,000 die of AIDS-related illnesses each year which means 290 children die of AIDS-related illnesses every day. Nearly 90% of HIV infected children live in Sub-Saharan Africa (SSA) (4). In Ethiopia it is estimated that 65,088 children are living with HIV. In 2016, over 3,100 children died due to AIDS related (5).

The introduction of antiretroviral therapy (ART) presented an enormous opportunity in terms of reducing morbidity and mortality due to AIDS, worldwide. Ethiopia has been engaged in the scale-up of ART access to its people since 2005 (6). It has been shown that the improvement in access to ART improves the quality of life and survival of children (7, 8).

Studies show that early access to ART could prevent 25% of HIV related deaths in Ethiopia (7-9). Therefore, to reduce child mortality attributed to HIV/AIDS, the provision of comprehensive treatment care, and support for HIV-infected children is very important.

Ethiopia has adopted World Health Organization's (WHO) recommendations for ART where 'regardless of their CD4 cell count, all HIV-infected individuals should start treatment to reduce morbidity and mortality associated with HIV infection' (3). The number of sites providing ART service in Ethiopia,

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including both public and private facilities, has increased from three to over 1,000, and persons initiated on treatment has increased from 24,000 to 308,000 during the period 2006-2016 with more than 23, 400 children under the age of 15 taking antiretroviral drugs (10).

Survival of HIV positive children in Ethiopia and other similar settings has improved as a result of increased access to ART; however, it is still low in the first six months after initiation of ART (11). Reports from Kenya, Zambia, and Malawi show that death among HIV positive children following ART initiation remains high, ranging from 7.5% to 15% (12-13). This contrast the substantially higher survival probability among HIV positive children initiated on ART in developed countries (15).

Findings from other studies elsewhere in Africa and other low income countries show that ART programs have resulted in decreased mortality among children on ART (16-18). Available evidences also depicted that the survival of the children is affected not only by the care delivered by ART programs, but also more fundamentally influenced by low CD4 count, advanced disease according to WHO staging, low hemoglobin (Hgb) level and opportunistic infections (OIs) like bacterial pneumonia and tuberculosis (19-21). However, as far as our search of the available literature has revealed, little is known about the effect of factors like viral load, nutritional status, Co-trimoxazole (CTZ) preventive therapy (CPT) and Isoniazid (INH) preventive therapy (IPT) on survival time of children below 15 years of age. Therefore, this study intended to estimate the survival time and identify associated factors by including viral load, nutritional status, CPT and IPT among HIV-infected children initiated on ART in public health facilities in Arba Minch town, Southern Ethiopia.

## Patients and Methods

***Study area and period*:** We conducted the study in Arba Minch town from March 20 to April 10, 2017. Arba Minch town is located about 495 km south-west of the capital city Addis Ababa, and about 275 km from Hawassa, the capital of the Southern Nations, Nationalities, and Peoples Region (SNNPR). Arba Minch town has one general hospital and one public health center, which provide ART service. Arba Minch Hospital was among the first few public hospitals to start ART in Ethiopia in August 2003. Arba Minch Health Center started ART service at the end of 2007. According to Gamo Gofa Zone Health Department (ZHD) report, the Arba Minch Hospital and Arba Minch Health Center provide HIV/AIDS interventions, including free diagnostic, treatment and monitoring services. Since August 2003, ART has been provided to children living with HIV regardless of CD4 count and WHO clinical stage, with financial support from the Norwegian Lutheran Mission. Data from ZHD show that a total of 664 children with HIV/AIDS were enrolled on chronic HIV care at the hospital and the health center since January 2009, but only 608 started ART (460 children at Arba Minch General Hospital and 148 children at Arba Minch Health Center) (22).

***Study design*:** A health facility-based retrospective cohort study was conducted to assess survival time and identify associated factors among children on ART in public health facilities of Arba Minch town.

***Source and study populations*:** All HIV infected children on ART and registered for HIV chronic care in public health facilities of Arba Minch town providing ART service from 2009 to 2016 constituted the source population. The study population included children <15 years of age who were living with HIV/AIDS and on ART, and registered for chronic care at public health institutions in Arba Minch town providing ART service from January 1, 2009 - December 30 2016.

***Sample size determination*:** The sample size was calculated by applying a two-population proportion formula using Epi-Info version 7. Co-trimoxazole preventive therapy (CPT), tuberculosis (TB) co-infection at baseline and anemia were considered and taking the most significant predictors of the three variables, anemia was used (17) with the following assumptions: 95% CI, power 80%, ratio of unexposed to exposed 1:1 and parameters outcome in exposed hemoglobin (Hgb)<10 gm/dl = 14.7%,outcome in unexposed Hgb ≥10 gm/dl)= 5.8% and Hazard Ratio (HR) = 2.5.This resulted in sample size 412 children. As there were a total of 421 children in the study area who fulfilled the inclusion criteria, we included all 421 in this study.

***Sampling procedure and sampling technique*:** A total of 608 children who started ART during the study period were identified in the two ART clinics. Charts were organized according to the hospital card number, in a chronological order, with each chart representing one child. As some of the charts in the hospital were not arranged in numerical order, the investigator assigned new numbers for all those registered between 2009 and 2016, starting from 1 to 608. Of these, the investigator drew 421 samples which fulfilled the inclusion criteria after reviewing the information transcribed to the pre-structured data abstraction form; 187 individuals did not fulfill the inclusion criteria; therefore, those charts were excluded from the study. Children ≤ 14 years of age and on ART, registered for chronic care at public health institutions of Arba Minch town from 1$^{st}$January 2009 to 30$^{th}$ December 2016 were included in the study. Those whose cards were incomplete with information on baseline CD4 count, WHO staging and date of ART start and current status were excluded from the study.

## Variables in the study

***Dependent variable*:** The response (outcome) variable in this study was "survival time" of HIV-infected children after starting ART.

***Independent variables*:** The predictor variables included five continuous covariates (age, hemoglobin

level, weight, height, and CD4 count) and nine categorical variables (gender, Co-trimoxazole prophylaxis, TB-co infection status, Isoniazid prophylaxis, functional status, clinical stage of the disease according to WHO scaling, type of ART drug , adherence to ART, and year of ART initiation).

**Operational definition of terms**

***Censored*:** includes lost-to-follow up, transfer out and live beyond the study time.

***Anemia:*** was defined as Hgb level below 10 gm/dl.

***Adherence to ART***: assessed by counting the number of tablets the children miss within the first three months after staring ART.

***Survival*:** absence of experience of death.

***Survival time*:** the length of time in months a child was followed-up from the time the child started ART until death, was lost to follow up, or was still on follow up.

***Incomplete card*:** considered when the indicator of the dependent variable and/or 10% of the independent variable is not registered.

***Data collection procedure and data quality control*:**
The standard data extraction tool, adapted from the revised 2014 Federal Ministry of Health HIV care/ART follow up form (9),was prepared in English. The data extraction tool was developed further by using different peer reviewed published literatures (23-25). The tool included sections on socio-demographic characteristics, clinical related information, immunological information, and ART and chemoprophylaxis related information. The data was collected by nine health professionals with diplomas and supervised by four professionals with Bachelor of Science (BSc) degrees and trained on comprehensive HIV care.

The data was collected by reviewing the patients' medical cards (follow up and ART intake forms) and ART electronic database; no contact was made with any of the study children. Data on death of HIV positive children while on ART was obtained from providers report on the medical cards. Death at home, after discharge, was ascertained by the drug adherence counselor using contact addresses. The most recent laboratory results before ART initiation were used as baseline values. If there was no pre-treatment laboratory test, results obtained within one month of ART initiation were considered as baseline values.

Data collectors and the supervisor were trained for one day on the objectives of the study, how to select study participants' card, how to keep confidentiality of information, on the contents of the questionnaire, how to extract the data and data quality management by the principal investigator. The principal investigator and supervisor conducted day-to-day follow up during the whole period of data collection. Each questionnaire was reviewed and checked for completeness by the supervisor and the principal investigator on a daily basis and the necessary feedback was given to the data collectors. The principal investigator supervised the overall activity of the study.

***Data processing and analysis*:** The completeness and consistency of the data was checked, coded and double entered into Epi-info version 7 and exported to Statistical Package for Social Sciences (SPSS) version 20 for analysis. Exploratory data analysis was carried out to check the levels of missing values and, presence of influential outliers. Descriptive statistics such as mean (standard deviation), frequencies and proportions were used to describe the characteristics of the cohort. Kaplan-Meier survival curve together with log rank test was used to assess survival experience of an individual at specific times and to compare survival between different independent variables.

The analysis was conducted in several steps. First, univariate Cox proportional hazards regression was performed for each independent variable and outcome of interest to identify potentially significant variables for consideration in the multivariable Cox proportional hazards regression model. Based on the univariate analysis, variables were selected for the multivariable analysis. Variables whose univariate significance test results were below p-value <0.25 were included in the multivariable regression model. In addition, context and findings of previous studies were considered in the identification of candidate variables for multivariable analysis.

Multivariable analysis was started with a model containing all of the selected variables. The model was built through a stepwise regression procedure, which added variables successively (the most significant at each step) until no variable added significant information and compared by likelihood ratio test and Harrell's concordance statistic test. Interactions and confounders were tested and the cutoff point of beta change greater than 20% was used. The results of the final model were expressed in terms of hazard ratio (HR) with 95% confidence intervals (CI) and interpreted accordingly. Kaplan-Meier survival curve together with log rank test was used to check for the existence of any significant differences in survival between the various categories of variables considered in this study. Statistical significance was declared if the p-value was less than 0.05.

***Ethical considerations*:** Ethical approval was obtained from ethical review committee of Arba Minch University, College of Medicine and Health Sciences with reference number CMHS/4268/09. Following the approval, official letter of co-operation was written to concerned bodies by the department of Public Health of Arba Minch University. Permission was granted from the Hospital and Health center administration as per the recommendation letter from the department. Personal identifiers were excluded during data extraction; rather codes were used. Considering the study was being conducted on secondary data, obtaining informed consents from the participants was not possible. However, the confidentiality of

information was maintained by not recording their name from the chart and the recorded data were not be accessed by a third person except by the principal investigator.

**Results**

***Baseline characteristics of the study participant*:** A total of 421 study participants (children under 15 years old) were included in the study. The sample comprised 241(57.2%) males and 180(42.8%) females. The ages of the cohort at ART initiation ranged from three to 168 months with a median age of 72 (IQR=33-108) months. Based on WHO clinical staging, 196 (47%) children initiated ART at an advanced stage of the disease i.e. WHO clinical stage III or IV. During the ART initiation 139 (33%) children were affected by one or more opportunistic illness, of which 41 children were found to have died at the end of the study. Sixty (14.3%) had history of TB at the start of ART and 36 died during the follow up time. At the initiation of ART, mean (SD) values for weight of children was 18.6 (± 9.65) kg and mean (SD) values for height of the cohort was 110.8 (± 32.19) cm. The baseline median values for Hgb was 10.9 (IQR= 8.8-12.3) g/dl and 181 (43.1%) of the children had absolute CD4 count below threshold for immune deficiency at initiation of ART.

Among the reviewed participants 410(97.4%) were on first line ART regimen while the rest were started on second line. Concerning the type of ART regimens, around 61% of children were taking D4T based drug regimens when they started the treatment (Table 1).

Table 1: **Demographic and clinical characteristics and chemoprophylaxis status among children on antiretroviral treatment at Arba-Minch Hospital and Health Center, Southern Ethiopia, 2017**

| Variables | Categories | Frequency | Percent |
|---|---|---|---|
| Sex | Male | 241 | 57.2 |
| | Female | 180 | 42.8 |
| Age category | <1 year | 30 | 7.1 |
| | 1-4 years | 169 | 40.1 |
| | 5-14 years | 222 | 52.7 |
| Primary care giver | Parents | 268 | 63.7 |
| | Relatives | 119 | 28.3 |
| | Guardian/orphan | 34 | 8.0 |
| Parental status | Both parents are alive | 260 | 61.8 |
| | Maternal orphan | 45 | 10.9 |
| | Paternal orphan | 31 | 7.4 |
| | Double orphan | 84 | 19.9 |
| WHO clinical staging at entry | Stage I | 91 | 21.6 |
| | Stage II | 135 | 32.1 |
| | Stage III | 147 | 34.9 |
| | Stage IV | 48 | 11.4 |
| TB at baseline | Yes | 60 | 14.3 |
| | No | 361 | 85.7 |
| Hemoglobin level at baseline | < 10 gm/dl | 78 | 18.5 |
| | ≥ 10 gm/dl | 343 | 81.5 |
| Absolute CD4 at baseline | CD4 above threshold | 239 | 56.9 |
| | CD4 below threshold | 181 | 43.1 |
| ART adherence status | Good | 335 | 79.6 |
| | Fair | 33 | 7.8 |
| | Poor | 53 | 12.6 |
| Cotrimoxazole preventive therapy | Yes | 314 | 74.6 |
| | No | 107 | 25.4 |
| INH prophylaxis | Yes | 302 | 71.7 |
| | No | 119 | 28.3 |

***Mean survival time after initiation of ART*:** After initiation of ART, children were followed for a minimum of 1 and maximum of 95 months with median follow up period of 50 (IQR = 24-80) months. At the end of follow up, 261 (62%) of the children were alive, 43 (10.2%) were lost to follow-up, 52 (12.4%) were transferred out to other facilities and 65(15.4%) were reported dead. The overall mean estimated survival time after ART initiation of children in the study was 82.3 (95% CI = 79.48 - 85.14) months.

There is a significantly different survival time between different factors considered in this study. Females have relatively lower survival time of 79.3 months than males with 84.6 months. Children 1-4 years of age had higher survival time of 86.8 months than those less than 1 and 5-14 years of age who had a mean survival time of 69.3 and 80.8 months, respectively**.**

C**omparison of survival curves**

The overall Kaplan-Meier survivor function estimate showed that most of the deaths occurred in the earlier months of ART initiation, which declined in the later months of follow up. Most of the graphs did not show differences between different categories. However, relatively larger gaps are observed in covariates such as WHO clinical stage, TB co-infection, low Hgb level (<10gm/dl), CTZ and INH prophylaxes.

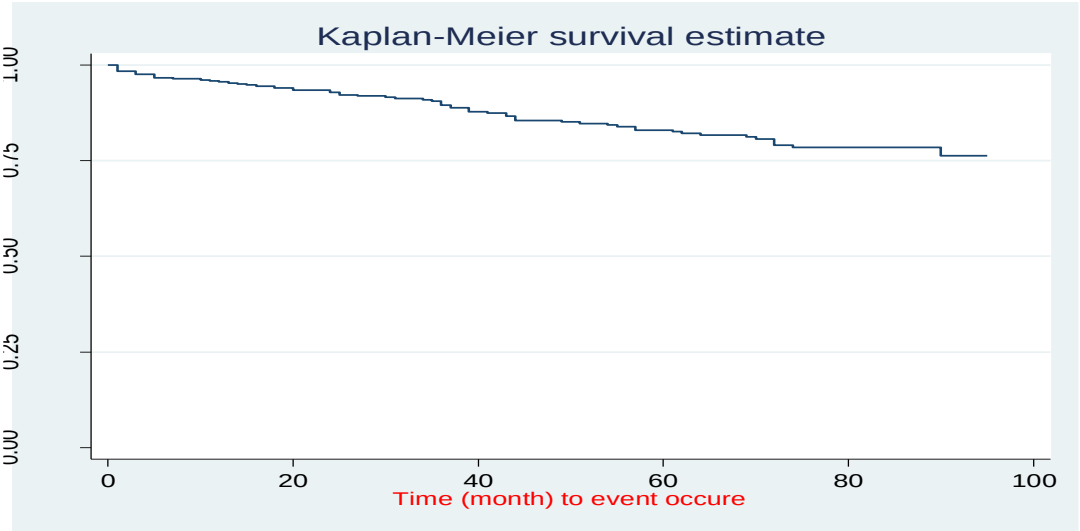


Figure 1: **The plot of the overall estimate of Kaplan-Meier survivor function among children on ART at public health facilities of Arba Minch Town, Southern Ethiopia, 2017**

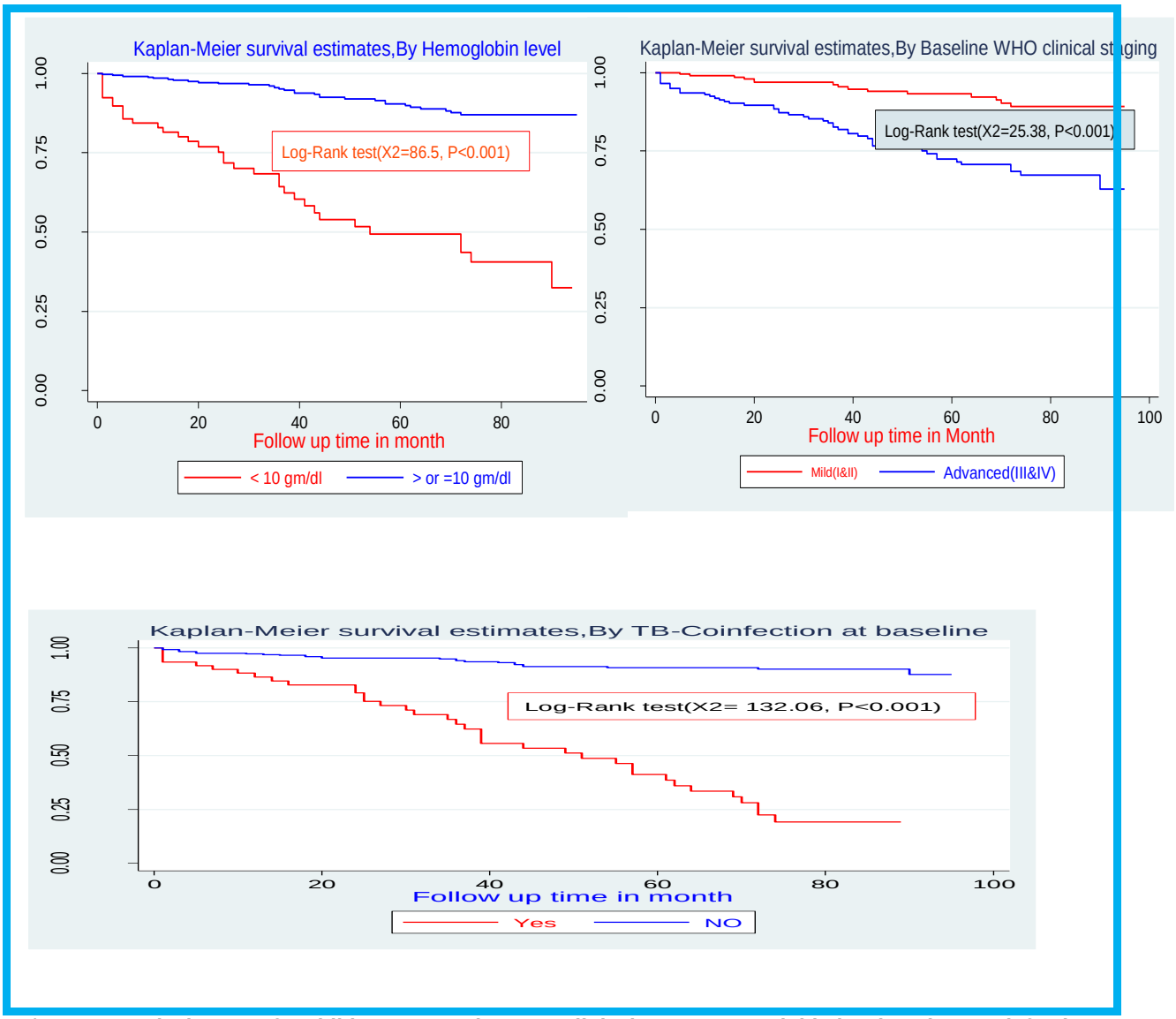


Figure 2: **Survival curves for children on ART by WHO clinical stage, Hemoglobin level, and TB-co infection after start on ART at public health facilities in Arba Minch town, 2017**

***Results of the Cox proportional hazards model*:** One important predictor of low survival time in univariable Cox regression analysis was advanced WHO staging. The risk of low survival chance in individuals with advanced disease according to WHO staging at baseline was nearly four times higher than that of those at the mild stage of the disease (P<0.001). The risk of surviving shorter time in individuals who had severe acute malnutrition (SAM) at baseline was nearly 2.5 times higher when compared to those with no malnutrition(P<0.006). Patients with baseline opportunistic infections (OI) survive nearly three times shorter than those without OIs (P<0.001) and children with TB co-infection were nearly eleven times more likely to survive shorter when compared to those without TB co-infection (P<0.001). Risk of surviving short duration was significantly higher with low hemoglobin level (CHR=7.3, 95% CI=4.47-11.9, P=0.001) and CD4 count below the threshold (CHR=1.7, 95% CI=1.02 -2.74, P=0.041) when starting ART compared to their counterparts. CTZ and INH had preventive effect against surviving for short duration (CHR=0.2, 95% CI=0.10-0.27 P=0.001) and (CHR=0.1, 95% CI= 0.07-0.20 P=0.001) when compared to their counterparts throughout the follow-up period, respectively (Table 2).

Table 2: **Univariable Cox regression analysis of socio-demographic characteristics and clinical and immunological status among children who were started on ART at public health facilities of Arba-Minch Town, 2017**

| Covariate/Factor | Categories | CHR | P–values |
|---|---|---|---|
| Sex | Male | | |
| | Female | 1.617 | 0.053* |
| Age group | <18 months | | |
| | 18-59 months | 1.259 | 0.336 |
| | 5-14 years | 0.655 | 0.069* |
| Nutritional Status | Normal | | |
| | Under weight | 1.903 | 0.010* |
| Anemia | No | | |
| | Yes | 2.702 | 0.001* |
| AbsoluteCD4count | Above threshold | | |
| | Below threshold | 1.293 | 0.041* |
| INH prophylaxis | No | | |
| | Yes | 0.408 | 0.001* |
| CPT prophylaxis | No | | |
| | Yes | 0.348 | 0.001* |
| ART Adherence on follow up | Good | | |
| | Fair | 6.256 | 0.001* |
| | Poor | 5.937 | 0.001* |
| WHO clinical staging at entry | Stage I&II | | |
| | Stage III | 2.360 | 0.009* |
| | Stage IV | 10.412 | 0.001* |
| Functional Status | Working | | |
| | Ambulatory | 1.302 | 0.350 |
| | Bed-ridden | 1.375 | 0.392 |
| ART Regimens at entry | D4t based regimen | 0.294 | 0.420 |
| | AZT based regimen | 0.513 | 0.290 |
| | TDF based regimen | 0.562 | 0.404 |
| | 2nd line ART | | |
| Evidence of TB during follow up | Yes | 1.383 | 0.050* |
| | No | | |

In multivariable Cox regression analysis, children with CD4 count below threshold for immunodeficiency at ART initiation were 2.3 times (AHR=2.26, 95% CI=1.32-3.88, P=0.003) more likely to survive shorter duration as compared to those with CD4 count above threshold. Children with low weight for age (underweight) at ART initiation were almost four times (AHR=4.1, 95% CI=2.41 - 6.9, P=0.001) more likely to survive shorter duration as compared to those with normal weight. Children that were presented for treatment with fair ART adherence and poor ART adherence were on follow up 3.4 times; (AHR=3.4, 95% CI=1.66 -6.9, P=0.001) and 3.3 times (AHR=3.3, 95% CI=1.73 - 6.23, P=0.001) more likely to survive shorter duration, respectively, as compared to those with good adherence on follow up. Estimated AHR for children on INH prophylaxis and CTZ prophylaxis were 0.4 (95% CI=0.21 - 0.65, P=0.001) and 0.3 (95%CI=0.14 -0.44, P=0.001); Short duration survival

hazard among children who took INH prophylaxis was 63% and CTZ prophylaxis was 75% (Table 3).

Table 3: **Multivariable Cox regression analysis of socio-demographic characteristics, and clinical and immunological status among children on ART at public health facilities of Arba-Minch town, 2017**

| Covariate | Categories | AHR | P -values |
|---|---|---|---|
| Nutritional status | Normal | 1 | |
| | Under weight | 4.08 | 0.001 |
| Absolute CD4 count | Above threshold | 1 | |
| | Below threshold | 2.26 | 0.003 |
| INH prophylaxis | No | 1 | |
| | Yes | 0.37 | 0.001 |
| CPT prophylaxis | No | 1 | |
| | Yes | 0.25 | 0.001 |
| ART Adherence on follow up | Good | 1 | |
| | Fair | 3.39 | 0.001 |
| | Poor | 3.28 | 0.001 |

**Discussion**

In this study the overall mean survival time was 82.3 months (95%CI: 79.48-85.14). The cumulative probability of survival of children on ART was 82.9% after 5 years (95% CI: 78.2%-86.7%). The major factors that affect the survival time of children with HIV/AIDS and on ART are nutritional status, absolute CD4 count below threshold, and poor/fair adherence to ART. Isoniazid prophylaxis and Co-trimoxazole prophylaxis were preventive factors.

Mean survival time in our cohort was 82.3 months(95% CI=79.48-85.14).This was in line with the finding of a study conducted in Southwest Ethiopia [83 months (95%CI=79- 87)] (26). However, our finding was higher when compared with study conducted in Northwest Ethiopia, which reported a survival time of 56.5 months(20). This difference might be associated with the high proportion (74.3%) of children in this study taking CTZ prophylaxis as compared to the finding of the study conducted in Northwest Ethiopia (52.3%-70.4%) and the difference might also be associated with increased access to ART services.

The cumulative probability of survival of children on ART in our study was 82.9% after five years (95% CI: 78.2%-86.7%). This was comparable with the report of a study conducted in Felege Hiwot Referral Hospital, Bahir Dar, northern Ethiopia (83%) (27) and another one in Northwest Ethiopia (83%) (20). However the cumulative survival probability from our study was much lower than that of the reports from Adama Referral Hospital and Medical College, Central Ethiopia (91.6%) (19)and Wolaita zone health facilities, Southern Ethiopia (92%)(20).These variations between our study and those from central and Southern Ethiopia may have to do with the variation in the quality of care provided at different institutions.

In this study we found that, having CD4 cell count below the threshold level was significantly associated with an increased probability of having short duration of survival among the children. This concurs with the findings of different studies previously done in Ethiopia (20,28).The similarity might be related to the fact that children, in our series, with absolute CD4 counts below the threshold level being more prone to OIs like TB. Another possible explanation could be ART was initiated in an advanced HIV stage (stages III&IV) where immunity of the children was already compromised.

Another covariate that had a significant effect on survival time was adherence to ART. The HR for poor adherence was 2.1 times and the HR for fair adherence was 2.2 times more likely to result in short duration of survival compared to children with good adherence. This finding was supported by studies conducted in North-west Ethiopia(28), and Wolaita zone health facilities(20). The poor adherence might be due to insufficient counseling and education of caregiver/patient.

The initiation of CTZ and INH at the start of ART in our cohort was associated with a longer duration of survival. This finding concurred with that of the studies conducted in Felege Hiwot referral hospital, northern Ethiopia(20) and rural Mozambique(29). The possible reason for higher risk of shorter survival time among children who did not receive CTZ at ART initiation could be due to occurrence of OIs such as- *Pneumocystis pneumonia*, toxoplasmosis, bacterial pneumonia, sepsis and diarrhea. Co-trimoxazole prophylaxis should be given at the initiation of ART to reduce OI and associated short duration survival among HIV positive children on ART, thereby improving their survival.

The hazards of short survival time for children on INH prophylaxis was 0.38, which means that, in those children who take INH prophylaxis, the hazard of short duration of survival was reduced by 62%. This finding corroborates the finding of the study conducted in Mizan-Aman General Hospital, in Southern Ethiopia (26), and that of a double blinded, placebo-controlled trial on INH efficacy among HIV children infected in Cape Town, South Africa(30). A possible reason could

be INH prophylactic therapy (IPT) prevented the occurrence TB.

There are some strengths and limitations of this study. The strengths of this study are the use of standard measurements which is enabled to make the comparison of findings with other national and international literatures to be valid. In addition, considering long duration of follow up period of children on ART, and the inclusion of important predictors like CTZ, INH and nutritional status also add the strength to this study. Since our study is retrospective based on available records, excluding those with incomplete information, survival time might be underestimated.

***Conclusion***:

In general, this study showed that the probability of survival of children on ART was 73.9% after 96 months and the overall mean survival time was 82.3 months. The main independent predictors of the survival time were nutritional status, absolute CD4 count below threshold, poor/fair adherence to ART, absence of INH prophylaxis and CTZ prophylaxis. However, sex, age, advanced disease according to WHO clinical stage, and presence of TB at baseline were not predictors of survival time. Therefore, children living with HIV should be encouraged to take prophylaxis drugs like CTZ and INH. This could be achieved by collective efforts of all concerned bodies on high risk groups such as children with OI especially TB, after initiation of ART and a careful monitoring and follow up of the children after initiation of ART.

**Competing interest:** The authors declare that there was no competing interest in connection to this research and its result.

**Authors' contribution:** NB conceived and designed the study, developed data collection instruments and supervised data collection. NB and SH participated in the testing and finalization of the data collection instruments and coordinated study progress. NB and SH performed the statistical analysis, SH wrote all versions of the manuscript. All authors read and approved the final manuscript.

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