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Original Research

Predictors of Survival Status Among Children on Antiretroviral Treatment at Dilchora Referral Hospital, Eastern Ethiopia: Cox Regression Model

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Abstract

Background: Despite expanded HIV care saving millions of children, over 1.6 million new infections occur annually, and child mortality remains high. Evidence on context-specific risk factors for mortality among children with HIV is limited. This study aimed to identify predictors of mortality among children on ART in Eastern Ethiopia.
Methods: A retrospective cohort study was conducted on 362 randomly selected pediatric ART records at Dilchora Referral Hospital (2017–2021). Data were collected from ART registers, intake forms, and follow-up charts. Descriptive statistics, life tables, Kaplan-Meier survival curves with log-rank tests, and Cox proportional hazards regression were used. Variables with $p < 0.25$ in bivariate analysis and clinically relevant factors were included in multivariable Cox regression. Crude and adjusted hazard ratios (AHR) with 95% CIs were reported; $p < 0.05$ indicated statistical significance.
Results: A total of 343 children were followed retrospectively for a median survival time of 80 months. During treatment, 57 (16.6%) (95% CI: 12.2, 20.8) of the children died. The hazard of death was highest during the first three years after ART initiation and declined thereafter, with nearly half of the deaths (28) occurring in the first year. The key predictors of mortality obtained from the study were wasting (AHR = 1.67, 95% CI: 0.90, 3.09), anemia (AHR = 1.72, 95% CI: 0.93, 3.17), advanced WHO clinical stage (AHR = 2.84, 95% CI: 1.08, 7.47), immunologic failure (AHR = 3.49, 95% CI: 1.79, 6.82), poor ART adherence (AHR = 2.36, 95% CI: 1.01, 5.50), and delayed or poor developmental milestones (AHR = 2.22, 95% CI: 1.15, 4.28). The adherence is influenced by multiple factors, including caregiver support, child behavior, and healthcare system engagement.
Conclusion: Mortality among children living with HIV remains a significant public health concern and is strongly associated with wasting, advanced disease stage, immunologic decline, poor adherence to ART, and delayed developmental milestones. Targeted interventions addressing these factors are critical to improving child survival.

Keywords: Antiretroviral Treatment, Child Survival, Ethiopia, Predictors, Survival Analysis

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1. Introduction

Human Immunodeficiency Virus (HIV) is a chronic viral infection that compromises the immune system, increasing susceptibility to opportunistic infections and contributing to significant morbidity and mortality, particularly among children [1,2]. Globally, an estimated 37.7 million individuals live with HIV, with more than 1.5 million new infections and 680,000 HIV-related deaths recorded annually. Alarmingly, over 1.7 million of these cases involve children under the age of 15 [3].

In recent decades, antiretroviral therapy (ART) has proven to be the most effective intervention in reducing HIV transmission and associated deaths. According to the United Nations, approximately 28.2 million HIV-positive individuals were receiving ART by 2021 [3]. Despite substantial progress, mother-to-child transmission (MTCT) remains a major concern, with over 160,000 new pediatric infections reported annually [4]. This may, in part, be attributed to the estimated 6.1 million people unaware of their HIV status, creating a hidden reservoir for continued MTCT.

In Ethiopia, although the incidence of HIV among children under five has declined by 76% over recent decades, the country remains off-track in meeting the 2030 global HIV targets [5]. Data from the most recent Demographic and Health Survey (DHS) indicate regional disparities, with the highest prevalence in Gambella (4.8%), followed by Addis Ababa (3.4%), and a national average of 1.55% [6]. Despite national and subnational efforts to expand ART coverage, reduce child mortality, and eliminate stigma, pediatric HIV-related deaths remain unacceptably high [7].

The primary mode of HIV acquisition in children is MTCT, with additional risks stemming from accidental exposures or sexual violence [8]. Once diagnosed, HIV-positive children require comprehensive chronic care, including Highly Active Antiretroviral Therapy (HAART), nutritional support, prophylactic treatment, and management of opportunistic infections [9,10]. When properly implemented, such integrated care can significantly reduce premature deaths. However, in many sub-Saharan African (SSA) countries, health system limitations such as poor follow-up, loss to care, and treatment interruptions continue to undermine survival outcomes [11].

Globally, only about 85% of pregnant women have access to ART to prevent MTCT, with access being significantly lower in low-resource settings [3]. Additionally, HIV status

disclosure rates in SSA range from 9% to 72%, delaying timely care and negatively impacting survival [12].

Mortality is particularly high during the early months of ART initiation, often exacerbated by poor adherence and weak patient retention systems [13]. The 2030 UNAIDS targets aim for 95% of people living with HIV to know their status, 95% of those diagnosed to receive sustained ART, and 95% of those on treatment to achieve viral suppression [10,14]. However, many countries are still far from reaching these goals. Furthermore, children remain 37% less likely to receive treatment compared to adults, indicating a significant gap in pediatric HIV care and service delivery [14]. Alarmingly, just 30 countries including Ethiopia account for 89% of new HIV infections globally [14].

Despite progress in ART availability and the expansion of comprehensive HIV services, pediatric mortality remains a significant concern in SSA. A recent meta-analysis estimated pooled mortality among children on ART at 7.9%, with mortality rates of 3%, 5%, 6%, and 7% at 3, 6, 12, and 24 months of treatment, respectively [15]. In Ethiopia, studies report even higher figures for example, one study in Addis Ababa showed a mortality rate of 21.8% among children on ART [16]. These findings highlight the urgent need for more localized evidence to identify and address the risk factors contributing to pediatric HIV mortality. Therefore, the present study aims to investigate the potential predictors of mortality among children receiving ART follow-up care in Eastern Ethiopia.

2. Methods and Materials

2.1.Study Design, Area, and Period

A hospital-based retrospective cohort study was conducted at Dilchora Referral Hospital to identify predictors of survival among children receiving Highly Active Antiretroviral Therapy (HAART). Dilchora Referral Hospital, located in Dire Dawa, serves as a major referral center for Eastern Ethiopia, providing specialized HIV/AIDS care and follow-up services. The study population consisted of pediatric patients enrolled in the HAART program at the hospital during the study period.

Dire Dawa, situated in the eastern part of Ethiopia, is an administrative city with both urban and rural communities. According to the 2012 Ethiopian Fiscal Year estimates from the Central Statistical Agency, the city had a total population of approximately 506,936. This setting was selected due to its high patient load and its central role in HIV/AIDS treatment and referral

services in the region. The city has two public hospitals, including Dilchora Referral Hospital, which offers both inpatient and outpatient services. The hospital provides comprehensive HIV care services for both pediatric and adult patients. Data collection for this study was conducted between May 1 and May 30, 2021.

2.2.Population

2.2.1. Target Population

- All pediatric patients (children under 15 years) on ART follow-up at Dilchora Referral Hospital.

2.2.2. Study Population

- A randomly selected sample of pediatric ART cases who had received chronic follow-up care during the specified study period.

2.2.3. Study Units

- Individual medical records (charts) of pediatric ART patients.

2.3.Eligibility Criteria

2.3.1. Inclusion Criteria

- Pediatric ART records with complete data regarding HIV treatment and outcomes.
- Records of children enrolled in HAART follow-up during the study period.

2.3.2. Exclusion Criteria

- Records with missing or incomplete data on survival status (HIV-related outcome).
- Cases missing more than 50% of key predictor variables.
- Records of children who died due to accidental, non-HIV-related causes (e.g., trauma or injury).

2.4.Sample Size Determination

The required sample size for the study was determined using two approaches:

2.4.1. For the First Objective (Estimating Mortality Proportion)

The sample size was calculated using a single population proportion formula, based on the following assumptions:

- Estimated proportion (p): 21.8% (mortality in children on ART, based on previous study) [17]
- Confidence level: 95%, Margin of error (d): 5% and Z-score for 95% CI: 1.96

$$n = \frac{Z^2 \cdot P \cdot (1-P)}{d^2} = \frac{(1.96)^2 \cdot 0.218 \cdot (1-0.218)}{(0.05)^2} \approx 248$$

After applying the formula and accounting for a 10% non-response rate, the final estimated sample size was 288 children.

2.4.2. For the Second Objective (Identifying Predictors Using Cox Regression)

Sample size estimation for the survival analysis was performed using STATA version 14.0, applying the Cox proportional hazards model. The calculation was based on the following assumptions:

- Power (1–β): 80%
- Significance level (α): 0.05
- Expected hazard ratio (HR): based on prior studies or clinical relevance
- Proportion of events (deaths): derived from previous literature
- Variance of covariates: estimated from prior data

The final sample size was determined by identifying the predictor variable that required the largest sample size to detect a statistically significant association with mortality. Accordingly, a total of 362 pediatric ART records were included in the analysis, ensuring sufficient statistical power for evaluating the effects of key predictors on survival outcomes (Table 1).

Table 1: Sample size determinants, for the predictor of survival among children on HAART at Dilchora referral hospital, Eastern Ethiopia

S. No	Factors	Statistics	Sample size
1	Under nutrition (malnourished versus Well nourished) [18]	Power = 80% Type I error = 5% Probability of failure (Outcome) = 0.067 AHR = 1.6 Variability of predictors =1.3	331
2	Low hemoglobin (anemic versus Non anemic) [17]	Power =80% Type I error =5% Probability of failure (Outcome) = 0.075 HR = 2.44 Variability of predictors = 1	139
3	ART adherence (poor versus Good) [18]	Power = 80% Type I error = 5% Probability of failure (outcome) = 0.067 HR = 2.5 Variability of predictors = 1	147

Considering the larger sample size calculated for the second objective and 10% card loss or withdrawals, the final sample became 362.

2.5.Sampling Procedures

A simple random sampling technique was employed to select medical records of pediatric patients receiving Highly Active Antiretroviral Therapy (HAART) from the pool of all pediatric ART clients documented in the ART register. Initially, pediatric records were listed using medical record numbers retrieved from the ART register. The sampling fraction (K) was calculated by dividing the total number of pediatric ART clients by the desired sample size. Based on the sampling interval, corresponding medical records were retrieved from the medical record unit.

2.6.Data Collection Methods

Data were collected using a pretested and cross-validated data abstraction form designed specifically for this study. The abstraction tool was developed in consultation with ART registers, follow-up forms, and medical charts, and was refined following a pilot test. Data sources included the ART enrollment forms, ART follow-up forms, and other relevant clinical documentation.

Trained health professionals specifically, Bachelor of Science (BSc) nurses and health officers with experience in ART care conducted the data extraction to ensure accuracy. The data collection tool captured a comprehensive range of variables, including sociodemographic information (age, sex), nutritional status, comorbidities, ART treatment details, prophylactic therapies, duration on ART, and treatment outcomes.

2.7.Study Variables

The dependent variable in this study was child survival, defined as either death or censorship. Death was determined from documented clinical records and excluded deaths due to accidental or unrelated causes. Censorship was defined as instances where the outcome (death) did not occur by the end of the follow-up period.

Independent variables included:

- **Sociodemographic factors**: Child's age and sex, parental marital status, and survival status of parents.
- **Clinical and treatment-related factors:** ART regimen, adherence, duration on therapy, CD4 count, nutritional status (wasting & stunting), prophylactic therapies (cotrimoxazole, isoniazid), and comorbidities (e.g., tuberculosis, anemia).
- **Other health indicators:** WHO clinical stage, functional status, and developmental status.

- Nutritional status was assessed using BMI-for-age Z-scores based on the WHO Growth Standards. Children with Z-scores below 2 were classified as undernourished, while those with Z-scores ≥ -2 were considered not undernourished.

2.8.Data Quality Assurance

Several quality assurance measures were undertaken. Data collectors received training on the use of the abstraction tool and methods for accurate data extraction. A pretest was conducted using 5% of the sample at a different health facility to identify and resolve potential ambiguities or technical issues in the tool. The data collection process was closely supervised by the principal investigators. Daily supervision and random spot-checks of collected data were conducted to ensure completeness and accuracy. Cross-verification of extracted information was carried out using multiple sources, including the ART intake form, ART register, and follow-up charts. Data were entered into EpiData software with validation features (e.g., legal values, skip patterns) to minimize entry errors. Prior to analysis, data cleaning procedures were conducted to ensure consistency and correctness.

2.9.Data Analysis Methods

After ensuring completeness and consistency, data were entered into EpiData Version 3.02 and exported to SPSS v. 23 for statistical analysis. Descriptive statistics, including frequencies, percentages, means, medians, and standard deviations, were computed. BMI-for-age Z-scores were calculated using WHO AnthroPlus software to assess nutritional status. To examine survival outcomes, time-to-event (survival) analysis was conducted. This included estimation of median survival time, life tables, hazard functions, and survival functions. The log-rank test was used to compare survival distributions across categories of predictor variables. A p-value < 0.05 was considered statistically significant.

Proportional hazards assumptions were assessed using global tests in STATA Version 14.0. Bivariable and multivariable Cox proportional hazards regression analyses were performed to identify factors associated with mortality. Variables with a p-value < 0.25 in the bivariable analysis, along with those identified in prior literature as important predictors, were included in the multivariable model. The final model was developed using a backward elimination approach. Crude and adjusted hazard ratios (C/AHR) with corresponding 95% confidence intervals (CI) and p-values were reported. Multicollinearity was assessed using Pearson correlation coefficients and the variance inflation factor (VIF), while interaction effects among key predictors were also examined.

3. Results

3.1.Socio-Demographic and Clinical Characteristics

In this study, a total of 343 medical charts of children receiving antiretroviral therapy (ART) were retrieved and reviewed, resulting in a card retrieval rate of 95%. The mean age of the children was 7.5 years (SD = 4.2). Of the total participants, 131 (38.2%) were between 5 and 10 years of age, while 116 (33.8%) were older than 10 years. More than half of the children were male (52.5%). Regarding parental survival status, 120 children (35%) had lost their mothers, 70 (20.4%) had lost their fathers, and 17 (5%) had lost both parents. With respect to the marital status of parents, more than one-third (37.3%) were reported to be married, while the remainder were separated, divorced, widowed, or living apart for other reasons.

At the time of ART initiation, 57 children (16.6%) were diagnosed with tuberculosis. In terms of prophylactic treatment, 204 children (59.5%) received cotrimoxazole prophylaxis for the prevention of opportunistic bacterial infections, while 144 children (42%) were given isoniazid prophylaxis to prevent mycobacterial infections. Regarding developmental status, the majority of children (70.3%) were developmentally appropriate for their age, whereas 83 (24.2%) exhibited delayed developmental milestones and 19 (5.5%) had regressed developmental progress. At baseline, 102 children (29.7%) had CD4 counts indicative of immunological failure. Additionally, 98 children (28.6%) and 31 (9%) were classified as being in advanced WHO clinical stages III and IV, respectively (Table 2).

Table 2: Sociodemographic and clinical characteristics of children on ART at DRH, Eastern Ethiopia.

Variables	Categories	Frequency	Percent (%)
Age in months	0-11 months	35	10.2
	12-59 months	61	17.8
	60-119 months	116	33.8
	120-168 months	131	38.2
Sex	Male	180	52.5
	Female	163	47.5
Orphan status	Both alive	136	39.7
	Maternal orphan	120	35.0
	Paternal orphan	70	20.4
	Double orphan	17	5.0
Paternal marital status	Single	84	24.5
	Married	128	37.3
	Divorced	85	24.8
	Widowed	46	13.4
Tuberculosis at baseline	Yes	57	16.6
	No	286	83.4
CPT prophylaxis	Yes	204	59.5

	No	139	40.5
INH prophylaxis	No	199	58.0
	Yes	144	42.0
Functional status	Appropriate	241	70.3
	Delay	83	24.2
	Regression	19	5.5
CD4 count	Above threshold	241	70.3
	Below threshold	102	29.7
WHO stage	Stage I	131	38.2
	Stage II	83	24.2
	Stage III	98	28.6
	Stage IV	31	9.0

Approximately 58% of the children demonstrated good adherence to ART, while 20% and 22% exhibited fair and poor adherence, respectively (Figure 1).

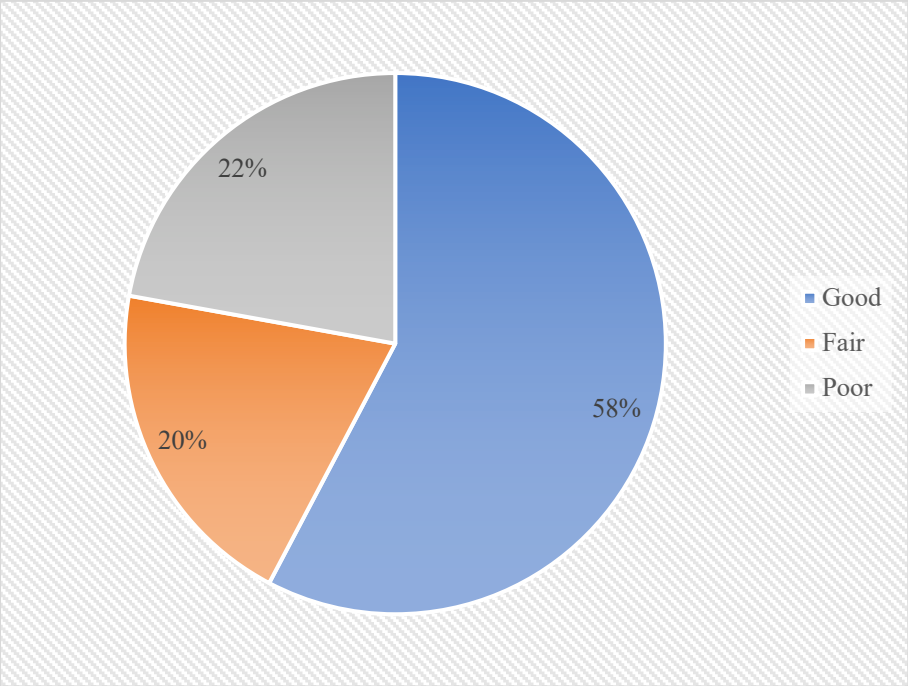

Figure 1. Recent ART medication adherence level of children on HAART at DRH, eastern Ethiopia

Regarding nutritional status among children on HAART follow-up, 144 (42%) were stunted, defined by height-for-age Z-scores (HAZ) below -2, and 102 (29.7%) were wasted, indicated by body mass index-for-age Z-scores (BAZ) below -2. Conversely, 32 children (9.3%) were classified as overnourished, including those who were overweight or obese, based on BAZ cutoff points (Figure 2).

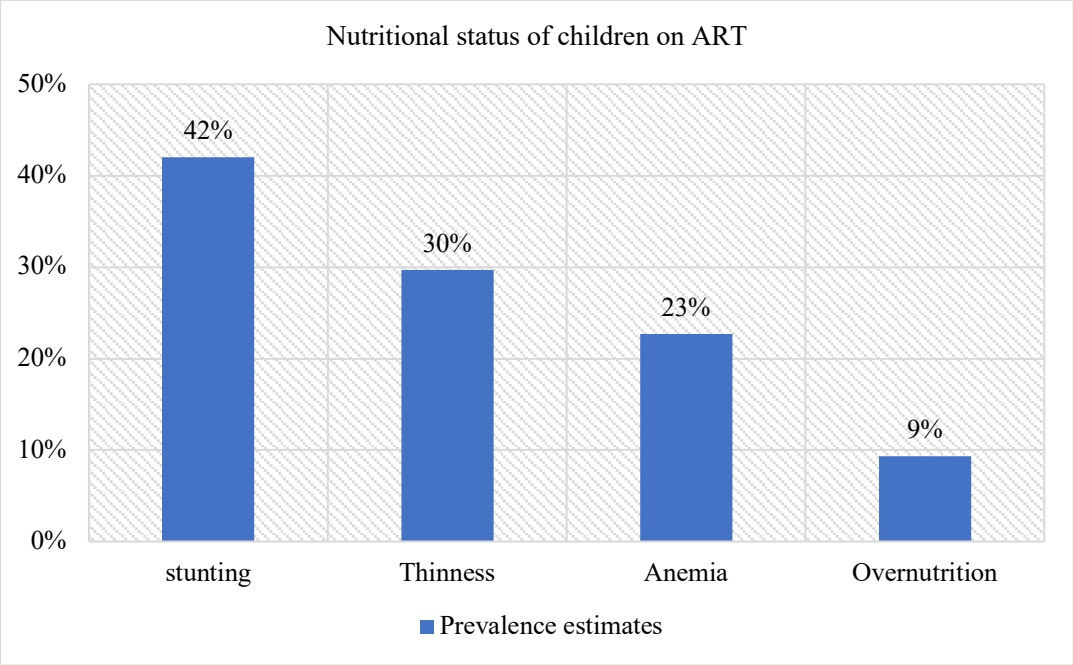

Figure 2. Prevalence estimates of malnutrition among children on ART at DRH, Eastern Ethiopia

Regarding treatment outcomes, 197 children (57.4%) remained actively engaged in HAART follow-up, while 34 (9.9%) were lost to follow-up and 55 (16%) were transferred to other healthcare facilities. During the course of treatment, 57 children (16.6%; 95% CI: 12.2, 20.8) died following ART initiation. The median duration of follow-up for the cohort was 80 months (Table 3).

Table 3. Life table showing the survival time and hazards of death among children on ART at Dilchora referral hospital, Eastern Ethiopia.

Month since ART	Number Entering Interval	Withdrawing No. during Interval	Number Exposed to Risk	No. of Terminal Events	Proportion Terminating
0	343	25	330.5	9	0.03
5	309	28	295	11	0.04
10	270	24	258	8	0.03
15	238	26	225	2	0.01
20	210	30	195	4	0.02
25	176	12	170	3	0.02
30	161	10	156	3	0.02
35	148	24	136	6	0.04
40	118	8	114	0	0
45	110	50	85	5	0.06
50	55	1	54.5	0	0
55	54	5	51.5	0	0
60	49	6	46	2	0.04
65	41	5	38.5	2	0.05
70	34	15	26.5	1	0.04
75	18	2	17	0	0
80	16	15	8.5	1	0.12

Proportion Surviving	CPS at End of Interval	SE of CPS at End of Interval	Probability Density	SE of Probability Density	Hazard Rate
0.97	0.97	0.01	0.005	0.002	0.01
0.96	0.94	0.01	0.007	0.002	0.01
0.97	0.91	0.02	0.006	0.002	0.01
0.99	0.9	0.02	0.002	0.001	0
0.98	0.88	0.02	0.004	0.002	0
0.98	0.87	0.02	0.003	0.002	0
0.98	0.85	0.02	0.003	0.002	0
0.96	0.81	0.03	0.007	0.003	0.01
10	0.81	0.03	0	0	0
0.94	0.76	0.03	0.01	0.004	0.01
10	0.76	0.03	0	0	0
10	0.76	0.03	0	0	0
0.96	0.73	0.04	0.007	0.005	0.01
0.95	0.69	0.04	0.008	0.005	0.01
0.96	0.67	0.05	0.005	0.005	0.01
10	0.67	0.05	0	0	0
0.88	0.59	0.09	0.016	0.015	0.03

Note: CPS - Cumulative Proportion Surviving, SE – Standard Error

The majority of the deaths were encountered after initiation of ART with in the first three years of age. Hence, the survival status of children drops significantly in the first three years immediately after starting the ART care. Thereafter, the fall in the survival status of children decline and the incidence of death declines. Almost half of the deaths (28 deaths) occurred during the first years of ART initiation. The hazards of death (hazard rate) were also higher during early and later years of after ART initiation (after five years) (Table 3 and Figure 3).

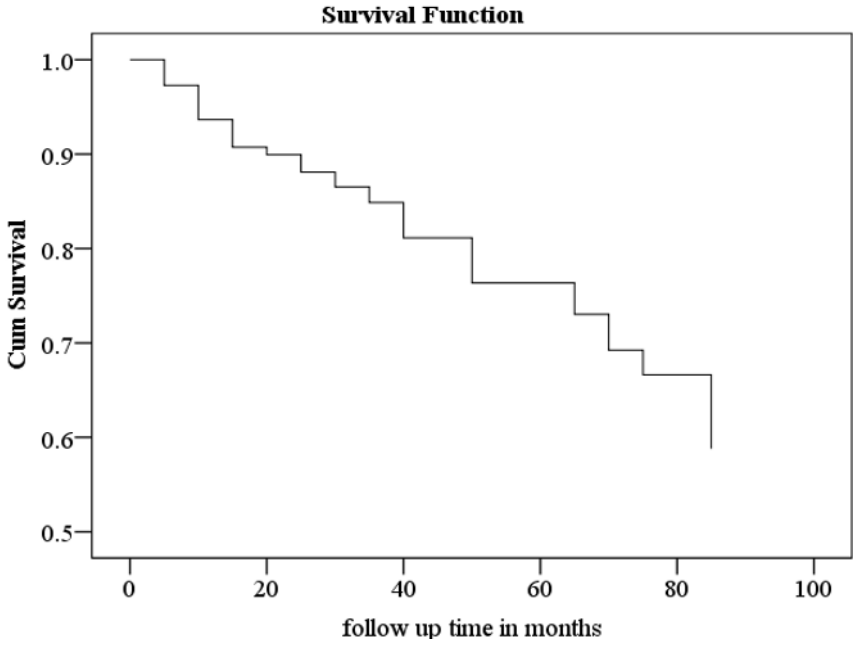

Figure 3. Survival curve depicting the probability of survival across the ART follow up periods among children on ART follow up in Dilchora referral hospital

3.2.Predictors of Mortality Among Children on ART

We explored the bivariable association between each predictor and the survival status of children. Hence, anemia status, history of TB, WHO stage, CD4 count, wasting, developmental status, adherence, and age were found to be significant predictors of survival status among children on ART follow-up.

Infants aged below one year exhibited an approximately four-fold increased risk of death compared to older children (CHR = 3.47; 95% CI: 0.72, 7.0). Similarly, children with a history of tuberculosis had a significantly elevated risk of mortality (CHR = 3.56; 95% CI: 2.07, 6.12) compared to those without TB. Anemic children were nearly six times more likely to die during ART follow-up than their non-anemic counterparts (CHR = 5.88; 95% CI: 3.47, 9.95).

Furthermore, children presenting with advanced WHO clinical stages of the disease had an eleven-fold higher risk of death (CHR = 11.1; 95% CI: 4.76, 26.0) compared to those with less advanced stages. Poor ART adherence was associated with a markedly increased risk of mortality (CHR = 9.75; 95% CI: 4.92, 19.3), as was immunological failure indicated by suboptimal CD4 counts (CHR = 7.59; 95% CI: 4.25, 13.6). Children with delayed or regressed developmental status had a seven-fold higher hazard of death relative to those with age-appropriate developmental milestones (CHR = 7.36; 95% CI: 4.12, 13.2).

Additionally, wasted children faced over twice the risk of mortality (CHR = 2.28; 95% CI: 1.34, 3.87), and those who did not receive isoniazid (INH) prophylaxis had a similarly increased risk (CHR = 2.36; 95% CI: 1.22, 4.58), compared to well-nourished children who received INH prophylaxis (Table 4).

Table 4. Bivariable cox regression to identify predictors of mortality among children who were on ART care at Dilchora referral hospital, eastern Ethiopia.

Predictors	Categories	Outcome		CHR 95% CI	P-value
		Dead	Censored		
Sex	Male	32	148	1.39 (0.82, 2.36)	0.216
	Female	25	138	1	
Age category	0-11 months	11	24	3.47 (0.72, 7.0)	0.0001**
	12-59 months	18	43	4.05 (2.22, 7.40)	0.0001**
	>-60 months	28	219	1	
Marital status	Married	14	114	1	
	Unmarried	43	172	1.70 (0.93, 3.11)	.085
History of TB at baseline	Yes	21	36	3.56 (2.07, 6.12)	0.0001**
	No	36	250	1	
Parent survival	Both alive	20	116	1	

	Lost parent/s	37	170	1.25 (0.72, 2.15)	0.429
Anemia status	<11 g/dl	32	46	5.88 (3.47, 9.95)	0.0001**
	≥11 g/dl	25	240	1	
WHO stage	Stage I or II	12	202	1	
	Stage III	35	63	7.14 (3.69, 13.8)	0.0001**
	Stage IV	10	21	11.1 (4.76, 26.0)	0.0001**
CD4 count	above threshold	16	225	1	
	below threshold	41	61	7.59 (4.25, 13.6)	0.0001**
ART adherence	Good adherence	10	188	1	
	Fair or poor	47	98	9.75 (4.92, 19.3)	0.0001**
Child developmental status	Appropriate	16	225	1	
	Fair or poor	41	61	7.36 (4.12, 13.2)	0.0001**
CPT	Yes	35	169	1	
	No	22	117	1.15 (.67, 1.96)	0.614
INH	No	46	153	2.36 (1.22, 4.58)	0.011*
	Yes	11	133	1	
wasting	Wasted	24	78	2.28 (1.34, 3.87)	0.002*
	Not wasted/thin	33	208	1	
Stunting	Stunting	28	116	1.03 (0.61, 1.75)	0.905
	Not stunted	29	170	1	

Note: Statistically significance of predictors was declared at a p-value below 0.05* and 0.001** in bivariable cox regression.

A multivariable Cox proportional hazard regression was conducted where WHO clinical stage, anemia status, child developmental status, INH prophylaxis, and ART adherence were found to be important predictors of survival from HIV. We further explored the possible multicollinearity and interaction effects, where we did not identify a statistically significant interaction among variables, and hence, we presented the adjusted association with the inclusion of seven predictors despite some changes in the AHR as compared to CHR estimates. However, INH prophylaxis and wasting parameter estimates showed a relatively stable hazard ratio compared to others.

As compared to non-wasted children and non-anemic children, wasting (AHR = 1.67; 95% CI: 0.90, 3.092) and being anemic (AHR = 1.72; 95% CI: 0.93, 3.17) predicted the time to death from HIV but did not reach statistical significance. Children with clinically advanced disease (WHO stage IV) (AHR = 2.84; 95% CI: 1.08, 7.47) and greater immunologic failure (AHR = 3.49; 95% CI: 1.79, 6.82) significantly increased the hazard of death among children on ART by 2.8 to 3.5 folds. Similarly, children with poor ART adherence (AHR = 2.36; 95% CI: 1.01, 5.50) and poor or delayed developmental milestones (AHR = 2.22; 95% CI: 1.15, 4.28) almost double the hazards of death from HIV (Table 5).

Table 5. Multivariable cox regression to identify predictors of mortality among children who were on ART care at Dilchora referral hospital, eastern Ethiopia.

Predictors	Categories	Outcome		AHR 95% CI	P-value
		Dead	Censored		
Anemia status	<11 g/dl	32	46	1.72 (0.93, 3.17)	0.083
	≥11 g/dl	25	240	1	
WHO stage	Stage I or II	12	202	1	
	Stage III	35	63	2.18 (1.03, 4.61)	0.042*
	Stage IV	10	21	2.84 (1.08, 7.47)	0.035*
CD4 count	Above threshold	16	225	1	
	Below threshold	41	61	3.49 (1.79, 6.82)	0.0001**
ART adherence	Good adherence	10	188	1	
	Fair or poor	47	98	2.36 (1.01, 5.50)	0.047*
Child developmental status	Appropriate	16	225	1	
	Fair or poor	41	61	2.22 (1.15, 4.28)	0.018*
INH	No	46	153	2.13 (0.97, 4.76)	0.060
	Yes	11	133	1	
Wasting	Wasted	24	78	1.67 (0.90, 3.092)	0.102
	Not wasted/thin	33	208	1	

Note: statistically significance of predictors was declared at a p-value below 0.05 (*) and 0.001(**)

4. Discussion

The revised 95-95-95 Fast-Track targets by the Joint United Nations Programme on HIV/AIDS (UNAIDS) aim to enhance access to care and improve survival among children living with HIV. Among those receiving care, the reduction of HIV-related mortality is considered a critical program-level indicator of treatment success [13]. In this retrospective cohort study conducted among children on HAART, we found that 16.6% died during the follow-up period, with a median survival time of 80 months. Most deaths occurred within the first year following ART initiation, a finding consistent with previous studies indicating that mortality risk is highest in the initial months of treatment [13].

Despite notable improvements in pediatric survival with increased access to ART, mortality among HIV-positive children remains unacceptably high, underscoring the need for integrated public health interventions in the study area. Similar mortality estimates have been reported across sub-Saharan Africa. For instance, studies from the region have shown mortality rates of 18.8% and 14.7% within five years of ART initiation [19].

However, the mortality rate reported in our study exceeds that of other Ethiopian studies, such as 5.4 deaths per 100 child-years [20] and 8.8% in Addis Ababa, where the median survival time was 27.9 months [21]. In contrast, research from northern Ethiopia reported a higher mortality rate of 21.8% with a shorter mean survival time of 22.4 months [16], and a study from Debre

Tabor showed a mortality rate of 23%, with over half of the deaths occurring early in treatment [22]. These discrepancies may be attributed to differences in baseline clinical and nutritional profiles, levels of ART adherence, parental survival status, and access to supportive care all of which significantly impact treatment outcomes.

In our study, nutritional status emerged as a significant predictor of mortality. Children who were wasted (AHR = 1.67; 95% CI: 0.90, 3.09) or anemic (AHR = 1.72; 95% CI: 0.93, 3.17) faced higher risks of death compared to their well-nourished counterparts. These findings are consistent with prior studies. For example, one study reported significantly shorter survival times among anemic children with lower hemoglobin levels ($p < 0.0001$) [16].

Evidence from Zewditu Hospital also demonstrated that wasted children (HR = 5.0; 95% CI: 2.4, 10.2) and anemic children (AHR = 2.9; 95% CI: 1.3, 6.7) had higher mortality risks [21]. Other studies further reinforce the critical role of nutritional status in predicting child survival, emphasizing how poor nutritional intake and weight loss compromise immune function and increase vulnerability to advanced disease and death.

Conversely, well-nourished children have been shown to experience significantly reduced risks of death. One study found that optimal nutritional status lowered the risk of mortality by 88% (AHR = 0.12; 95% CI: 0.07, 0.19) [23]. Given that an estimated 50–100% of children living with HIV suffer from either recent or chronic weight loss due to both disease-related and medication-related factors [24], maintaining adequate nutritional status is essential. Nutritional interventions, including supplementation and promotion of a balanced diet, are thus vital components of pediatric HIV care [25].

Advanced disease stage and immunologic failure were also independently associated with higher mortality. Children with advanced WHO clinical stages (AHR = 2.84; 95% CI: 1.08, 7.47) and those with low CD4 counts (AHR = 3.49; 95% CI: 1.79, 6.82) had significantly increased risks of death. These findings align with prior studies linking advanced disease status and low immune function to shorter survival times and higher mortality [16, 21]. For instance, one study found that children in WHO stages III or IV had an AHR of 4.5 (95% CI: 2.80, 8.40), and those with low CD4 counts had an AHR of 1.6 (95% CI: 1.19, 7.85) [22]. Similarly, data from Zewditu Hospital indicated that low CD4 count was associated with a three-fold increase in the hazard of death (AHR = 3.0; 95% CI: 1.02, 8.96) [21].

Poor ART adherence and developmental delays were also associated with increased mortality risk. Children with poor adherence (AHR = 2.36; 95% CI: 1.01, 5.50) and those with delayed or regressed developmental milestones (AHR = 2.22; 95% CI: 1.15, 4.28) faced nearly twice the hazard of death. Given that HIV treatment requires lifelong adherence for sustained viral suppression and immune recovery, poor adherence can lead to treatment failure and disease progression.

Adherence is influenced by multiple factors, including caregiver support, child behavior, and healthcare system engagement. A previous study showed that children receiving psychosocial support to improve adherence had significantly lower mortality (AHR = 0.3; 95% CI: 0.1, 0.7) [22], highlighting the importance of ongoing adherence counseling for both children and their caregivers.

Developmental delay may have a bidirectional relationship with HIV infection. Children with delayed development are often more clinically ill and nutritionally compromised, which can further exacerbate their vulnerability to mortality [26]. Therefore, the regular developmental monitoring is essential for early identification of high-risk children and timely intervention to improve outcomes [27]. Additionally, the high proportion of children in this cohort who had lost one or both parents likely contributed to reduced access to consistent care, emotional support, and proper nutrition, further compromising survival.

In conclusion, this study assessed mortality and its predictors among children receiving ART in Eastern Ethiopia and found a concerning rate of death, particularly during the first few months following ART initiation. These findings have important implications for HIV care programs and should inform future intervention strategies focused on early identification of high-risk children, nutritional support, enhanced adherence counseling, and psychosocial care. However, the retrospective nature of the study may limit the ability to capture critical psychosocial and household-level factors that could also influence child survival.

5. Conclusion

Child survival remains a significant public health concern among HIV-positive children receiving chronic care. Mortality in this population is closely associated with modifiable factors such as wasting, advanced clinical disease, immunosuppression (low CD4 count), poor ART adherence, and delayed developmental milestones. Based on these findings, we strongly recommend that healthcare providers and non-governmental organizations collaborate to

reduce preventable deaths among HIV-infected children. Targeted interventions should focus particularly on younger children with advanced disease stages and poor nutritional status. Enhanced care strategies, including therapeutic food supplementation, early developmental monitoring, improved nutritional intake, and prevention of opportunistic infections, are essential to improving child survival in this setting.

Abbreviations

AHR: Adjusted Hazard Ratio, AIDS: Acquired Immune Deficiency Syndrome, BMI: Body Mass Index, CHR: Crude Hazard Ratio, CI: Confidence Interval, HAART: Highly Active Antiretroviral Therapy, HIV: Human Immune Virus, SSA: Sub-Saharan Africa, TB: Tuberculosis, UNICEF: United Nations Children Education Fund, WFA: Weight for Height, WFH: Weight for Age, WHO: World Health Organization

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Authors Contribution

AO and ID contributed substantially to the study conception, design, data collection, analysis, funding acquisition, and manuscript preparation. MK, KN, and MY, were involved in data collection and critically reviewed and edited the manuscript for intellectual content. All authors agreed on the final manuscript for publication.

Ethical Approval

Ethical clearance for this study was obtained from the Institutional Research Ethical Review Committee of Dire Dawa University. A formal support letter was submitted to the Dire Dawa Regional Health Bureau and Dilchora Referral Hospital. Written consent was secured from the hospital administration due to the retrospective and secondary nature of the data used.

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Conflict of Interests

The authors declare no conflicts of interest related to this study.

Availability of Data and Materials

All data generated or analyzed during this study are included in the manuscript. Additional data may be made available by the corresponding author upon reasonable request.

References

1. Becerra JC, Bildstein LS, Gach JS. Recent Insights into the HIV/AIDS Pandemic. Microb Cell. 2016: 3(9): 451-475. https://doi.org/10.15698/mic2016.09.529
2. Amuche NJ, Emmanuel EI, Innocent NE. HIV/AIDS in sub-Saharan Africa: current status, challenges and prospects. Asian Pac J Trop Dis. 2017: 7(4): 239-256. http://dx.doi.org/10.12980/apjtd.7.2017D6-366
3. UNAIDS. Fact sheet-latest statistics on the status of the AIDS epidemic. UNAIDS. 2021.
4. UNAIDS. Fact sheet-latest statistics on the status of the AIDS epidemic. UNAIDS. 2019.
5. Mirkuzie AH, Ali S, Abate E, Worku A, Misganaw A. Progress towards the 2020 fast track HIV/AIDS reduction targets across ages in Ethiopia as compared to neighboring countries using global burden of diseases 2017 data. BMC Public Health. 2021;21(1):1–10.
6. Kibret GD, Ferede A, Leshargie CT, Wagnew F, Ketema DB, Alebel A. Trends and spatial distributions of HIV prevalence in Ethiopia. Infect Dis Poverty. 2019;8(1):1–9.
7. Kalembo FW, Zgambo M. Loss to Follow up: A Major Challenge to Successful Implementation of Prevention of Mother-to-Child Transmission of HIV-1 Programs in Sub-Saharan Africa. ISRN AIDS. 2012 31;2012:589817. https://doi.org/10.5402/2012/589817
8. McNairy ML, Teasdale CA, El-Sadr WM, Mave V, Abrams EJ. Mother and child both matter: reconceptualizing the prevention of mother-to-child transmission care continuum. Curr Opin HIV AIDS. 2015;10(6):403-410. https://doi.org/10.1097/COH.0000000000000199
9. Kassa GM. Mother-to-child transmission of HIV infection and its associated factors in Ethiopia: a systematic review and meta-analysis. BMC Infect Dis. 2018;18(1):1–9.
10. World Health Organization. Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. Geneva: WHO; 2021.
11. Oumer, A., Kubsa, M.E. & Mekonnen, B.A. Malnutrition as predictor of survival from anti-retroviral treatment among children living with HIV/AIDS in Southwest Ethiopia: survival analysis. BMC Pediatr. 19(1): 1-10. https://doi.org/10.1186/s12887-019-1823-x
12. Doat A-R, Negarandeh R, Hasanpour M. Disclosure of HIV status to children in Sub-Saharan Africa: a systematic review. Medicina. 2019;55(8):433.
13. Davies M-A, Gibb D, Turkova A. Survival of HIV-1 vertically infected children. Curr Opin HIV AIDS. 2016;11(5):455–464. https://doi.org/10.1097/COH.0000000000000303
14. UNAIDS. Understanding Fast Tracks: Accelerating Actions to End the AIDS Epidemics By 2030. UNAIDS. (Year unknown): 5–15.
15. Ahmed I, Lemma S. Mortality among pediatric patients on HIV treatment in sub-Saharan African countries: a systematic review and meta-analysis. BMC Public Health. 2019;19(1):1–13.
16. Atnafu H, Wencheko E. Factors affecting the survival of HIV-infected children after ART initiation in Bahir-Dar, Ethiopia. Ethiop J Health Dev. 2012;26(3):193–199.
17. 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(1):161.
18. Mulugeta A, Assefa H, Tewelde T, Dube L. Determinants of survival among HIV positive children on antiretroviral therapy in public hospitals, Addis Ababa, Ethiopia. Qual Prim Care. 2017;25(4):235–241.
19. Haas AD, Zaniewski E, Anderegg N, Ford N, Fox MP, Vinikoor M, Dabis F, Nash D, et al. African regions of the International epidemiologic Databases to Evaluate AIDS (IeDEA). Retention and mortality on

antiretroviral therapy in sub-Saharan Africa: collaborative analyses of HIV treatment programmes. J Int AIDS Soc. 2018:21(2):e25084. https://doi.org/10.1002/jia2.25084

20. Molla M, Kebede F, Kebede T, Haile A. Effects of undernutrition and predictors on the survival status of HIV-positive children after started antiretroviral therapy (ART) in Northwest Ethiopia. Int J Pediatr. 2022;2022:1046220. https://doi.org/10.1155/2022/1046220
21. Taye B, Shiferaw S, Enquselassie F. The impact of malnutrition in survival of HIV infected children after initiation of antiretroviral treatment (ART). Ethiop Med J. 2010;48(1):1–10.
22. Arage G, Assefa M, Worku T, Semahegn A. Survival rate of HIV-infected children after initiation of antiretroviral therapy and its predictors in Ethiopia: a facility-based retrospective cohort. SAGE Open Med. 2019;7:2050312119838957. https://doi.org/10.1177/2050312119838957
23. Shabangu P, Beke A, Manda S, Mthethwa N. Predictors of survival among HIV-positive children on ART in Swaziland. Afr J AIDS Res. 2017;16(4). https://doi.org/10.2989/16085906.2017.1386219
24. Houtzager L. Nutrition in HIV: a review. Benin J Postgrad Med. 2009;11(1)
25. De Pee S, Semba RD. Role of nutrition in HIV infection: review of evidence for more effective programming in resource-limited settings. Food Nutr Bull. 2010;31(4 Suppl 4):S313–S344.
26. Walker SP, Wachs TD, Grantham-McGregor S, Black MM, Nelson CA, Huffman SL, et al. Inequality in early childhood: risk and protective factors for early child development. Lancet. 2011;378(9799):1325–1338.
27. Sherr L, Croome N, Castaneda KP, Bradshaw K, Romero RH. Developmental challenges in HIV infected children: an updated systematic review. Child Youth Serv Rev. 2014;45:74–89.